HIV/HCV/SUD Virtual Symposium

Treating HCV in Persons with Mental Health & Substance Use Disorders

Jeffrey J. Weiss, PhD, MS

November 18, 2020

Disclosures

None

Objectives

1. Understand how a substance use disorder diagnosis is relevant to the HCV care cascade

2. Conduct PREP-C assessment

3. Discuss evidence for efficacy of PREP-C

Higher Prevalence of HCV in Marginalized Groups

Rates of HCV infection:

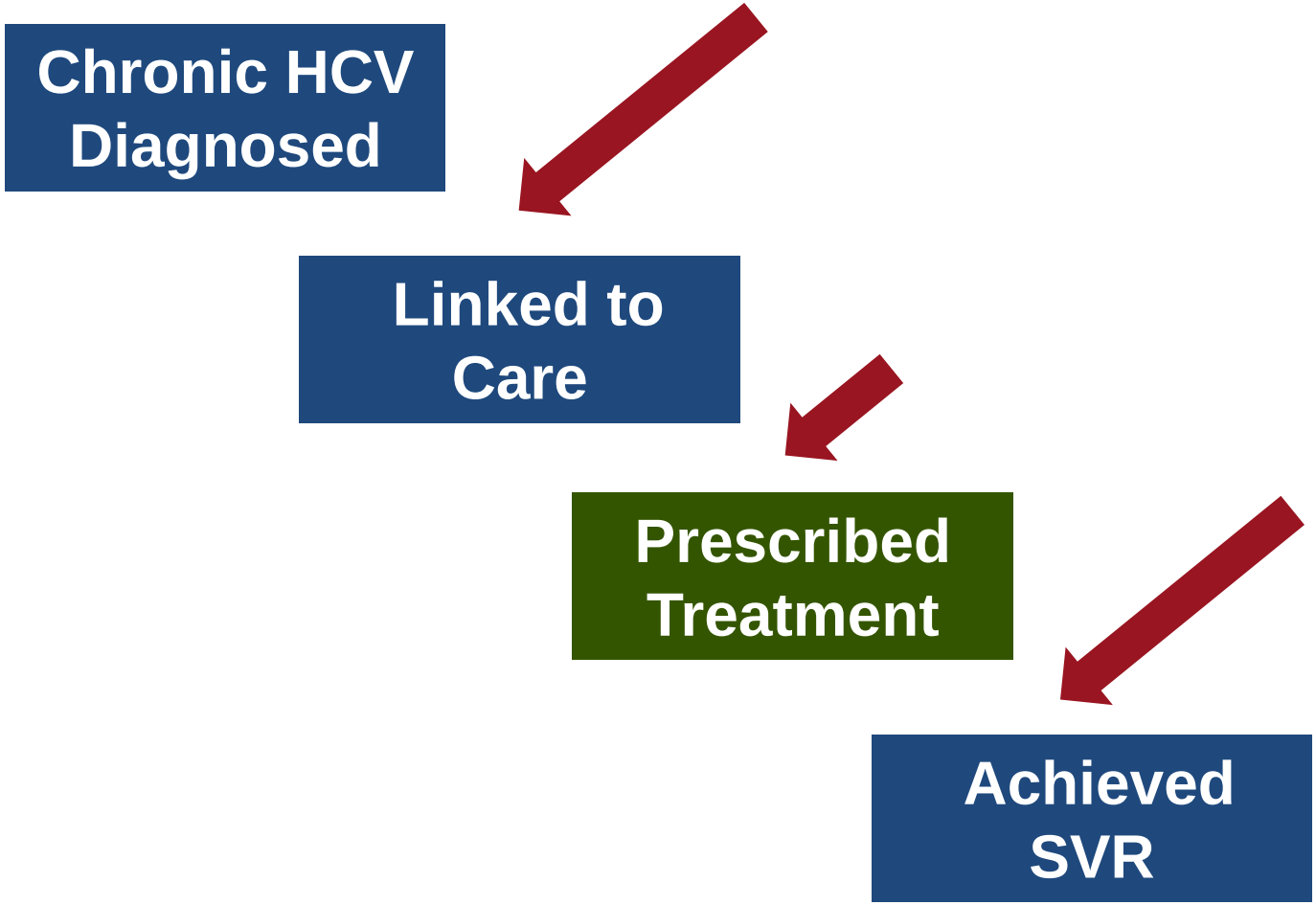
• IDU > 10 years of use	90% *(Tseng et al. 2007)*
• IDU < 9 years of use	66% *(Tseng et al. 2007)*
• Homeless persons	15% *(Hofmeister et al. 2019)*
• Incarcerated	16% *(Hofmeister et al. 2019)*
• Severely mentally ill	20% *(Rosenberg et al. 2001)*
• US population (reference)	1.5% *(Hofmeister et al. 2019)*

Tseng et al. (2007) Hepatology, 46 (3) 666-71.
Hofmeister et al. (2019) Hepatology 69(3) 1020-1031.
Rosenberg et al. (2001) Am J Pub Health 91(1) 31-37.

HCV Adherence Challenge in 2020

- Psychiatric disorders, substance use disorders and cognitive impairment have been shown to be general risk factors for medication non-adherence across multiple medical conditions
- As we progress toward HCV elimination, the patients who remain to be treated will present with increasingly complex neuropsychiatric profiles

HCV Cascade – Mental Health & Substance Use Relevant at Every Step



Access to HCV Treatment for Patients with Mental Health or SUD

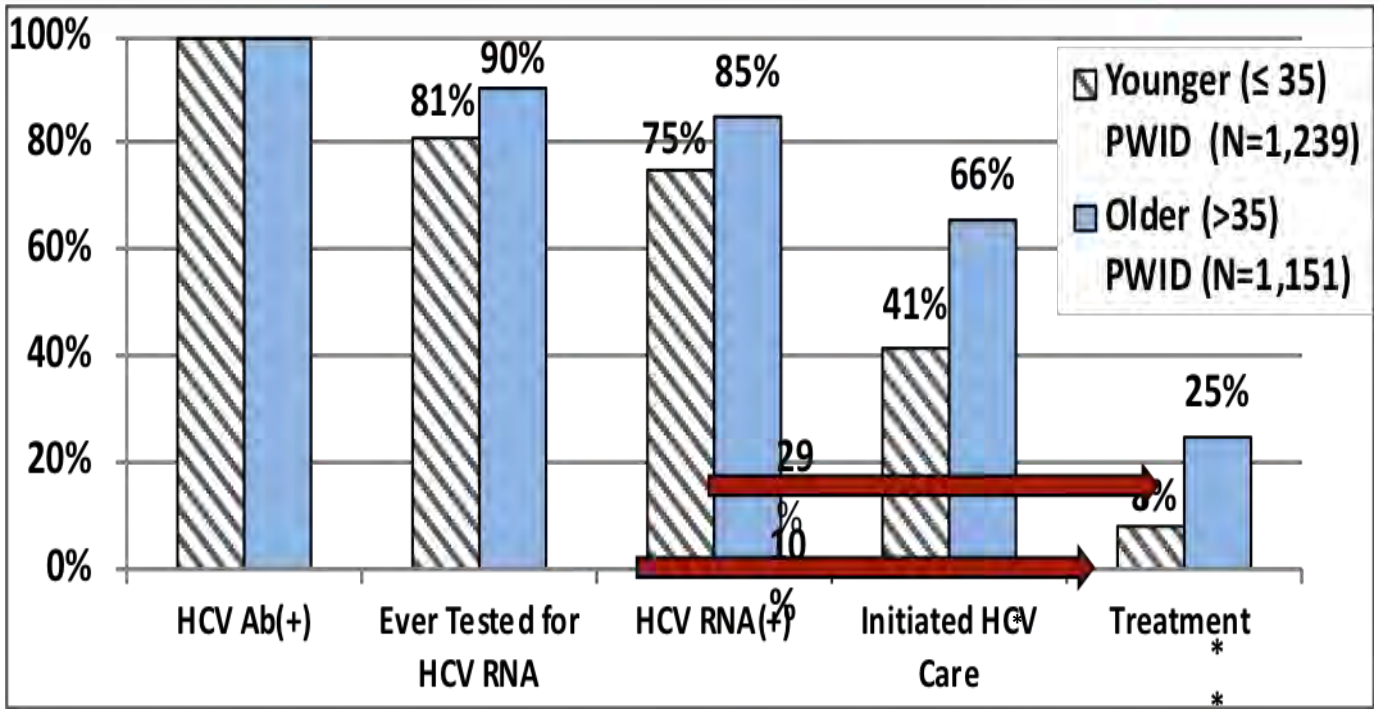
Predictors of HCV treatment in the pre-DAA (1/1/11 – 12/31/13) and post-DAA (1/1/14-2/28/17) in 4 clinical cohorts of 14,501 persons (Dallas, Oakland, New Orleans, Richmond)

	Pre-DAA			Post-DAA		
	% of Untreated with	% of Treated with	P value	% of Untreated with	% of Treated with	P value
Major Depression	8.6	4.9	0.0476	5.8	4.0	0.0543
Other Mood/psychiatric disorder	12.8	5.3	0.0008	8.1	3.5	<0.0001
Manic/bipolar disorder	5.5	0	0.0003	3.6	0.3	<0.0001
Alcohol Use Disorder	12.0	3.5	<0.0001	9.0	4.0	<0.0001
Opioid Use Disorder	4.4	0.4	0.0035	4.5	0.2	<0.0001

Jain et al. 2019, Hepatology, 69, 51-63

Continuum of care in PWID

The continuum of care for PWID in Philadelphia 2013-17



*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

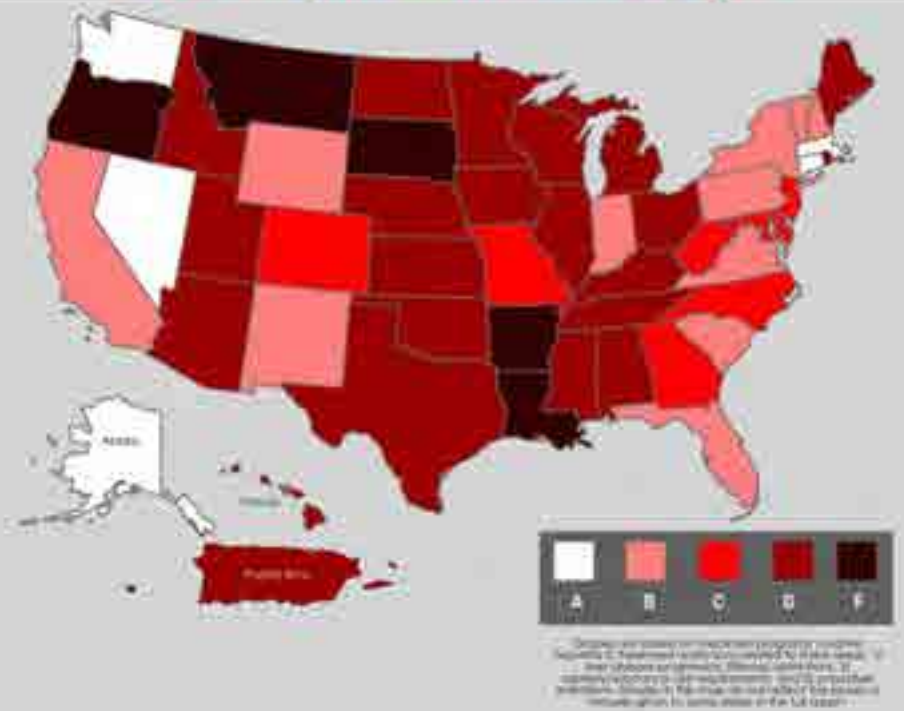
Poor linkage to care and very low treatment rates, especially in younger PWID

Trooskin et al, AASLD 2018, Abstract 1632

Hepatitis C: State of Medicaid Access

A report by the National Viral Hepatitis Roundtable (NVHR) and the Center for Health Law and Policy Innovation of Harvard Law School (CHLPI) finds that most Medicaid programs are restricting access to a cure for hepatitis C, which kills more Americans each year than all other infectious diseases combined. More than half of Medicaid programs received a "D" or an "F" for severely restricting access to hepatitis C treatment.

See how your state matches up...



BEST 5 STATES

Alaska
Connecticut
Massachusetts
Nevada
Washington

WORST 5 STATES

Arkansas
Louisiana
Montana
Oregon
South Dakota

#StateofHepC

NVHR

StateofHepC.org

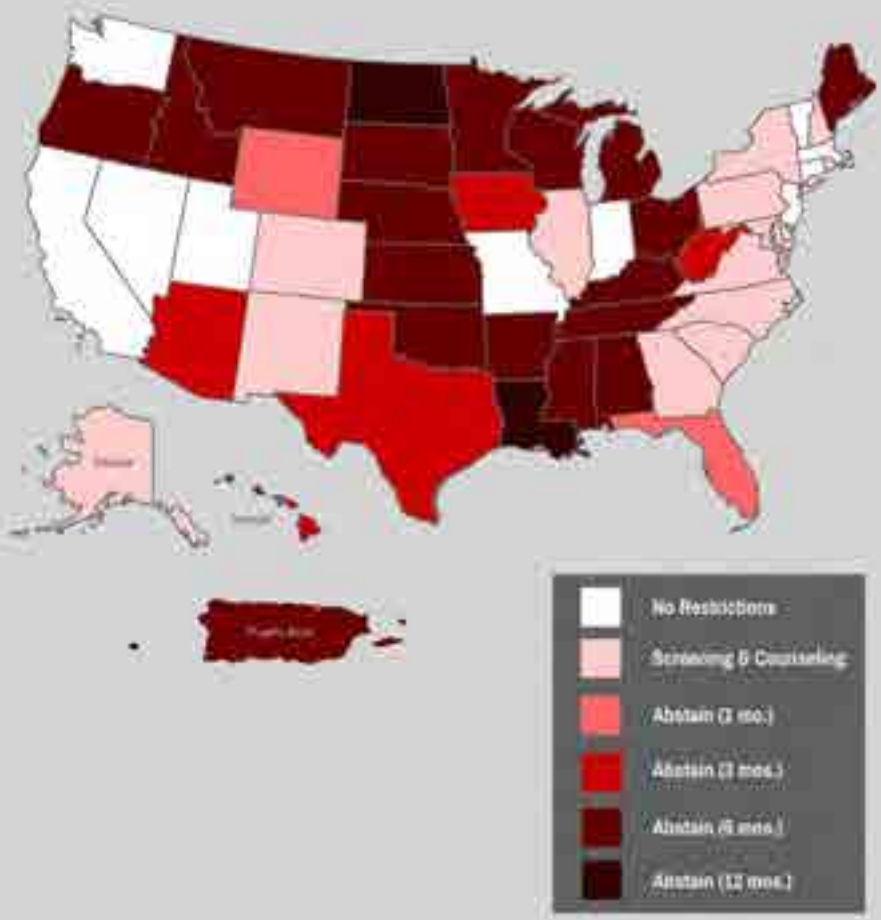
stateofhepc.org

Hepatitis C: State of Medicaid Access

Sobriety Restrictions

An analysis of 2017 Fee-For-Service (FFS) Medicaid data demonstrates that several Medicaid programs have eliminated sobriety requirements for patients seeking to access hepatitis C (HCV) cures, while others highly restrict access.

2017 Medicaid FFS Sobriety Restrictions for HCV Treatment



#StateofHepC NVHR CENTER for HEALTH LAW and POLICY INNOVATION StateofHepC.org

Hepatitis C: State of Medicaid Access Report Card

Texas

Estimated Number of Individuals Living with Hepatitis C: 376,600[1]

Grade	Summary
D+	**Liver Damage (Fibrosis) Restrictions:** Fee-For-Service (FFS) requires severe liver damage (F3 or greater). Thirteen of 15 Managed Care Organizations (MCOs) impose the same liver damage requirements as FFS: Aetna, Amerigroup, BlueCross BlueShield, Cigna HealthSpring, Christus Health Plan, Community Health First Plans, El Paso First Health, FirstCare STAR Health Plans, Molina Healthcare, Scott & White, Sendero Health Plans, Superior HealthPlan and UnitedHealthcare. Community Health Choice and Parkland Community Health do not provide hepatitis C coverage criteria publicly. **Sobriety Restrictions:** FFS requires screening for substance use within 90 days prior to submitting a prior authorization request. Thirteen of 15 MCOs impose the same sobriety criteria as the FFS program: Aetna, Amerigroup, BlueCross BlueShield, Cigna HealthSpring, Christus Health Plan, Community Health First Plans, El Paso First Health, FirstCare STAR Health Plans, Molina Healthcare, Scott & White, Sendero Health Plans, Superior HealthPlan and UnitedHealthcare. Community Health Choice and Parkland Community Health do not provide hepatitis C coverage criteria publicly. **Prescriber Restrictions:** FFS requires a prescription be written by or in consultation with a specialist. Thirteen of 15 MCOs impose the same prescribing requirements as FFS: Aetna, Amerigroup, BlueCross BlueShield, Cigna HealthSprung, Christus Health Plan, Community Health First Plans, El Paso First Health, FirstCare STAR Health Plans, Molina Healthcare, Scott & White, Sendero Health Plans, Superior HealthPlan and UnitedHealthcare. Community Health Choice and Parkland Community Health do not provide hepatitis C coverage criteria publicly. **Recommendations to Improve Patient Access:** • Remove liver damage, sobriety and prescriber restrictions. • Maintain coverage parity across the FFS and MCO programs and ensure transparency regarding hepatitis C coverage in all MCOs *Grade Rationale: Texas Medicaid FFS and MCOs severely restrict access to hepatitis C medications, requiring severe liver damage, 90 days of sobriety and a prescription written by or in consultation with a specialist. With these restrictions, very few people with hepatitis C have access to treatment. Texas Medicaid requires MCOs to apply the FFS coverage criteria. However, plans are allowed to impose less stringent requirements. In recognition of parity across FFS and MCOs and the potential for MCOs to have less severe restrictions than FFS, a "plus" has been added to the state's D grade.*

Psychiatric and Substance Use Disorders

	Psychiatric Disorder	No Psychiatric Disorder
Substance Use Disorder	**Comorbid**	**Substance Use**
No Substance Use Disorder	**Psychiatric**	**None**

578 persons with OUD in NESARC sample

Grella et al. (2009) *Addictive Behaviors* 34:498-504

52% Major Depression (7% general pop)

39% Any anxiety disorder (19% general pop)

50% Any personality disorder (9% general pop)

NESARC, NCS, ECA: Odds Ratio of Association between Alcohol or Drug Dependence and other Disorders

	Alcohol	Drug
Major Depression	1.6 - 4.0	2.0 - 9.0
Dysthymia	2.3 - 3.8	1.3 - 11.3
Bipolar Disorder	4.6 – 8.0	8.3 – 13.9
Panic Disorder with Agoraphobia	2.6 – 3.6	4.4 – 10.5
Social Phobia	1.6 – 2.5	2.2 – 5.4
PTSD	3.4	3.8
ADHD	2.8	7.9
Antisocial Personality	8.3 – 14.7	15.6 – 18.5

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Edward V. Nunes, MD

What Level of Adherence is Required?

- Resistance
- Relapse
- 90%
- 12 week course = no more than 8 missed days
- 8 week course = no more than 5 missed days

3 Groups of People Who Use Drugs (PWUD) with HCV

- Clinical trials: *proof of concept*
- Clinical practice: *current opportunity*
- Not yet linked to care: *ongoing challenge*

Research in IFN era finds that IDUs (including active users) can do equally well on:

→ Adherence to HCV treatment
→ Outcome of HCV treatment – SVR

Context of adequate access to food, housing, medical care, medication, psychiatric care, syringe exchange, opioid substitution therapy, Safer Injection Facilities (8 countries).

Robaeys et al. (2006) Eur J Gastroenterol Hepatol (Benelux)
Bruggmann et al. (2008) J Viral Hepatitis (Switzerland)
Grebely et al. (2010) Eur J Gastroenterol Hepatol (Vancouver)

Lower adherence and SVR has been observed in persons with frequent injecting drug use (daily/every other day) during treatment (Grebely et al. 2015 J Hepatology)

C-EDGE CO-STAR: EFFICACY OF GRAZOPREVIR / ELBASVIR FIXED DOSE COMBINATION FOR 12 WEEKS IN HCV-INFECTED PERSONS WHO INJECT DRUGS ON OPIOID AGONIST THERAPY

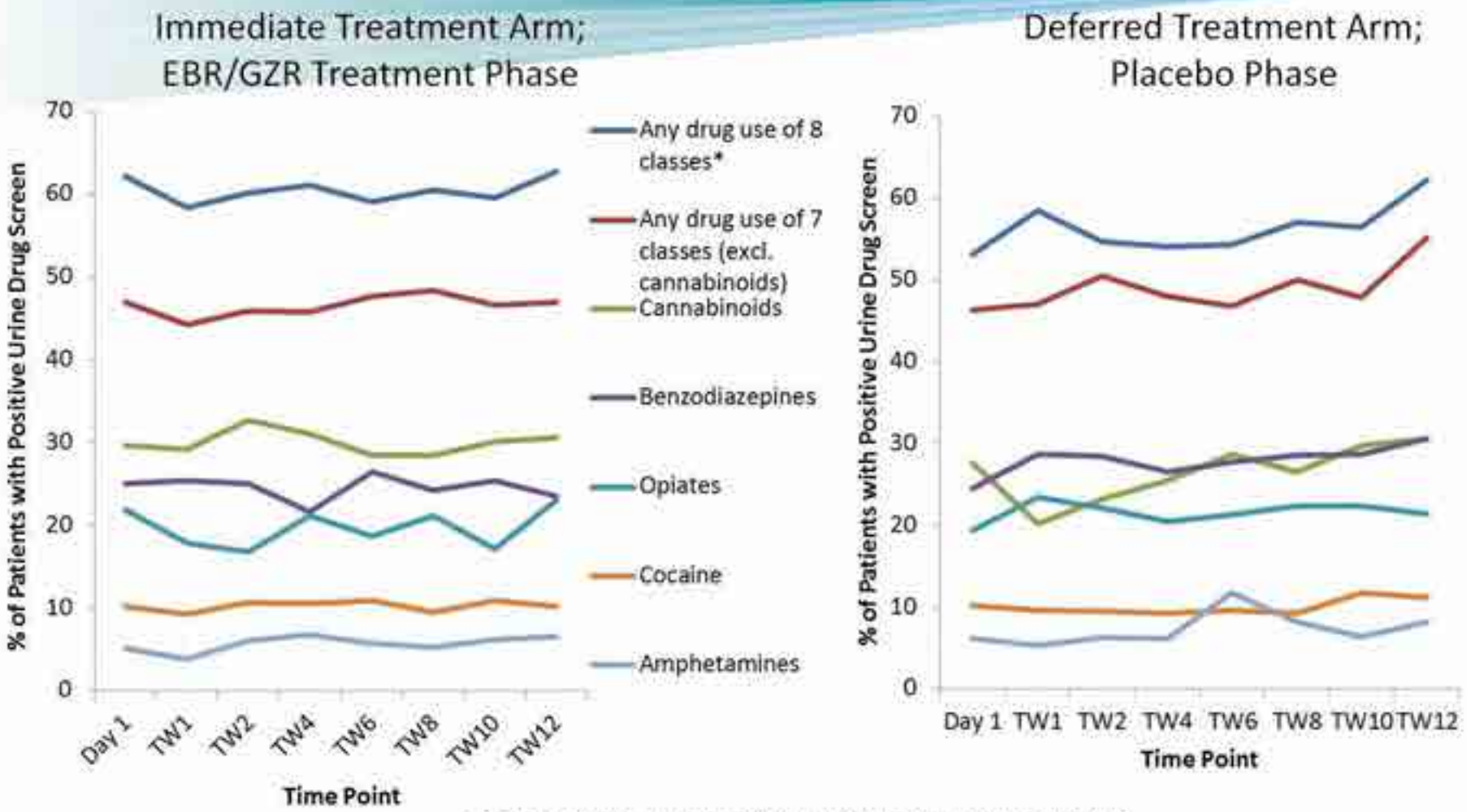
Dore GJ[1], Altice F[2], Litwin AH[3], Dalgard O[4], Gane E[5], Shibolet O[6], Luetkemeyer A[7], Nahass R[8], Peng CY[9], Conway B[10], Grebely J[1], Howe A[11], Nguyen BY[11], Wahl J[11], Barr E[11], Robertson M[11], Platt HL[11]

[1]The Kirby Institute, UNSW Australia, [2]Yale School of Medicine, [3]Montefiore Medical Center and Albert Einstein College of Medicine, [4]Institute of Clinical Medicine, [5]Auckland Clinical Studies, [6]Tel-Aviv Medical Center, [7]University of California, San Francisco, [8]ID Care, [9]China Medical University Hospital, [10]Vancouver Infectious Diseases Centre, [11]Merck & Co., Inc.

MERCK

C-EDGE CO-STAR

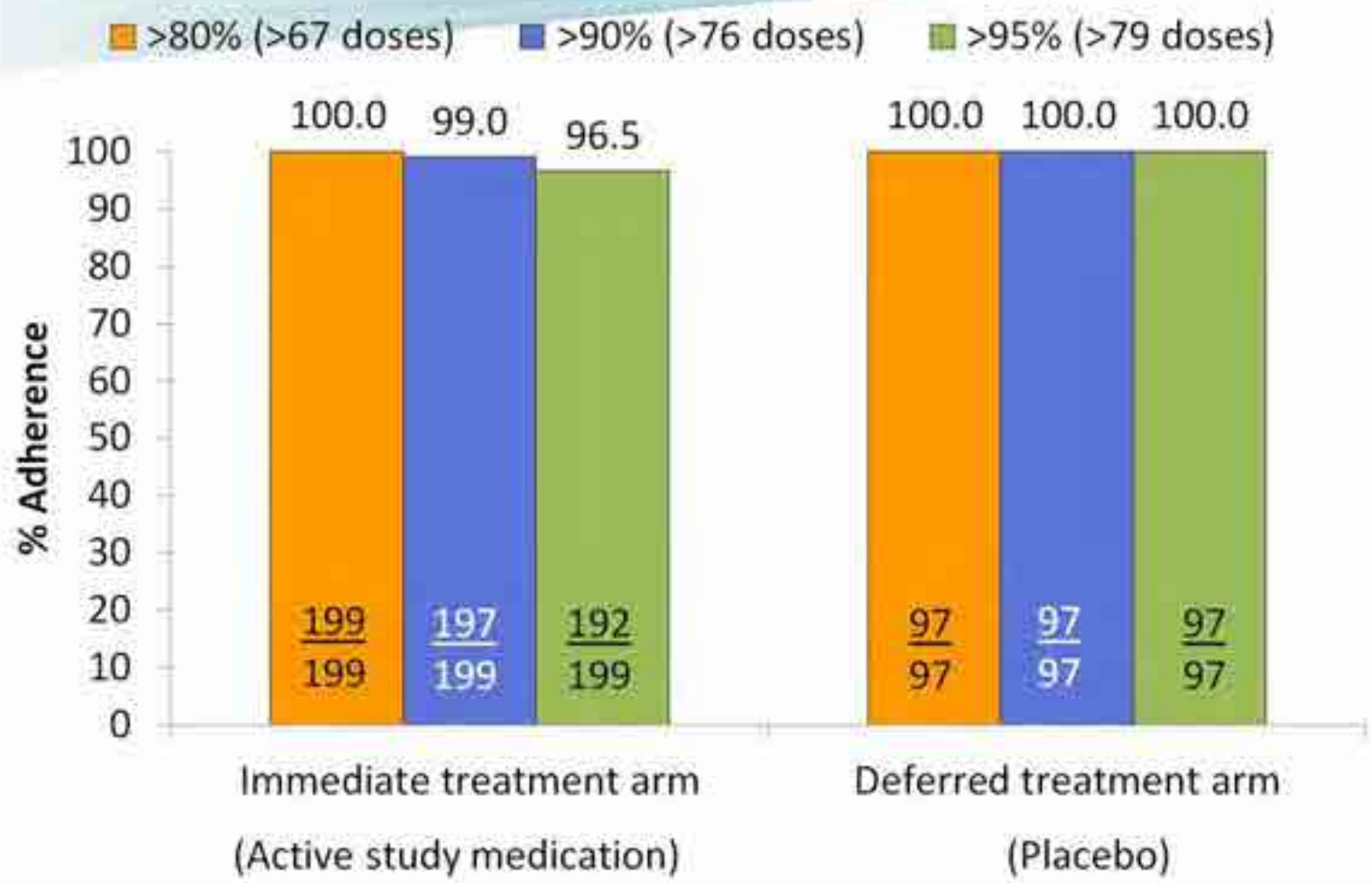
URINE DRUG SCREEN RESULTS: DAY 1 TO TREATMENT WEEK 12



* 8 drug classes: amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, opiates, phencyclidine, propoxyphene

C-EDGE CO-STAR

ADHERENCE


>80% (>67 doses)
>90% (>76 doses)
>95% (>79 doses)
% Adherence
100
90
80
70
60
50
40
30
20
10
0
100.0
99.0
96.5
100.0
100.0
100.0
199/199
197/199
192/199
97/97
97/97
97/97
Immediate treatment arm
(Active study medication)
Deferred treatment arm
(Placebo)

Models of HCV Treatment in PWID (Akiyama et al. 2019)

158 PWID with HCV receiving opioid agonist therapy (OAT) were randomized to one of 3 study conditions at 3 OAT programs in the Bronx (Oct 2013-April 2017):

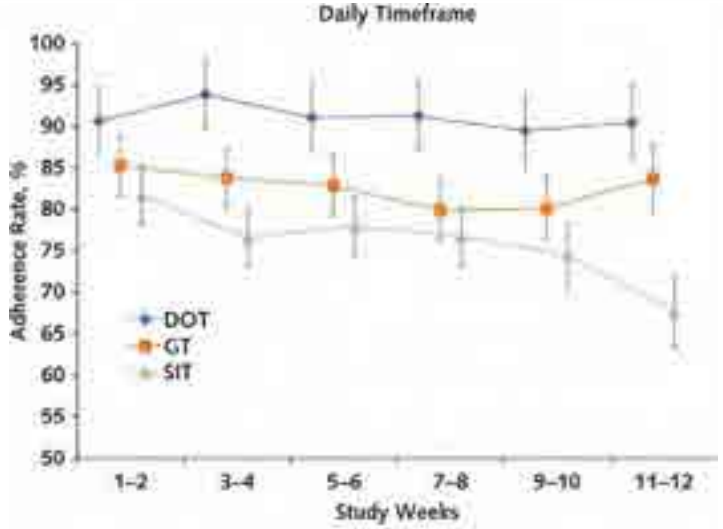
Directly observed treatment (DOT)

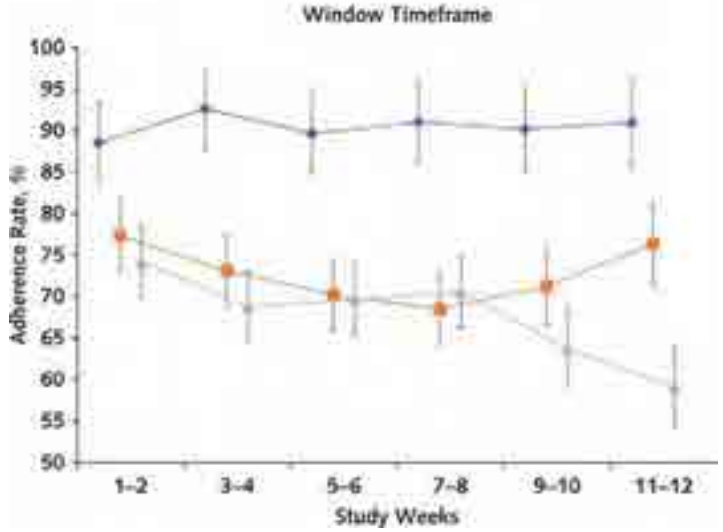
Group treatment (GT)

Self-administered individual treatment (SIT)

Intensive Models of Hepatitis C Care for People Who Inject Drugs Receiving Opioid Agonist Therapy: A Randomized Controlled Trial
Annals of Internal Medicine, May 7 2019

Dosing and Timing Adherence
Akiyama et al. 2019





SVR rates
Akiyama et al. 2019

Appendix Table 1. SVR, by Group, for Study Participants Overall and for Those Receiving a Combination DAA Regimen*

Group	Overall			Combination DAA Regimen		
	Patients, *n*	SVR, *n* (%)	SVR, 95% CI, %	Patients, *n*	SVR, *n* (%)	SVR, 95% CI, %
Overall						
DOT	51	50 (98)	90 to 100	36	36 (100)	90 to 100
GT	48	45 (94)	83 to 99	40	38 (95)	83 to 99
SIT	51	46 (90)	79 to 97	39	35 (90)	76 to 97
Total	150	141 (94)	89 to 97	115	109 (95)	89 to 98
		Difference in SVR (95% CI), *percentage points*			**Difference in SVR (95% CI), *percentage points***	
Comparison						
DOT vs. GT	–	4 (−7 to 16)		–	5 (−8 to 18)	
DOT vs. SIT	–	8 (−4 to 20)		–	10 (−4 to 25)	
GT vs. SIT	–	4 (−10 to 17)		–	5 (−10 to 21)	

DAA = direct-acting antiviral; DOT = directly observed therapy; GT = group treatment; SIT = self-administered individual treatment; SVR = sustained virologic response.

* No significant differences in SVR were found across the 3 groups ($P = 0.152$) among all participants or among those receiving combination DAA treatment ($P = 0.056$), on the basis of multivariable exact logistic regression adjusting for site and the 3 stratifying variables. No missing data were observed for this analysis.

Adherence
Akiyama et al. 2019

- Greater adherence was associated with SVR, with the odds of SVR 1.81 times higher for each 10% increase in daily adherence and 1.71 times higher for each 10% increase in window adherence
- Factors significantly associated with poor daily adherence were psychiatric illness at baseline (p=0.048) and drinking alcohol to intoxication in the 30 days before baseline (p=0.028). Drug use was not associated with poor adherence.

Impact of Prescribed Treatment Duration on Hepatitis C Treatment Adherence: Comparison of 8- and 12-Week Treatment With Glecaprevir/Pibrentasvir

Data was pooled from
10 phase 3 clinical trials
of naïve patients GT 1-6.
G/P for 8 or 12 weeks
N= 2086

Not significant:
Current alcohol use
History of IDU

Overall SVR12=97.7%

Jacobson IM et al. Hep Dart 2019

Table 2. Predictors of Non-adherence

Variable	Odds ratio (95% CI)	*P* value
[illegible]		
History of psychiatric disorder (yes vs no)	2.62 (1.54–4.46)	<.001
Race (black vs nonblack)	2.45 (1.07–5.64)	.035
Treatment duration (12 vs 8 weeks)	1.77 (1.03–3.02)	.037
[illegible]		
Treatment duration (12 vs 8 weeks)	1.92 (1.39–2.63)	<.001
Age, years	0.98 (0.97–0.99)	.003
HCV GT6 vs GT1	2.37 (1.27–4.42)	.007
Geographic region (North America vs Europe)	1.63 (1.12–2.36)	.011
History of psychiatric disorder (yes vs no)	1.52 (1.08–2.14)	.016
Race (black vs nonblack)	1.93 (1.12–3.33)	.017
Sex (male vs female)	1.45 (1.06–1.98)	.021
Presence of polypharmacy[i] (yes vs no)	1.44 (1.00–2.06)	.047
HCV GT3 vs GT1	1.47 (1.00–2.15)	.050

[illegible]

NYS Medicaid Pharmacy PA Program
Treatment Readiness

Provider utilized scales/assessment tools to evaluate the readiness of the patient:

- SAMHSA HRSA Center for Integrated Health Solutions- Drug & Alcohol Screening Tools- available at:

https://www.integration.samhsa.gov/clinical-practice/screening-tools#drugs

or

- Psychosocial Readiness Evaluation and Preparation for Hepatitis C Treatment (PREP-C) available at: https://prepc.org/

SAMHSA Screening Tools

- Alcohol Use Disorders Identification Test-C (AUDIT-C) 3 items alcohol screen
- Drug Abuse Screen Test (DAST-10) 10 item
- CAGE-AID – 5 item alcohol and drug use screen
- Screening, Brief Intervention, and Referral to Treatment (SBIRT)
  https://www.integration.samhsa.gov/clinical-practice/sbirt

Recommendations for Screening and Treatment of HCV Infection in People Who Inject Drugs (PWID)

RECOMMENDED	RATING
Annual HCV testing is recommended for PWID with no prior testing, or past negative testing and subsequent injection drug use. Depending on the level of risk, more frequent testing may be indicated.	IIa, C
Substance use disorder treatment programs and needle/syringe exchange programs should offer routine, opt-out HCV-antibody testing with reflexive or immediate confirmatory HCV-RNA testing and linkage to care for those who are infected.	IIa, C
PWID should be counseled about measures to reduce the risk of HCV transmission to others.	I, C
PWID should be offered linkage to harm reduction services when available, including needle/syringe service programs and substance use disorder treatment programs.	I, B
Active or recent drug use or a concern for reinfection is **not** a contraindication to HCV treatment.	IIa, B

Recommendation for Testing for Reinfection in People Who Inject Drugs (PWID)

RECOMMENDED	RATING
At least annual HCV-RNA testing is recommended for PWID with recent injection drug use after they have spontaneously cleared HCV infection or have been successfully treated.	IIa, C

Recommendations For the Management of HCV Infection Among PWID

RECOMMENDATION:

Pre-therapeutic assessment should include an evaluation of housing, education, cultural issues, social functioning and support, finances, nutrition and drug and alcohol use. PWID should be linked into social services, and peer support if available.

Class I, Level B

Grebely et al. on behalf of INHSU. Intl J of Drug Policy 2015

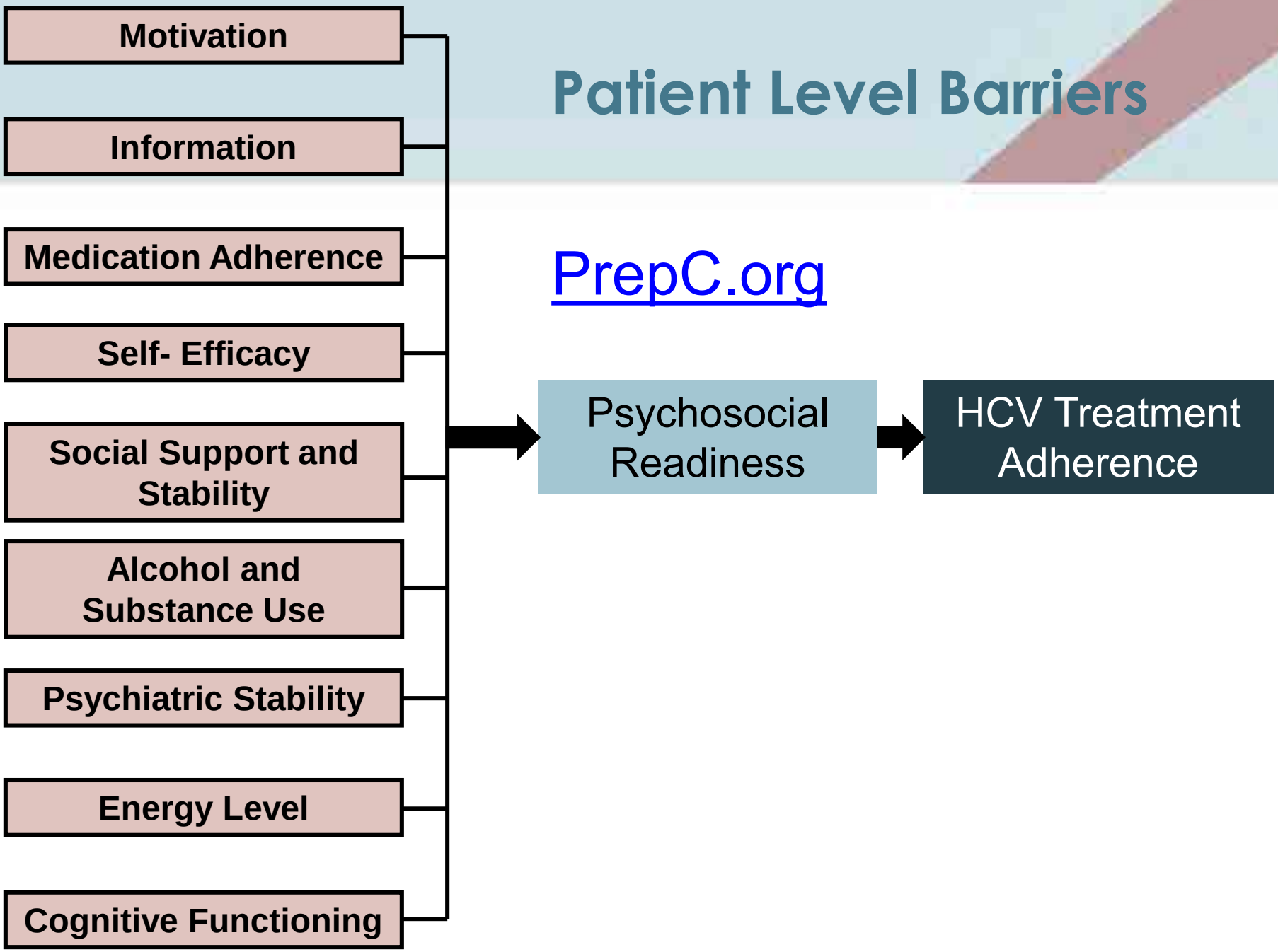
Psychosocial Readiness Evaluation & Preparation for HCV Treatment (PREP-C)

Developed to guide how best to prepare patients to succeed on treatment; not to decide who should go on treatment

Goals of Using PREP-C

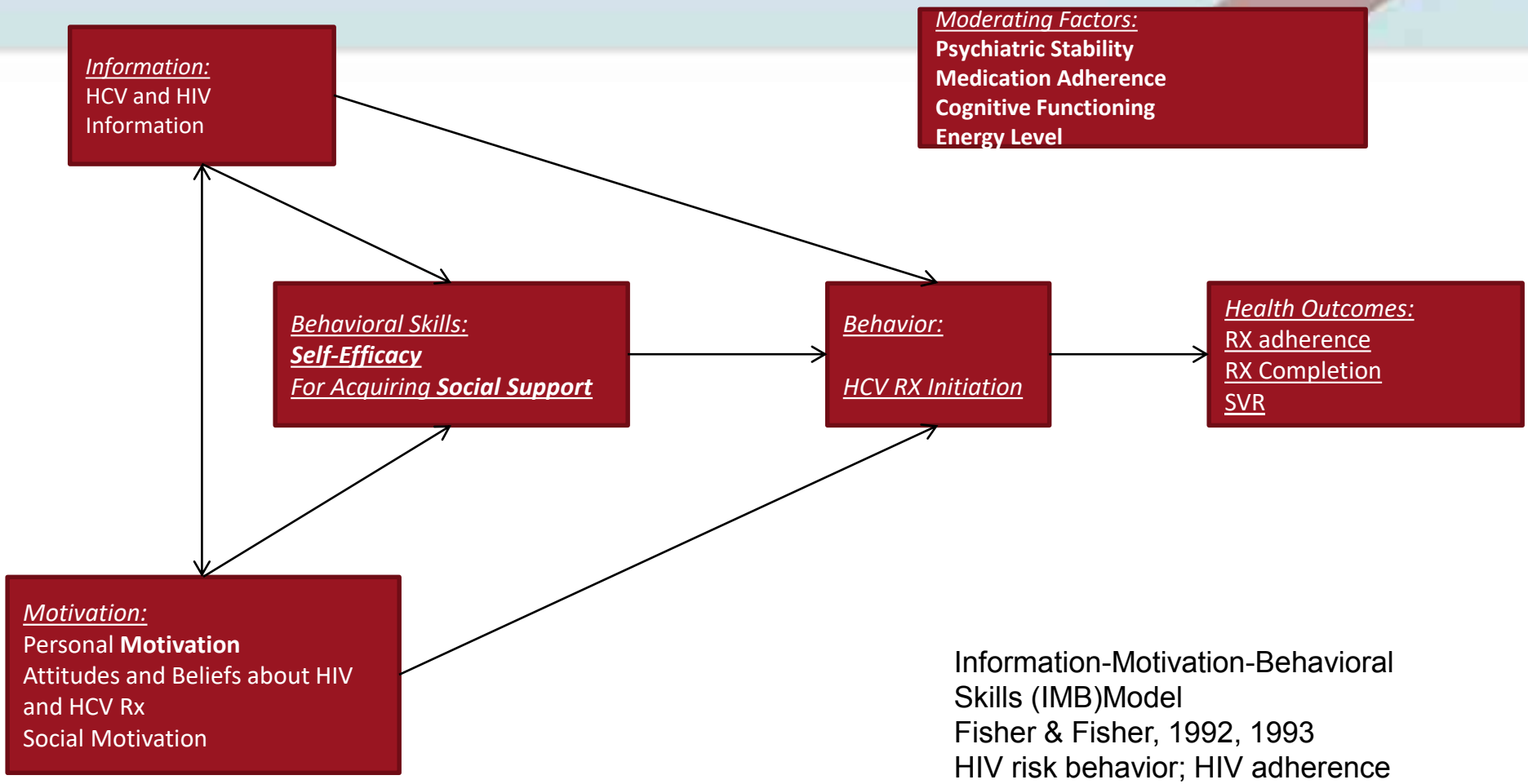
- Identify modifiable areas of psychosocial functioning which are predictive of HCV treatment adherence prior to HCV treatment initiation in order to be able to create a treatment plan to improve functioning in these areas prior to HCV treatment initiation
- Identify non-modifiable areas of psychosocial functioning which are predictive of HCV treatment adherence prior to HCV treatment initiation in order to be able to plan for and take these factors into account during treatment
- Level of support and resources available in treatment setting can be used to inform evaluation of readiness

Patient Level Barriers



Principles Guiding Development of PREP-C Assessment Tool

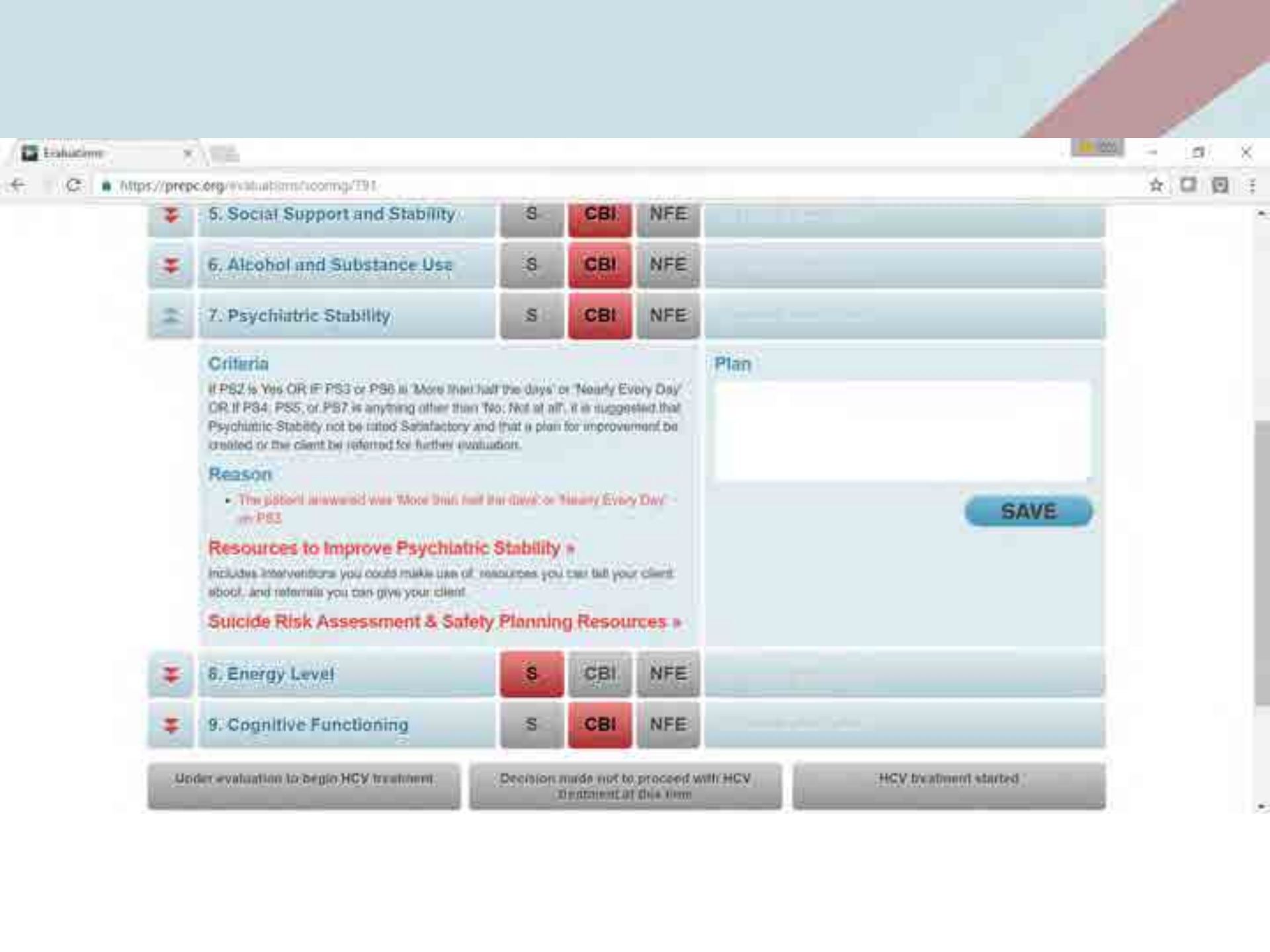
- Suitable to be administered by service providers from diverse disciplines
- Structured interview rather than self-report
- Not to be used to “screen people out” of treatment but to identify areas which can be improved
- Can be used with HCV mono-infected and HIV/HCV co-infected clients
- Provides opportunity for immediate intervention and provision of resources
- Leads to plan for (referral to) further evaluation and treatment
- Can be used in a diverse range of HCV treatment settings



Information-Motivation-Behavioral Skills (IMB)Model
Fisher & Fisher, 1992, 1993
HIV risk behavior; HIV adherence


PREP-C
Psychosocial Readiness Evaluation and Preparation for Hepatitis C Treatment
HOME PORTAL NEWS ABOUT TRAINING RESOURCES CONTACT ACCOUNT LOGOUT ADMIN EDIT
Mount Sinai Hospital
9. Cognitive Functioning (CF1)
CF1 CF2 CF3 CF4 CF5
Q
En el último mes, ¿se le han olvidado cosas que han sucedido recientemente, como dónde puso cosas, citas, etc.?
A
Nunca
Muy pocas veces
Algunas veces
Mas de la mitad de las veces
La mayoría de las veces
Todo el tiempo
Notes


PREP-C - Provider Portal
https://prepc.org/providers
Healthcare Provider Portal
SEARCH
ADD NEW PATIENT
Sorty by: Patient ID
Date Created
Date Last Edited
124
123
122
121
120
M
I
MA
SE
SS
SU
PS
EL
CF
Under evaluation to begin HCV treatment
Training


https://prepc.org/evaluations/scoring/791
5. Social Support and Stability
S
CBI
NFE
6. Alcohol and Substance Use
S
CBI
NFE
7. Psychiatric Stability
S
CBI
NFE
Criteria
If PS2 is Yes OR IF PS3 or PS6 is 'More than half the days' or 'Nearly Every Day' OR If PS4, PS5, or PS7 is anything other than 'No; Not at all', it is suggested that Psychiatric Stability not be rated Satisfactory and that a plan for improvement be created or the client be referred for further evaluation.
Reason
The patient answered was 'More than half the days' or 'Nearly Every Day' on PS3
Resources to Improve Psychiatric Stability »
Includes interventions you could make use of, resources you can tell your client about, and referrals you can give your client
Suicide Risk Assessment & Safety Planning Resources »
Plan
SAVE
8. Energy Level
S
CBI
NFE
9. Cognitive Functioning
S
CBI
NFE
Under evaluation to begin HCV treatment
Decision made not to proceed with HCV treatment at this time
HCV treatment started

Intervention to Improve Hepatitis C (HCV) Treatment Uptake and Adherence in HIV/HCV Co-infection (NIMH R34-MH099930)

Study Aims:

1. To formally adapt existing behavioral medicine interventions based on PREP-C assessment to target individual **patient-level barriers** to HCV treatment initiation in HIV/HCV co-infected patients who are medically eligible for HCV treatment
2. To conduct a pilot randomized clinical trial on HIV/HCV co-infected patients comparing the nurse-administered PREP-C intervention with attention control in order to evaluate patient acceptance, satisfaction, enrollment, retention as well as preliminary efficacy (initiation of HCV treatment within 6 months of randomization and persistence and adherence to the first 12 weeks of treatment in those who did initiate treatment)

Research was supported by the National Institute of Mental Health of the National Institutes of Health R34MH099930
EASL, 2017, Weiss et al.

Barriers to Treatment Initiation – Why have some people still not been treated?

- Patient-level barriers
- Provider-level barriers
- Structural barriers

Barriers to Treatment Initiation

- Patient-level barriers
- **Provider-level barriers**
  - Perceptions about poor adherence, ongoing substance use, relapse to substance use
  - Concern about reinfection with HCV
  - Provider inexperience in treating HCV
- Structural barriers

Barriers to Treatment Initiation

- Patient-level barriers
- Provider-level barriers
- **Structural barriers**
  - Poor access to HCV treatment
  - Lack of collaborative relationships across medical provider disciplines
  - Inadequate insurance coverage for costly HCV treatments
  - Inexperience with or insufficient staff for the prior authorization process

Inclusion/Exclusion Criteria

Inclusion Criteria

1. Co-infection with HIV and HCV
2. Age: 21 years and older
3. Primary language: English or Spanish
4. Two most recent HIV RNA levels are both less than <1000 copies/mL
5. Has attended appointment with HIV primary care provider in previous 6 months
6. Has not attended appointment with HCV provider in last year

Exclusion Criteria

1. Presence of active malignancy (except for squamous or basal cell skin cancers), not otherwise in remission
2. Chronic kidney disease on dialysis
3. Decompensated cirrhosis

Study Overview

Phase I: Intervention Development

- Random assignment to PREP-C intervention or attention control

Phase II: Pilot Randomized Clinical Trial

- Random assignment to PREP-C intervention or attention control

	PREP-C Intervention	Attention Control
1	Administration of web-based PREP-C assessment	Administration of web-based personality interview (SCID-II)
2	Hepatitis C Virus & Liver Education	HIV and Antiretroviral (ARV) Therapy
3	Motivation Interviewing and Behavioral Skills I	HIV Adherence and ARV Resistance
4	Motivation Interviewing and Behavioral Skills II	Psychiatric & Medical Comorbidities

The HIV-Positive Patient Guide to Hepatitis C Treatment

Cindy J. Aaronson, MSW, PhD
Lizeth Cervantes, RN
Theodore Miller, BA
Jeffrey J. Weiss, PhD, MS

Study Flow

- Identify eligible participants
- Consent
- Attend appointment with HCV provider
- Randomize
- Study Baseline Interview
- 4 Nurse Intervention Sessions
- Study Follow-up Interview
- 6 month follow-up/Adherence Phone calls

Baseline demographics – RCT- 11/14 – 5/16

Variable	Total Sample (n=53)	PREP-C (n=28)	AC (n=25)	P-value
Age, years, mean ± SD	54.4 ± 9.2	54.1 ± 8.3	54.7 ± 10.3	0.81
Sex, male, n (%)	38 (71.7)	21 (75.0)	17 (68.0)	0.57
Race/ethnicity, n (%)				0.98
Hispanic, not black	24 (45.3)	13 (46.4)	11 (44.0)	
Black, not Hispanic	22 (41.5)	11 (39.3)	11 (44.0)	
White, not Hispanic	5 (9.4)	3 (10.7)	2 (8.0)	
Black Hispanic	2 (3.8)	1 (3.6)	1 (4.0)	
Primary language, English, n (%)	39 (73.6)	20 (71.4)	19 (76.0)	0.71
Education, years, mean ± SD	11.7 ± 2.4	11.8 ± 2.3	11.6 ± 2.6	0.87
Monthly income, USD, mean ± SD	1034 ± 517	1032 ± 582	1038 ± 445	0.76

Baseline HIV and HCV clinical characteristics

Characteristic	Total Sample (n=53)	PREP-C (n=28)	AC (n=25)	P-value
CD4+ count, cells/µL, mean ± SD	**660 ± 340**	**762 ± 358**	**545 ± 283**	**0.031**
CD4+ count, <500 cells/µL, n (%)	22 (41.5)	10 (35.7)	12 (48.0)	0.37
HIV-1 viral load, copies/mL, n (%)				0.66
<20	48 (90.6)	26 (92.9)	22 (88.0)	
20-450	5 (9.4)	2 (7.1)	3 (12.0)	
AIDS diagnosis, n (%)				0.15
Yes	35 (66.0)	16 (57.1)	19 (76.0)	
No	18 (34.0)	12 (42.9)	6 (24.0)	
HCV genotype, n (%)				0.82
1a/1b	46 (86.8)	24 (85.7)	22 (88.0)	
2b	4 (7.5)	2 (7.1)	2 (8.0)	
3	1 (1.9)	1 (3.6)	0 (0.0)	
4	2 (3.8)	1 (3.6)	1 (4.0)	
Fibrosis-4 score (FIB-4), n (%)				0.84
<1.45	17 (32.1)	10 (35.7)	7 (28.0)	
1.45-3.25	26 (49.1)	13 (46.4)	13 (52.0)	
>3.25	10 (18.9)	5 (17.9)	5 (20.0)	
HCV Treatment, n (%)				0.10
Naïve	39 (74.0)	18 (64.0)	21 (84.0)	
Experienced	14 (26.0)	10 (36.0)	4 (16.0)	

Baseline Neuropsychiatric profile

Characteristic	Total Sample (n=53)	PREP-C (n=28)	AC (n=25)	P-value
Depression score (BDI-II), mean ± SD	16.4 ± 12.8	18.3 ± 14.1	14.2 ± 11.1	0.30
Fatigue score (FSS), mean ± SD	37.2 ± 16.5	39.0 ± 16.8	35.1 ± 16.2	0.41
Executive Functioning, T-score, mean ± SD	42.0 ± 6.7 *[n=45]*	40.5 ± 7.0 *[n=25]*	43.8 ± 6.0 *[n=20]*	0.10
Speed of Information Processing, T-score, mean ± SD	42.6 ± 9.5 *[n=50]*	40.7 ± 10.4 *[n=27]*	44.8 ± 8.1 [n=23]	0.13
Psychiatric Disorder – Lifetime Diagnosis, n (%)	39 (73.6)	19 (67.9)	20 (80.0)	0.32
Substance Use Disorder – Lifetime Diagnosis, n (%)	45 (84.9)	24 (85.7)	21 (84.0)	1.00
History of IVDU, n (%)	30 (56.6)	18 (64.3)	12 (48.0)	0.23

Intervention Session Attendance

Intervention Session Attendance (max=4)	PREP-C (n=28)	AC (n=25)	P-value
Sessions attended, n (%)			0.38
All 4 sessions	21 (75.0)	16 (64.0)	
<4 sessions	7 (25.0)	9 (36.0)	

Intervention Session Satisfaction

Satisfaction	PREP-C (n=28)	AC (n=25)	P-value
12 item self-report (range12-60)	58.0 (3.8)	53.4 (5.9)	0.04

Nurse Fidelity Ratings

Nurse Fidelity	PREP-C (n=28)	AC (n=25)	P-value
Audio Recorded Sessions (0-100%)	93.2 (0.06)	87.8(0.88)	0.13

Primary Outcome: HCV Treatment Initiation in 6 months

19/21 Sof/Led; 1 Sof/Dac; 1 Sof/Vel

Primary Outcome	Total Sample (n=53)	PREP-C (n=28)	AC (n=25)	P-value
HCV treatment initiation ≤6 months post-randomization, n (%)				**0.028**
Yes	**21 (39.6)**	**15 (53.6)**	**6 (24.0)**	
No	**32 (60.4)**	**13 (46.4)**	**19 (76.0)**	

AOR 4.40, 95% CI [1.17-16.60]

All 21 subjects who initiated HCV treatment achieved SVR

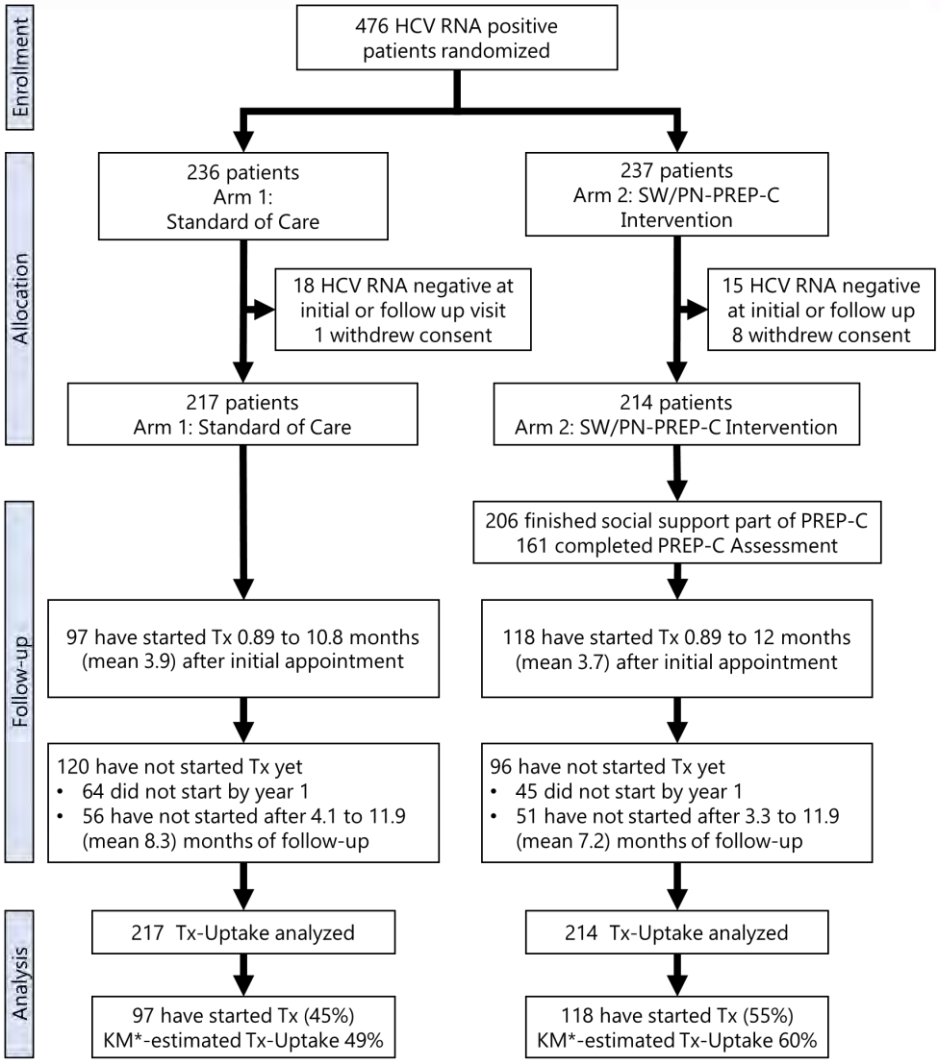
Community Access, Retention in care and Engagement for hepatitis C (CARE-C)

- University of Kentucky Hepatology Clinic
- Funded by Gilead Sciences (PI: Jens Rosenau, MD)

- Patients were **randomized 1:1** at the first clinic visit to either a **standard of care arm** (HCV management by an interdisciplinary care team with specialty provider (advanced practice provider or hepatologist), specialty pharmacist, nurse case manager with access to addiction specialists) or an **intervention arm** (SW/PN-PREP-C added to standard of care). The **primary endpoint is HCV treatment uptake** within one year after initial visit.

AASLD, 2020, Hooman et al.

Study flow diagram (8/18-12/19)



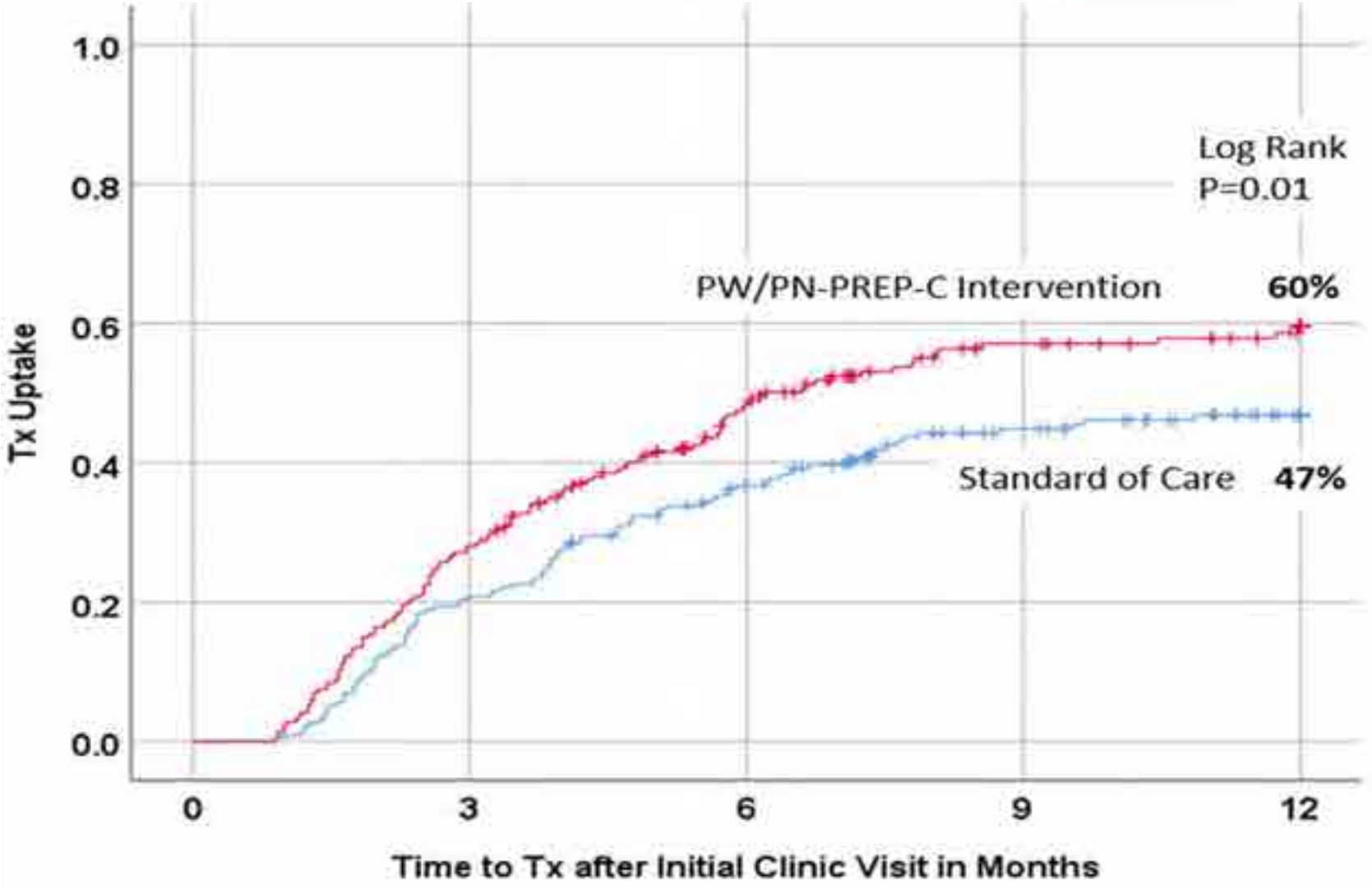
Baseline characteristics (n=431)

		Total n=431	Standard of Care n=217	SW-PN-PREP-C-Intervention n=214	P
Age	Mean	40.9 (±12.2)	41.1 (±12.0)	40.6 (±12.4)	
	Median	38 (32-50)	38 (32-50)	38 (31-50)	
Age Group	<30	75 (17.4)	31 (14.3)	44 (20.6)	0.51
	30 to <40	159 (36.9)	85 (39.2)	74 (34.6)	
	40 to <50	89 (20.7)	47 (21.7)	42 (19.6)	
	50 to <60	67 (15.6)	34 (15.7)	33 (15.4)	
	>=60	41 (9.5)	20 (9.2)	21 (9.8)	
Gender	Male	247 (57.3)	125 (57.6)	122 (57.0)	0.90
	Female	184 (42.7)	92 (42.4)	92 (43.0)	
Race	White	400 (92.8)	200 (92.2)	200 (93.5)	0.82
	Black	26 (6.0)	15 (6.9)	11 (5.1)	
	Hispanic	2 (0.5)	1 (0.5)	1 (0.5)	
	Others	3 (0.7)	1 (0.5)	2 (0.9)	
BMI (overall)	Mean	28.0 (±6.1)	28.1 (±6.5)	27.9 (±5.7)	
	Median	27 (24-31)	27 (24-31)	27 (24-31)	
Rural/Urban	Urban	310 (72.3)	160 (74.1)	150 (70.4)	0.40
	Rural	119 (27.7)	56 (25.9)	63 (29.6)	
Appalachian	No	254 (58.9)	129 (59.5)	125 (58.4)	0.83
	Yes	177 (41.1)	88 (40.6)	89 (41.6)	
Insurance	Medicaid	326 (75.8)	164 (75.6)	162 (76.1)	0.90
	Medicare	41 (9.5)	21 (9.7)	20 (9.4)	
	Commercial	53 (12.3)	28 (12.9)	25 (11.7)	
	Others	10 (2.3)	4 (1.8)	6 (2.8)	
Genotype	1	256 (63.7)	131 (63.9)	125 (63.5)	0.15
	2	39 (9.7)	14 (6.8)	25 (12.7)	
	3	100 (24.9)	55 (26.8)	45 (22.8)	
	Others	7 (1.7)	5 (2.4)	2 (1.0)	
Cirrhosis	No	356 (83.6)	175 (82.2)	181 (85.0)	0.43
	Yes	70 (16.4)	38 (17.8)	32 (15.0)	
Treatment Experience	No	418 (97.2)	209 (96.3)	209 (98.1)	0.25
	Yes	12 (2.8)	8 (3.7)	4 (1.9)	
Drug History	Recent	126 (29.7)	47 (22.0)	79 (37.4)	**0.002**
	Remote	236 (55.5)	134 (62.6)	102 (48.3)	
	unspecified	25 (5.9)	10 (4.7)	15 (7.1)	
	Never	38 (8.9)	23 (10.8)	15 (7.1)	
Heavy Alcohol History	Recent	56 (13.1)	16 (7.5)	40 (18.7)	**0.003**
	Remote	101 (23.6)	51 (23.8)	50 (23.4)	
	unspecified	36 (8.4)	16 (7.5)	20 (9.4)	
	Never	235 (54.9)	131 (61.2)	104 (48.6)	

Predictors of HCV treatment initiation

OVERALL		Total Tx Starts	Univariate		Multivariate	
			OR (95% CI)	P-value	OR (95% CI)	P-value
Age	Per year		1.012 (0.996-1.028)	0.14		
Gender	Male	118 (47.8)	1			
	Female	97 (52.7)	1.22 (0.83-1.79)	0.31		
Race	White	197 (49.3)	1			
	Black	17 (65.4)	1.95 (0.85-4.47)	0.12		
	Hispanic					
	Others					
BMI	Per unit		0.997 (0.967-1.029)	0.87		
Rural/Urban	Urban	153 (49.4)	1			
	Rural	61 (51.3)	1.08 (0.71-1.65)	0.72		
Appalachian	No	125 (49.2)	1			
	Yes	90 (50.8)	1.07 (0.73-1.57)	0.74		
Insurance	Medicaid	159 (48.8)	1			
	Medicare	19 (46.3)	0.91 (0.47-1.74)	0.77		
	Commercial	34 (64.2)	1.88 (1.03-3.43)	0.04		
	Others	3 (30.0)	0.45 (0.11-1.77)	0.25		
Genotype	1	139 (54.3)	1		1	
	2	29 (74.4)	2.44 (1.14-5.22)	0.02	2.55 (1.13-5.75)	0.02
	3	42 (42.0)	0.61 (0.38-0.97)	0.04	0.60 (0.37-0.98)	0.04
	others	5 (71.4)	2.10 (0.40-11.05)	0.38		
Cirrhosis	No	181 (50.8)	1			
	Yes	34 (48.6)	1.10 (0.66-1.83)	0.73		
Treatment Experience	Naive	209 (50.0	1			
	Experienced	6 (50.0)	1.0 (0.32-3.15)	1.0		
Drug History	Recent	52 (41.3)	1		1	
	Unspecified	6 (24.0)	0.45 (0.17-1.20)	0.11		
	Remote	135 (57.2)	1.90 (1.23-2.95)	0.004	1.96 (1.25-3.08)	0.004
	Never	18 (47.4)	1.28 (0.62-2.65)	0.51		
Heavy Alcohol History	Recent	26 (46.4)	1		1	
	Unspecified	8 (22.2)	0.33 (0.13-0.85)	0.02		
	Remote	57 (56.4)	1.49 (0.78-2.88)	0.23	2.02 (1.19-3.43)	0.009
	Never	122 (51.9)	1.25 (0.69-2.23)	0.46		
Care Model	1	97 (45.0)	1			
	2	118 (55.0)	1.52 (1.04-2.22)	0.03	2.00 (1.29-3.09)	0.002

Kaplan Meier estimates of HCV treatment uptake



Summary

- Persons with psychiatric and/or substance use disorders can be effectively treated for HCV
- Assessed appropriately, information about the patient's substance use behavior can be used to optimize the patient's chances of achieving SVR
- Tailored educational and behavioral interventions based on the PREP-C can increase rates of HCV treatment initiation in diverse groups of persons with HCV

Next Steps

- Piloting PREP-C assessment in HCV treatment program at syringe exchange program
- Piloting PREP-C as part of telemedicine protocol to treat persons for HCV while in residential substance use treatment program
- PREP-C part of NIH KeY Treat HCV Elimination study among PWID in rural Kentucky
- Factor analysis to create brief PREP-C assessment

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