



# Overcoming Barriers to Hepatitis C Treatment Among Substance Users

Marija Zeremski, PhD

*Project Director*

Clinical Directors Network, Inc. (CDN)

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# Overview and Learning Objectives

- HCV Overview
  - Transmission routes
  - Acute vs. chronic infection
  - Prevalence among specific patient populations
  - New developments in HCV treatment
- Define barriers to hepatitis C treatment among people with substance use disorders
- Review strategies to overcome barriers to HCV treatment among substance users

# HCV Overview

- Virus discovered in 1989
- A blood borne pathogen
  - Direct blood-to-blood contact is the most efficient mode of transmission
- Prior to HCV isolation, principal transmission routes were:
  - Blood transfusions
  - Unsafe injections including procedures in health care settings
  - Injection drug use
- After introduction of HCV serologic screening of the blood supply (1992), injection drug use become the primary mode of transmission
- Sexual contact is very inefficient transmission route
  - Exception are HIV-positive men who have sex with men and rough sexual acts

# HCV Overview - Transmission

- Most common chronic blood borne infection in US
- HCV prevalence among people who inject drugs (PWID) between 30-70%
- Of an estimated 12 million people who inject drugs worldwide:
  - 6.1 million live with HCV
  - 1.6 million lives with HIV
  - 1.3 million live with HCV and HIV

# Transmission Via Contact with Contaminated Blood

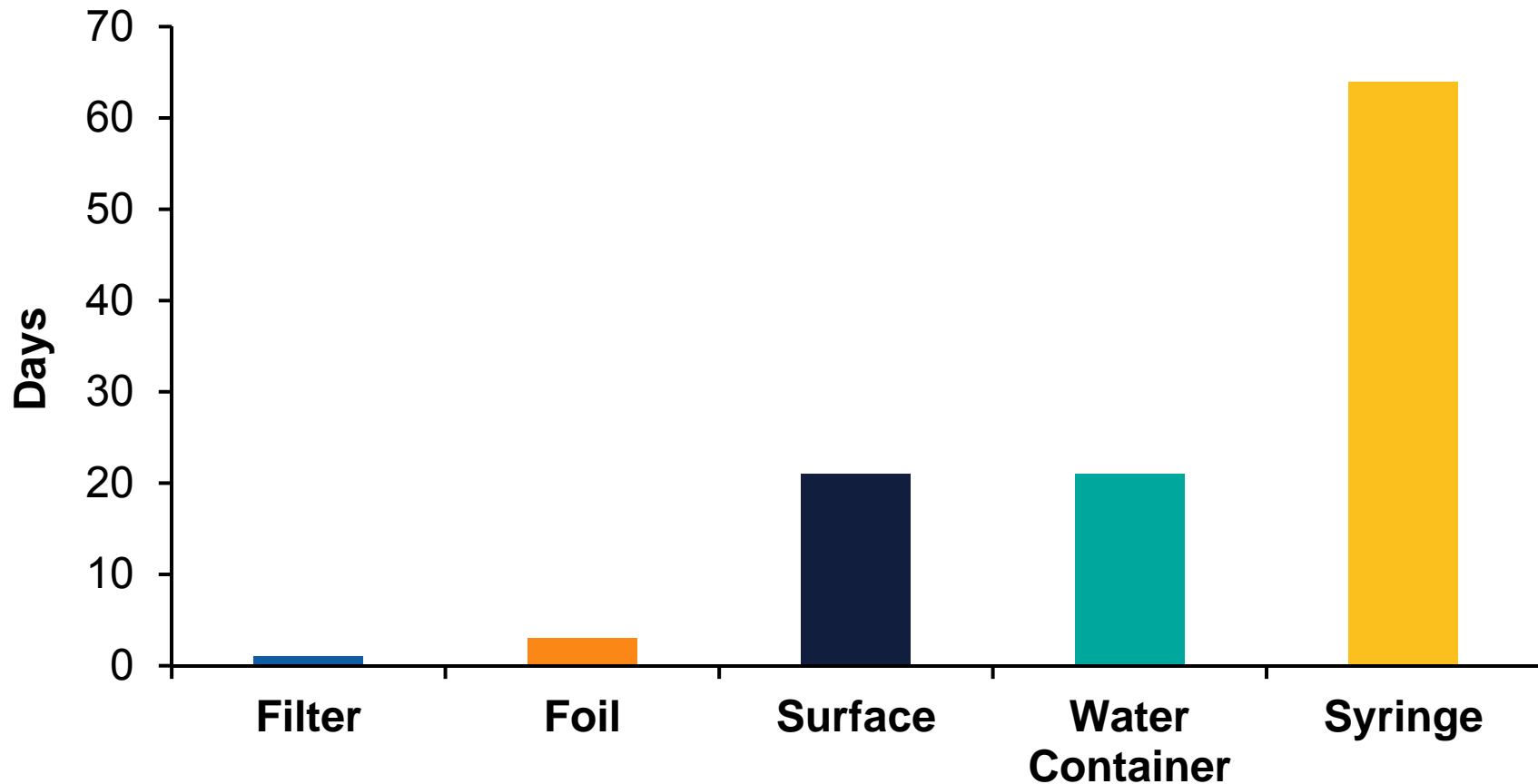
## Needles and Syringes:



## Preparation Equipment:

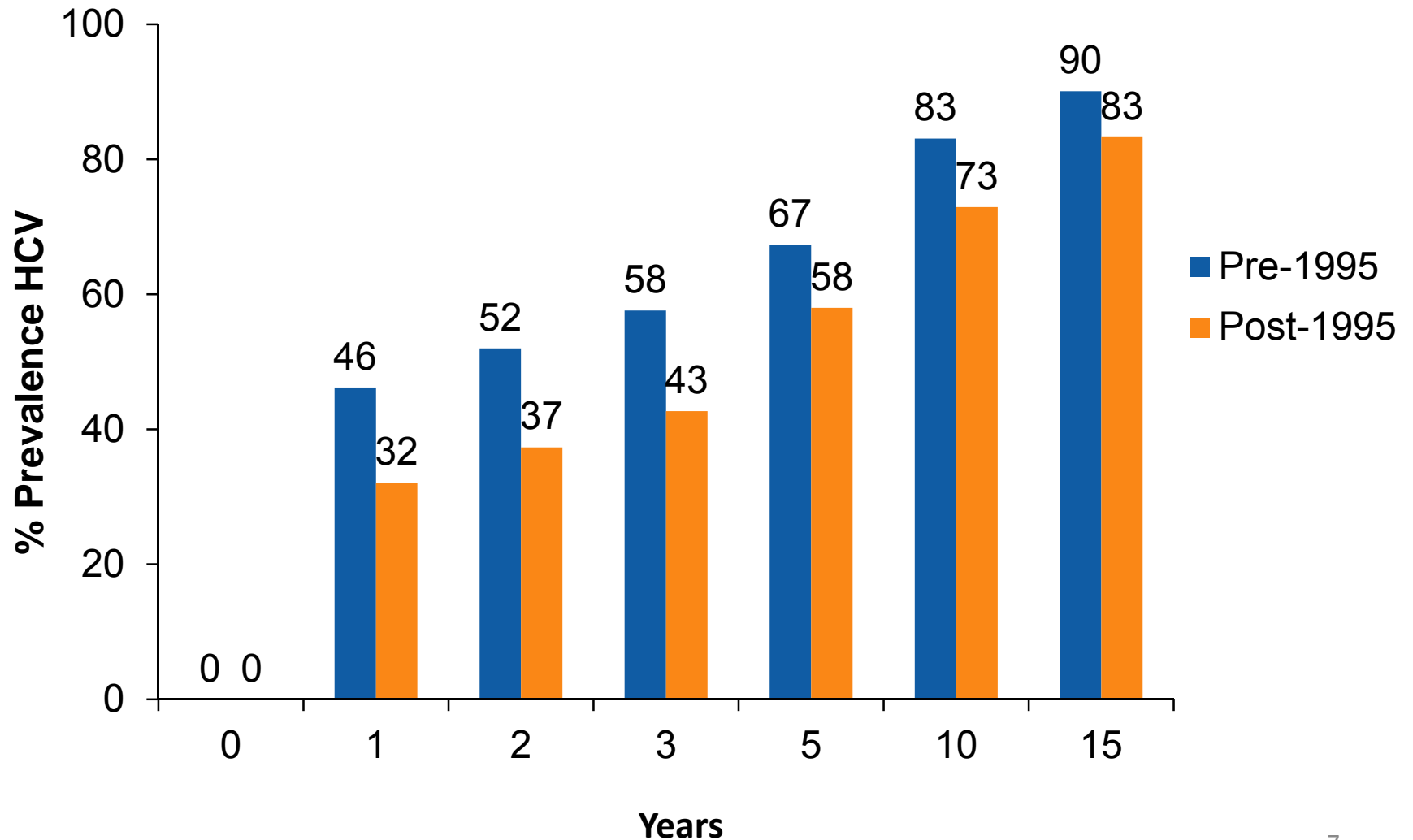


# How Long Can HCV Survive on Inanimate Objects?



HCV-contaminated solution needs to be heated for almost **90 seconds** and reach temperatures of **65-70°C** for the virus to be at undetectable levels.

# Likelihood of HCV Infection: Duration of IDU



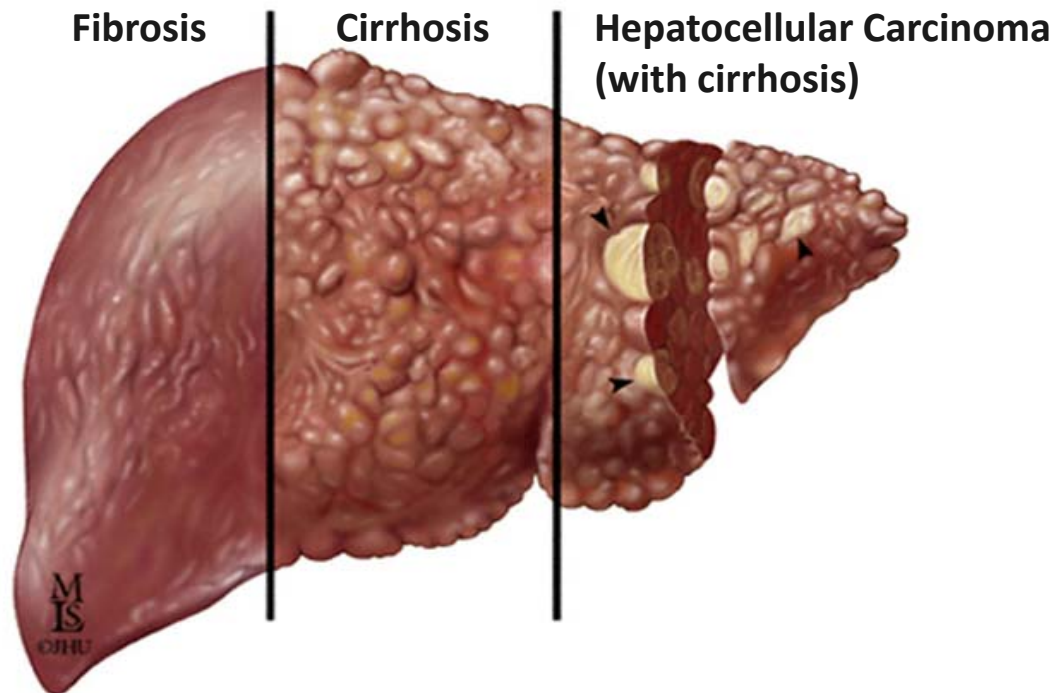
# Acute HCV Infection

- The acute phase of HCV infection is asymptomatic in the majority of patients and therefore is rarely diagnosed
- Some patients (15-25%) spontaneously clear acute HCV infection
  - The reasons for this are not well known
- Patients that spontaneously clear HCV infection test positive for HCV antibodies but are HCV RNA negative
  - A positive anti-HCV test result is not a diagnosis for chronic HCV infection
- The majority of people exposed to HCV develop chronic hepatitis C



# Chronic HCV Infection

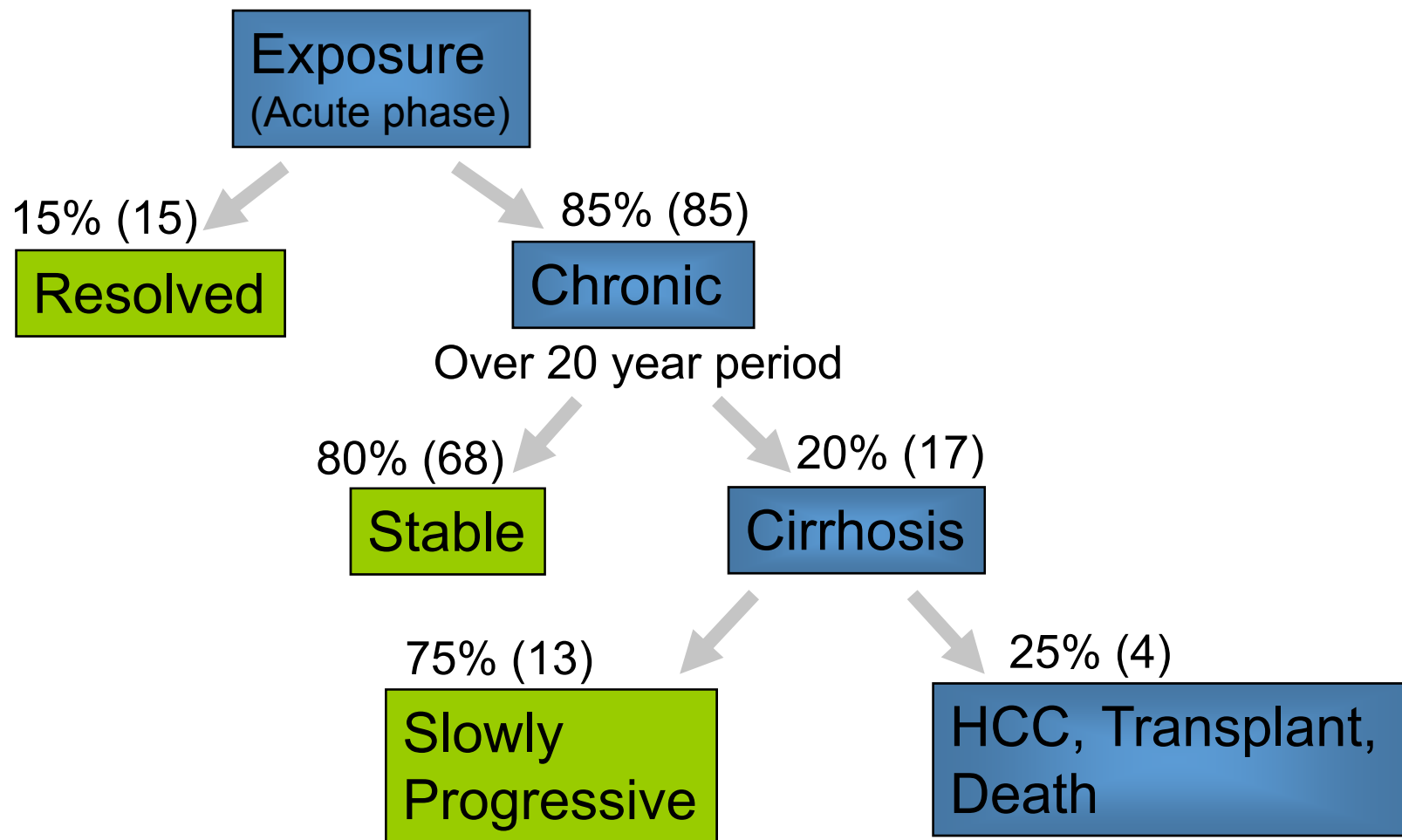
- A major cause of chronic liver disease resulting in liver fibrosis, cirrhosis and liver cancer
  - 75%-85% of HCV-infected patients will develop chronic infection and ~65% of those are expected to develop chronic liver disease



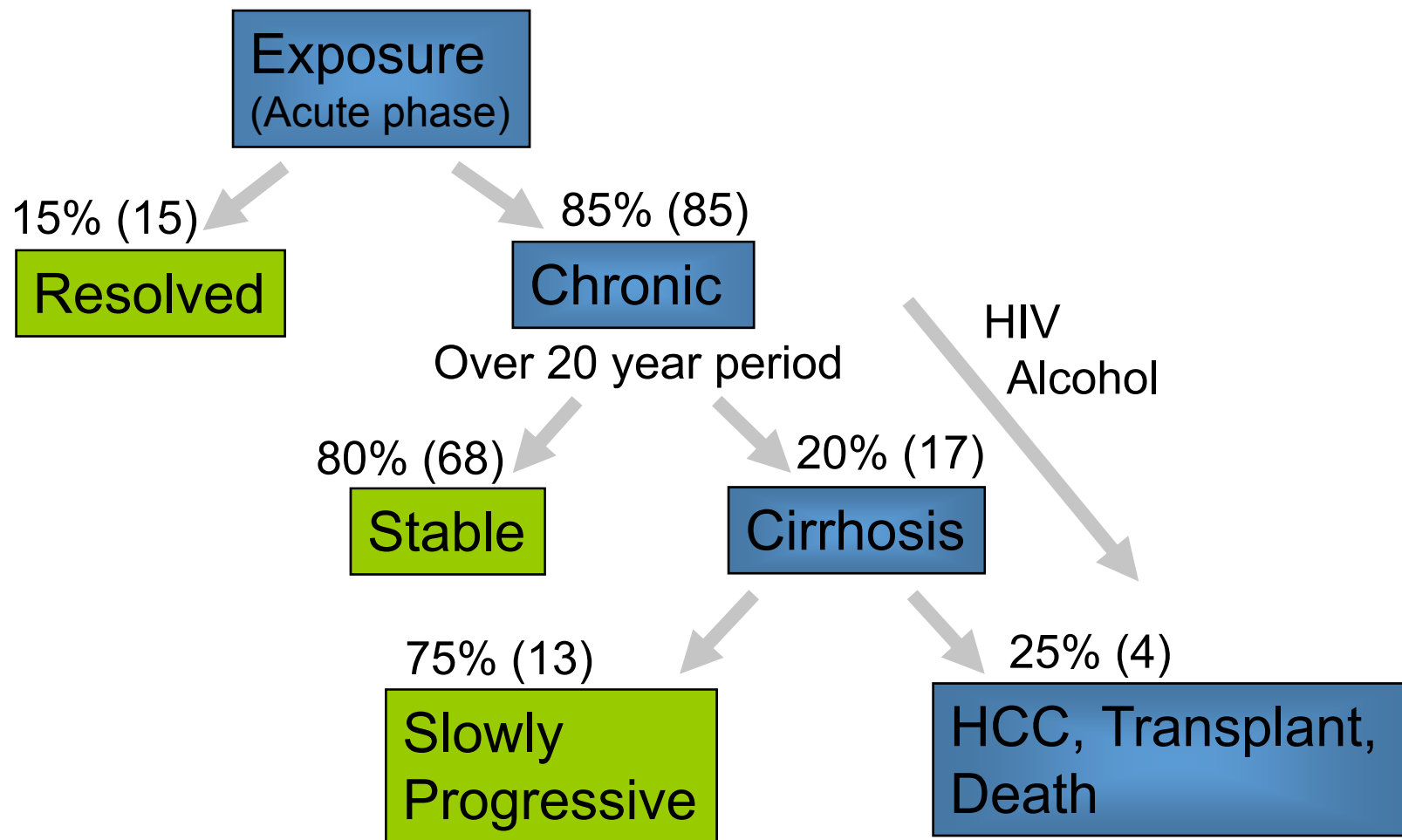
# Chronic HCV Infection

- Chronic HCV infection is asymptomatic in most patients
- Symptoms of infection usually do not develop until liver disease is far advanced
- Symptoms are generally vague and unspecific
  - Fever
  - Fatigue
  - Loss of appetite, weight loss
  - Nausea, vomiting, abdominal pain, diarrhea
  - Jaundice
  - Dark urine
  - Clay-colored bowel movements

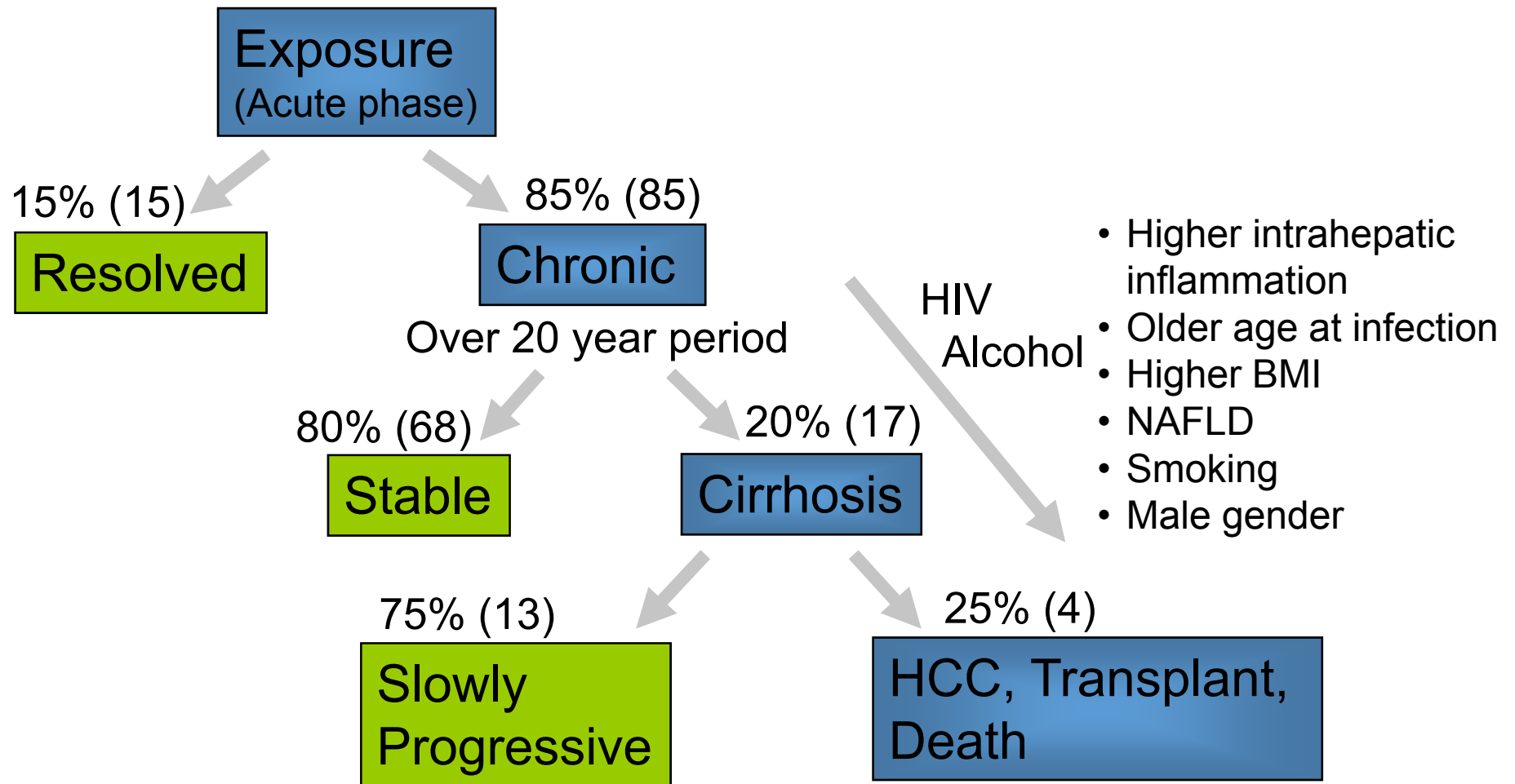
# Natural History of HCV Infection



# Natural History of HCV Infection



# Natural History of HCV Infection



# Chronic HCV Infection

- The leading indication for liver transplantation
- Accounts for > 50% incident hepatocellular carcinoma
  - The fastest growing cause of cancer-related death in the US
- Almost 500,000 persons worldwide die of HCV-related conditions each year
- Annual HCV-associated mortality in the US increased over 50% from 1999 to 2007
  - HCV-associated deaths reached an all-time high of 19,659 in 2014
  - HCV-associated deaths are now more frequent than deaths caused by HIV

# HCV Prevalence

- 130-170 million persons, 2% to 3% of the world's population, have been infected with HCV
  - An estimated 71 million people worldwide have chronic hepatitis C infection
- Almost 5 million people in the United States have ever been infected with HCV
- Approximately 3 million or more persons in the United States have chronic HCV infection

# HCV Prevalence

- US populations with higher HCV prevalence:
  - People who inject drugs (PWID)
  - Homeless individuals (up to 50% prevalence)
  - Veterans (6.2% prevalence)
  - Incarcerated
    - Approximately 33% of people with chronic HCV infection have been to jail and/or prison at some time
  - People born between 1945 and 1965 (baby boomers)
    - 3.25% prevalence compared to 0.8% prevalence of all other
    - Account for 75% of all HCV infections



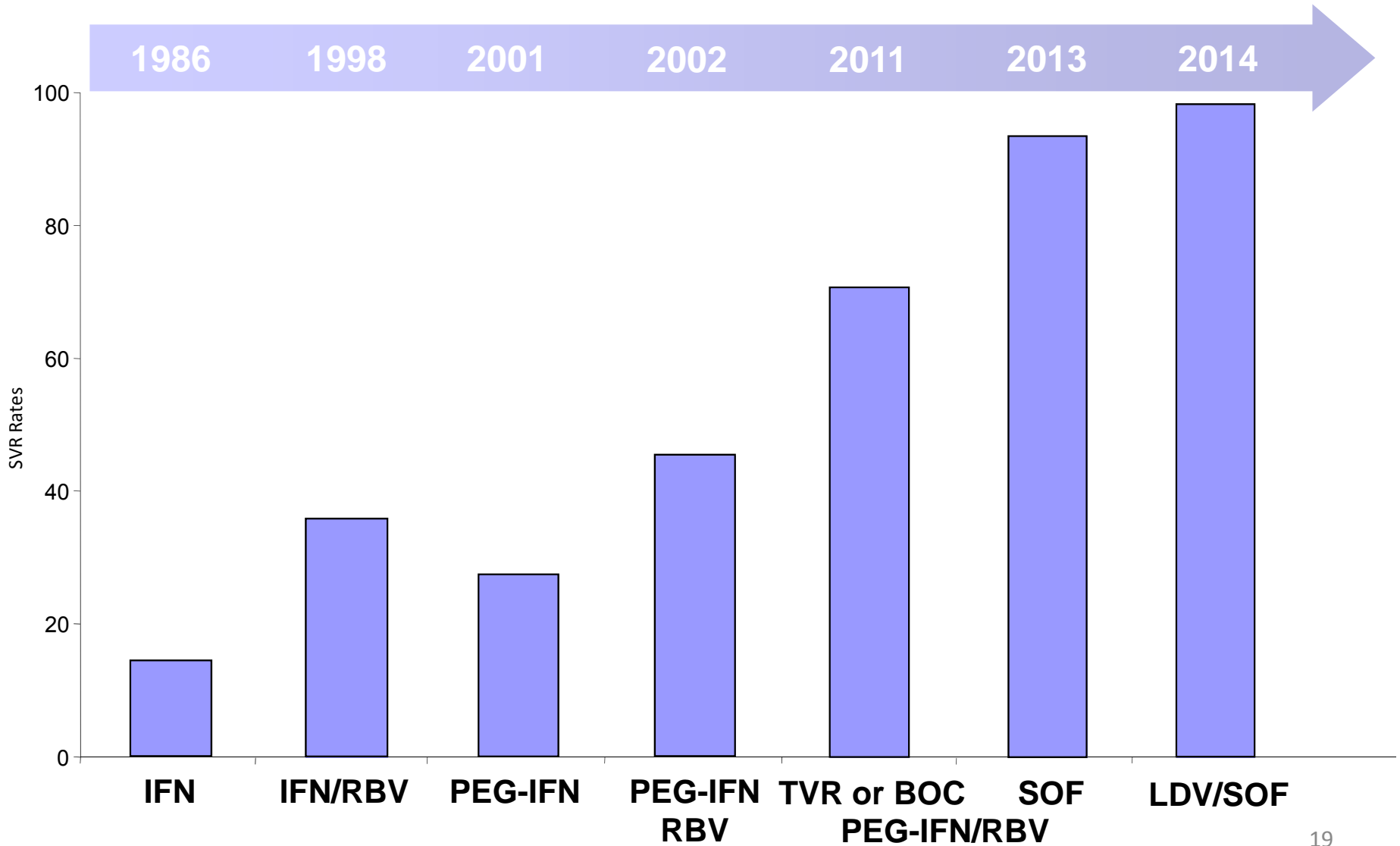
# HCV Testing

- 45% to 85% of US adults with chronic HCV infection are unaware of their condition
- HCV Ab testing is suboptimal even for high-risk populations for whom routine testing is recommended
- An estimated 30% of anti-HCV positive people never receive an HCV RNA test to confirm current infection

# HCV Treatment

- Unlike HIV and HBV infection, HCV infection is a curable disease
- What does cure mean?
  - Undetectable HCV RNA 12 weeks after completion of antiviral therapy for chronic HCV infection
  - SVR = sustained virologic response
- Recently approved highly effective interferon-free regimens can cure HCV in more than 90% of patients
  - Near universal efficacy
  - Shortened duration of therapy
  - Adverse events have minimal impact on patient's quality of life

# The Evolution of HCV Therapy



# Direct-Acting Antivirals (DAA)

- First DAAs approved in 2011
- First all-oral DAA regimens approved in Oct. 2014
  - **Harvoni** (sofosbuvir/ledipasvir)
  - **Olysio** (simeprevir) + **Sovaldi** (sofosbuvir)
  - **Viekira Pak** (Technivie = ombitasvir/paritaprevir/ritonavir + dasabuvir)
  - **Daklinza** (daclatasvir) + **Sovaldi** (sofosbuvir)
  - **Zepatier** (elbasvir/grazoprevir)
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**Is eradication of HCV possible?**

# Obstacles to HCV Eradication

## **Inadequate HCV testing**

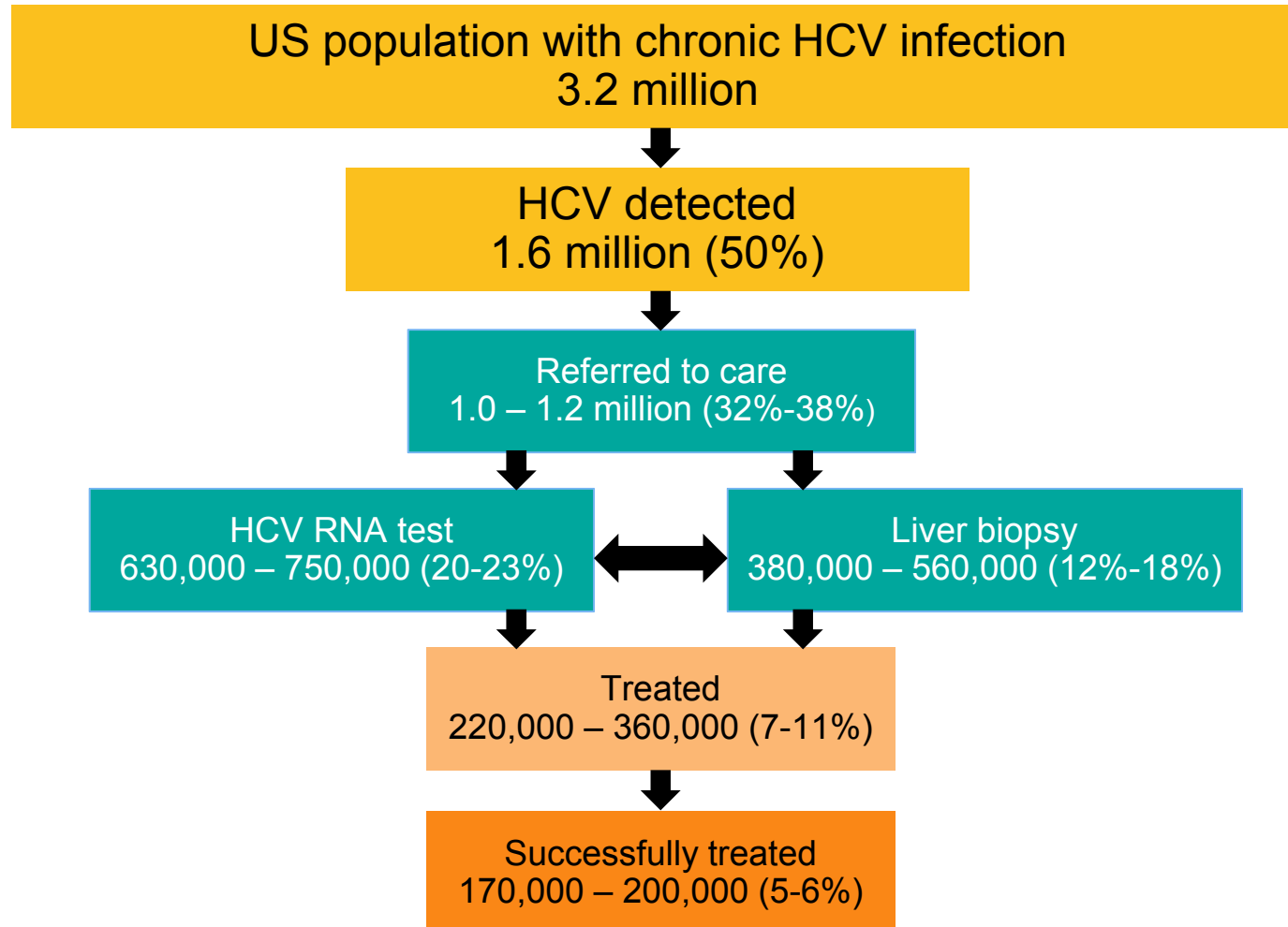
- Accuracy of the estimated HCV prevalence is poor
  - National prevalence estimates based on the mainstream population and generally excluded high-risk groups
  - In low income countries suboptimal testing due to high cost of testing
- Targeted outreach to high-risk populations and alternative testing algorithms might improve HCV diagnosing

# Obstacles to HCV Eradication

## **Sub-optimal linkage to care**

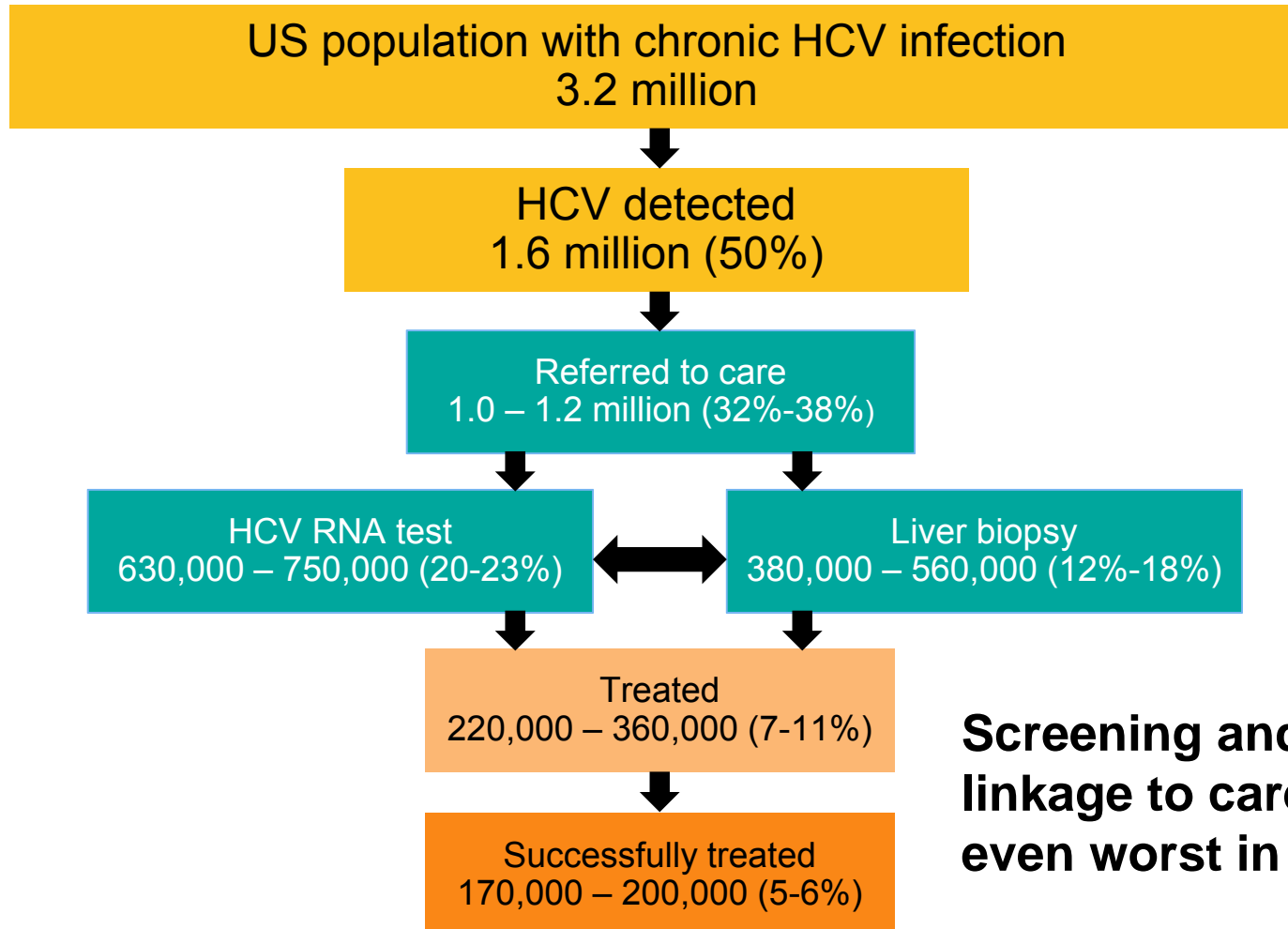
- High medication cost
- Inadequate insurance coverage
  - PWID are more likely to be uninsured or have limited access to health care system
- Insufficient numbers of clinicians
  - In rural areas
  - Willing to treat PWID
- Insufficient support services

# Screening and Linkage to Care in the US





# Screening and Linkage to Care in the US



**Screening and linkage to care is even worst in PWID**

## Polling Question:

Do you work with injection drug users or other substances users?

1. Yes
2. No

## Linkage to HCV Care in PWID

- PWID have the highest HCV prevalence, but their treatment uptake remains low
  - PWID are less likely to be referred for HCV evaluation
  - Less than 1/3 of those referred to specialty clinics appear for appointments
  - Less than 20% of those evaluated initiate antiviral therapy
- The majority of PWID (> 70%) express willingness to undergo HCV treatment but only a small minority (1%-6%) receives therapy
- Reasons for low treatment uptake emanate from patients, providers, and the health care system

# Treatment Barriers in PWID - Patients

- Lack of knowledge about HCV status
  - 45%-85% of HCV-infected people unaware of their status
- Lack of HCV related knowledge
  - Low perceived need for treatment (asymptomatic disease)
  - Few patients cognizant that treatment is curative
- Fear of side effects
  - IFN-related
  - Some patients unaware of new treatment options

# Treatment Barriers in PWID - Patients

- Mistrust of the health care system
  - Face stigmatization in general health care venues
  - Often experience providers as judgmental, unresponsive to their medical needs and disdainful
- PWID are more likely to be uninsured, be affected by poverty, and have reduced social support

# Treatment Barriers in PWID - Providers

- Reluctant to treat PWID
  - PWID are less likely to be referred and less likely to be HCV treated<sup>1</sup>
  - Perceive PWID as challenging patients – more likely to be diagnosed with psychiatric co-morbidities
- Concerns about re-infection
  - Reinfections can occur but the rate is low even in persons who continue injection drug use during and after treatment<sup>2</sup>

# Treatment Barriers in PWID - Providers

- Concerns about treatment adherence
  - Drug use in the 6 months preceding the initiation of HCV therapy is **not** associated with poorer treatment response<sup>1-3</sup>
  - Therapy can be successful for pts. who currently inject drugs<sup>1-5</sup>
    - Occasional drug use during treatment does not seem to impact adherence and treatment completion rates<sup>5</sup>
    - More frequent use (daily/every other day) is correlated with lower adherence and SVR rates<sup>1,2,4,5</sup>
  - Psychiatric diagnosis was more clearly associated with poorer treatment outcome than moderate drug use<sup>1</sup>
  - Social functioning may be a better indicator of treatment outcome than injection drug use<sup>4</sup>

# System-Based Treatment Barriers

- Complex and difficult to navigate
- Stigmatization in health venues
  - PWID often experience health care providers as judgmental and unresponsive to their medical needs
- Insurance coverage
  - PWID are more likely to be uninsured and to have less financial resources



# Determinants of HCV Treatment Adherence and Outcomes in PWID

**Meta-analysis performed to assess factors that influence HCV treatment adherence and outcomes in PWID**

- SVR rates for PWID are very similar to those obtained in registration trials (general population)
- Treatment of addiction during HCV therapy results in higher HCV treatment completion rates
- Involvement of multidisciplinary team was associated with higher SVR rates
  - Systematic program for HCV treatment that includes specialists from 2 or more areas

# Determinants of HCV Treatment Adherence and Outcomes in PWID

**Meta-analysis performed to assess factors that influence HCV treatment adherence and outcomes in PWID<sup>1</sup>**

- Support services offered during HCV treatment significantly increase treatment completion rates among PWID
  - Needle exchange programs
  - Counseling
  - Case management
  - Educational interventions
  - Directly observed therapy (DOT)
  - Motivational interviewing

## Overcoming Barriers – Patients

- Most patient-related barriers are based on misconceptions and lack of HCV-related knowledge
- Support services during HCV treatment increase treatment completion rates among PWID

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HCV-related educational interventions and peer-support groups could be utilized to overcome patient-related barriers

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hepatology, addiction medicine, general practice, mental health

## Overcoming Barriers – Treatment Venues

- Well stabilized addiction seems to be critical for successful HCV treatment of PWID
- Support services further improve HCV treatment outcomes in PWID
- PWID mistrust medical community and often avoid general healthcare venues



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Co-localizing HCV management services at venues where PWID receive care for drug addiction may increase HCV treatment uptake

## Opiate Agonist Treatment (OAT) facilities as HCV treatment venues

- May provide an infrastructure to circumvent many obstacles of HCV treatment in PWID
  - Stabilize patients' addiction
  - Provide portal for PWID entry into the healthcare system
  - Provide support services (educational programs, support groups, counseling and case management, DOT)
  - Employ multidisciplinary teams capable of addressing medical comorbidities or offering social support
- The majority of OAT facilities do not have capabilities to offer HCV care and treatment

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- The majority of OAT facilities do not have capabilities to offer HCV care and treatment

New models for HCV care and management in OAT venues are urgently needed

# PET-C Project

## Prevention, Evaluation, and Treatment of Hepatitis C in Opiate Agonist Treatment

- Objective of testing the feasibility of telemedicine-based care model for HCV management and treatment for PWID enrolled in OAT
- Collaboration of 3 institutions:
  - Weill Cornell Medical College
  - University at Buffalo, State University of New York
  - START Treatment & Recovery Centers
- Supported by the CDC Foundation through the Viral Hepatitis Action Coalition

## PET-C Project – Survey

- Initiated with the survey of patients from 2 MMTPs in Harlem (NYC)
- The objective:
  - To assess the level of HCV-related knowledge and willingness to participate in HCV-related education and treatment**
- 320 MMTP patients participated in the survey
- All patients attending MMTP and willing to participate were included in the survey
  - Participants compensated with a 5-ride transportation card (\$11.25)

# PET-C Project – Survey

- 30 item survey
- The first 23 questions assessed:
  - Demographics (age, gender, race/ethnicity)
  - Education level and employment/disability status
  - Drug use history
  - Willingness to attend HCV-related educational session
  - Willingness to be treated for HCV
- The last 7 questions assessed HCV-related knowledge

# Survey – Patient Characteristics

Variable	n Respondents	n (%) or Mean (SD)
Age, yr	319	53.15 (8.72)
Sex	316	
Male		188 (59.49)
Female		128 (40.51)
Race	312	
White		28 (8.97)
African American		172 (55.13)
Mixed		21 (6.73)
Other		91 (29.17)
Ethnicity	308	
Hispanic		118 (38.31)
Non-Hispanic		190 (61.69)
Duration of OAT program attendance, yrs	314	7.03 (6.70)
Education	320	
No GED/high school diploma		127 (39.69)
GED/high school		154 (48.13)
Associates degree		22 (6.88)
College degree		14 (4.38)
Masters or doctorate degree		3 (0.94)
Employed	320	21 (6.56)
On disability	318	198 (62.26)

# Survey – Patient Characteristics

- 56.9% reported history of injection drug use
  - 6.9% in the last 6 months (heroin, cocaine and crack)
- 93.8% reported history of non-injection drug use
  - 37.3% in the last 6 months (heroin, cocaine and crack)
- 46% reported positive HCV status
  - Self-reported HCV positive respondents were slightly older than other patients
  - HCV positivity associated with the history of injection drug use and recent injection drug use
- Only 5.4% did not know their HCV status



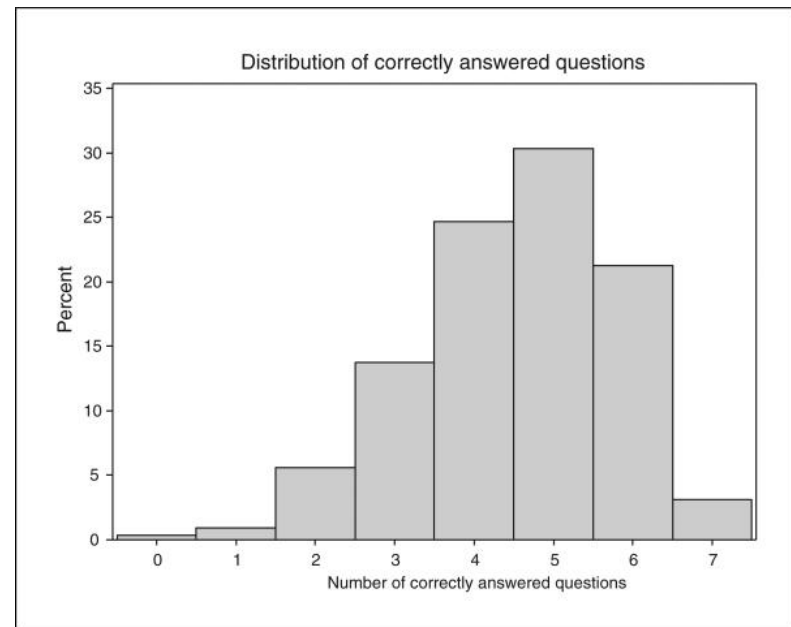
## Survey Results – HCV Education

- 58.3% of respondents were aware of the on-site HCV-related educational activities
  - 35.5% attended such activities; additional 25.5% attended similar educational activities elsewhere
- 78% expressed willingness to participate in HCV-related educational activities in the future
- Willingness to participate in the educational activities was associated with
  - Female gender
  - Unemployment
  - Previous participation in an educational program
  - Willingness to receive HCV treatment

# Survey Results – HCV Knowledge

- Respondents demonstrated substantial HCV-related knowledge

- 54.7% correctly responded to at least 5 of 7 HCV-related knowledge questions



- Patients who previously attended HCV educational activity scored higher on HCV knowledge questions

## Survey Results – HCV Treatment

- The majority of patients (78%) expressed willingness to be treated for HCV
- Patients who scored higher on HCV knowledge questions were more likely to accept HCV treatment

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Educational activities likely improved HCV-related knowledge in PWID resulting in increased willingness to be treated for HCV

# Education Provides Significant Benefits to Hepatitis Patients

Systematic review of studies that analyzed role of educational interventions for patients with HCV and HBV infection

- Even simple educational interventions can significantly increase knowledge about HBV and HCV infections
- Complex, multimodal educational interventions can cause behavioral changes that increase rates of testing, vaccination, and treatment uptake

# PET-C Project: Educational Intervention

- HCV-related educational interventions conducted in two MMTPs in Harlem (NYC)
  - Initiated in June 2013
- Over a 3 year period, 204 patients completed HCV-related educational intervention
- Results obtained from the first 110 patients who participated in the intervention were analyzed and published

# Educational Intervention

- Offered to all MMTP patients willing to participate who previously completed HCV-related survey
- Two 30-60 minutes sessions separated by 1 week
  - Patients unable to complete session 2 the following week were allowed to do it on any subsequent week
    - Average time between 2 sessions was  $12 \pm 14$  days
  - 10 participants per session
- Sessions were interactive
  - Participants stimulated to ask questions and share thoughts and experiences with the group
- Patients received \$50 compensation after the second session

# Educational Intervention

- Blood obtained before the first session for HCV RNA assessment
  - After the second session patients informed about their HCV status
- HCV-related knowledge was assessed before and after the intervention
- Post-educational 15-item questionnaire
  - 7 HCV-related knowledge questions
  - 8 questions about employment/disability status, recent drug use, and HCV treatment willingness



# Educational Intervention

## Session 1:

- Virus as a cause of disease
- Routes of transmission
- Acute vs. chronic infection
  - Spontaneous resolution
  - Ab development
  - Potential symptoms
- Function of the healthy liver
- Consequences of the chronic disease

## Session 2:

- Diagnostic testing
  - (HCV Ab vs. HCV RNA)
- Treatment
- Prevention

# Educational Intervention Patient Characteristics

Variable	n Respondents	n (%) or Mean (SD)
Age, yr	110	54.7 (7.8)
Male sex	109	64 (59)
Race	108	
White		5 (5)
African American		76 (70)
Mixed		2 (2)
Other		25 (23)
Hispanic Ethnicity	103	31 (30)
Education	109	
No GED/high school diploma		41 (38)
GED/high school		54 (50)
Associates degree		11 (10)
College degree		1 (1)
Masters or doctorate degree		2 (2)
History of IDU	110	65 (59)
History of non-IDU	110	105 (95)
Years attending OAT program	105	6.85 (5.36)

## Educational Intervention HCV-Related Knowledge

- Educational intervention significantly improved HCV related knowledge in patients
  - 66% of patients answered 5 or more questions correctly before the intervention
  - 84% of patients answered 5 or more questions correctly after the educational intervention
  - The mean number of correctly answered questions significantly increased ( $4.95 \pm 1.14$  vs.  $5.40 \pm 1.08$ ,  $p < 0.001$ )

## Educational Intervention HCV-Related Knowledge

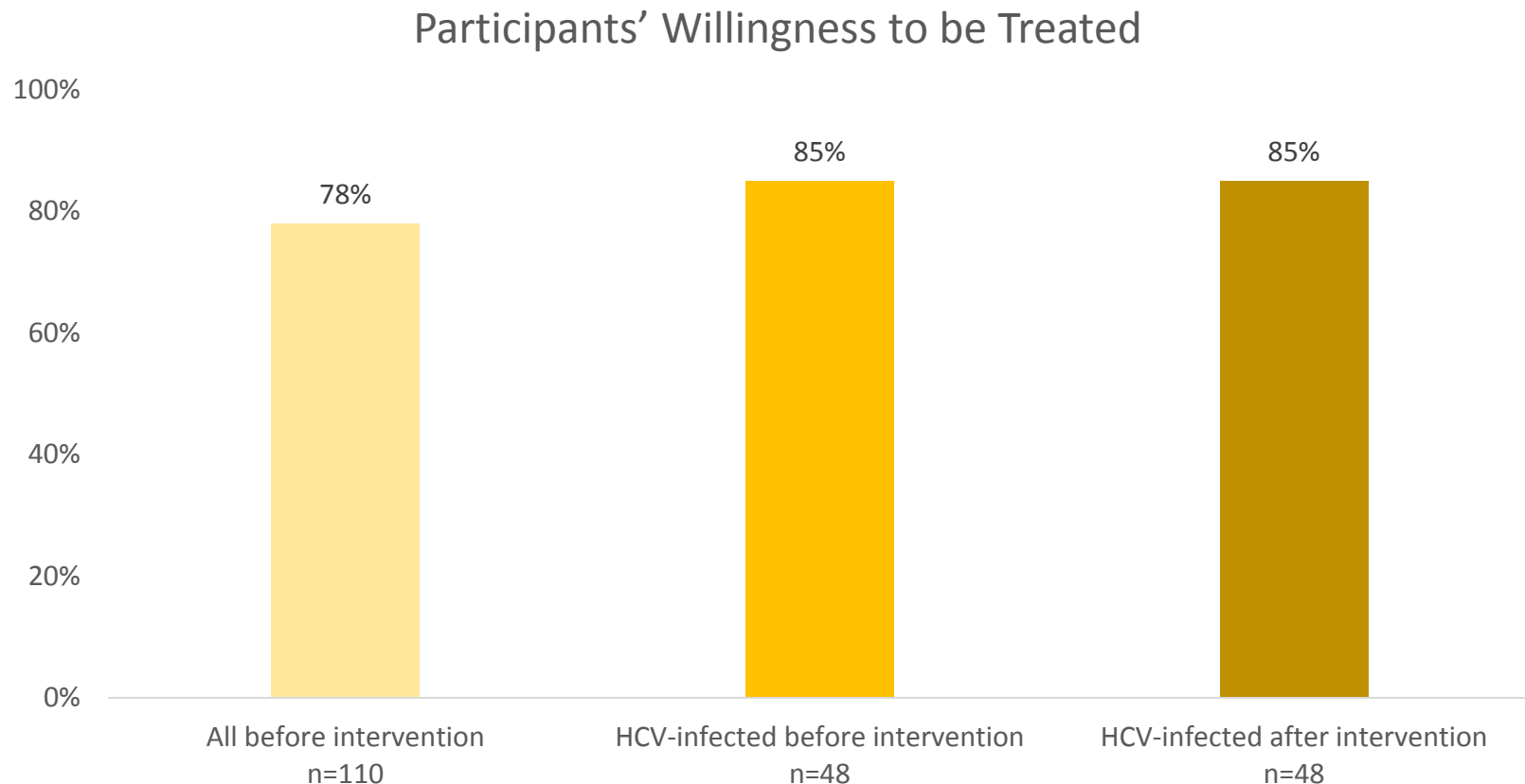
- Pre-intervention HCV-related knowledge did not change significantly over time
  - Analyzed in patients who completed the survey more than 6 months prior to educational intervention,
- Ever being tested for HCV was significantly associated with higher HCV-related knowledge after the intervention

## Educational Intervention HCV Status

- 66 (60%) participants were HCV-seropositive and 48 (43%) were HCV RNA positive
  - 37 (77.1%) participants were previously diagnosed with HCV
  - 4 (8.3%) were unaware of their HCV status
  - 7 (14.5%) thought they didn't have the disease
- 18 participants were HCV-seropositive but HCV RNA negative
  - 17 participants spontaneously resolved the infection
  - 1 participants previously treated for HCV

# Educational Intervention Willingness to be Treated

- Participants' willingness to be HCV treated did not change after the educational intervention



# Participants Perspective

- The majority of attendees had a very positive disposition towards the educational intervention
- Many participants expressed gratitude for the opportunity to learn more about HCV and current treatment options
  - Some participants expressed interest to participate in other educational activities related to other diseases
- Many HCV-infected participants expressed interest to be enrolled in HCV treatment on-site

# Conclusions

- Co-localization of HCV management with substance abuse treatment may facilitate HCV diagnosis and promote treatment acceptance
  - OAT venues may provide a portal for PWID to enter into the health care system
- Many barriers for HCV treatment of PWID are based on misconceptions and could be modified through educational activities
- Multidisciplinary approaches with healthcare providers from different specialties may increase HCV treatment efficacy among PWID



# Collaborators

## **Weill Cornell Medicine**

- Marija Zeremski, PhD

## **University at Buffalo**

- Andrew H. Talal, MD, MPH
- Rositsa B. Dimova, PhD

## **START Treatment and Recovery Centers**

- Lawrence S. Brown Jr, MD, MPH
- Clewert Sylvester, MD
- Steven Kritz, MD
- Roberto Zavala, MD
- Anthony McLeod

## **CDC**

- Bryce D. Smith, PhD
- Jon E. Zibbell, PhD

# Thank You!

Marija Zeremski, PhD  
Project Director  
Clinical Directors Network, Inc. (CDN)  
[erla@CDNetwork.org](mailto:erla@CDNetwork.org)



# Knowledge Questions

1. The easiest way to get hepatitis C is through sharing equipment to inject drugs. Yes No
2. The majority of people with chronic hepatitis C do not have any symptoms. Yes No
3. What can hepatitis C do?
  - A. Infect cells in the liver
  - B. Cause inflammation of the liver
  - C. Cause cirrhosis of the liver
  - D. Cause liver cancer
  - E. All of the above
  - F. a and b only
4. Everybody with a positive hepatitis C antibody test has chronic hepatitis C disease (infection). Yes No
5. There is medication to treat hepatitis C. Yes No
6. There is a vaccine for hepatitis C. Yes No
7. People who clear the hepatitis C virus, either spontaneously or after medical treatment can be infected again. Yes No