Psychosocial Readiness Evaluation and Preparation for hepatitis C treatment: PREP-C

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Hepatitis C disproportionately impacts marginalized groups

Rates of infection:

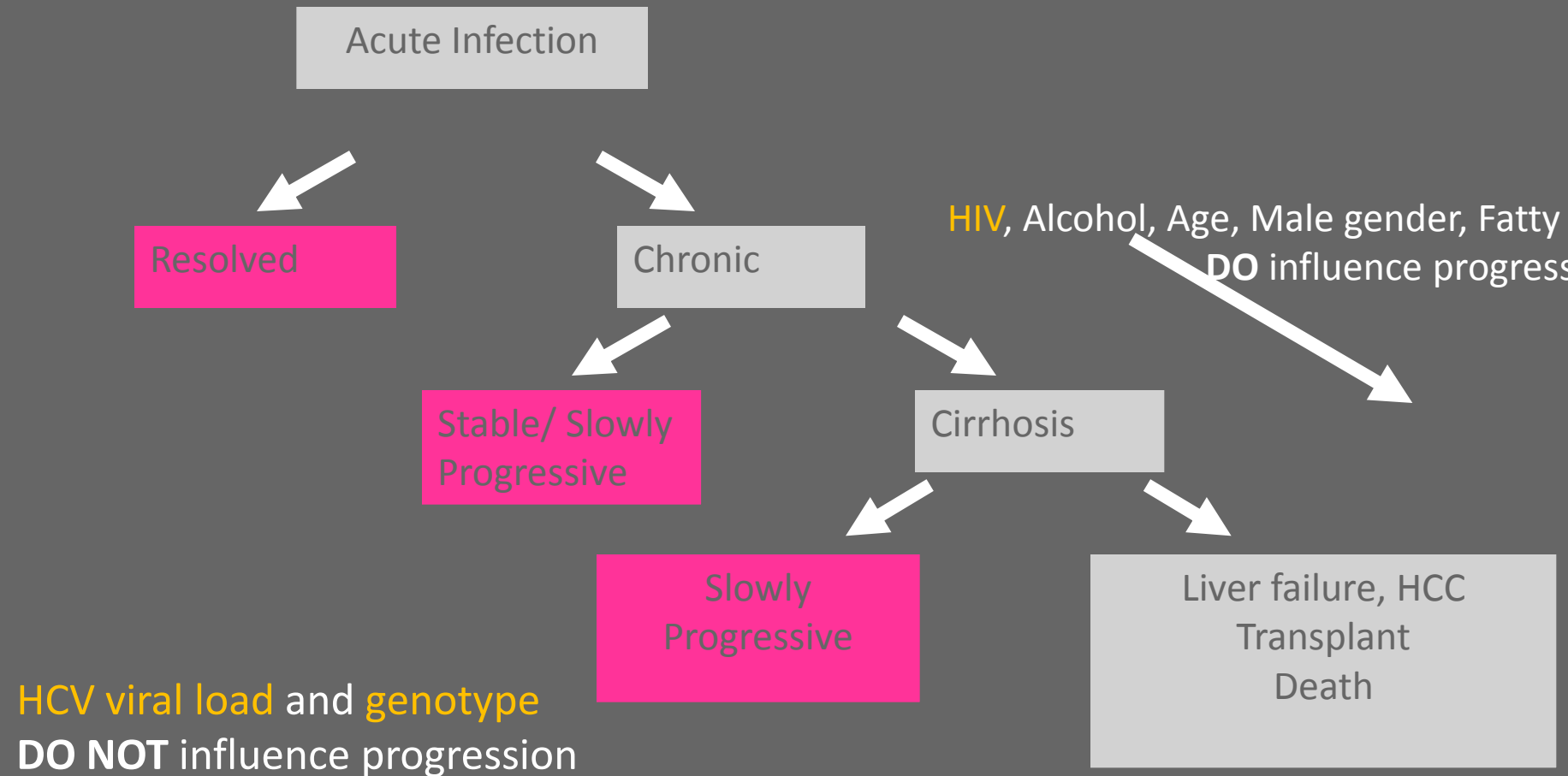
- IDU > 10 years of use 90%
- IDU < 10 years of use 50%
- Homeless persons 35%
- HIV-positive 25-30%
- Prisoners 29%
- Severely mentally ill 19%
- US population 2%

Chak et al. Liver Int. 2011

‘Stigma is the process by which the reaction of others spoils normal identity'.

E. Goffman, STIGMA: Notes on the Management of Spoiled Identity 1963

Natural History of HCV Infection



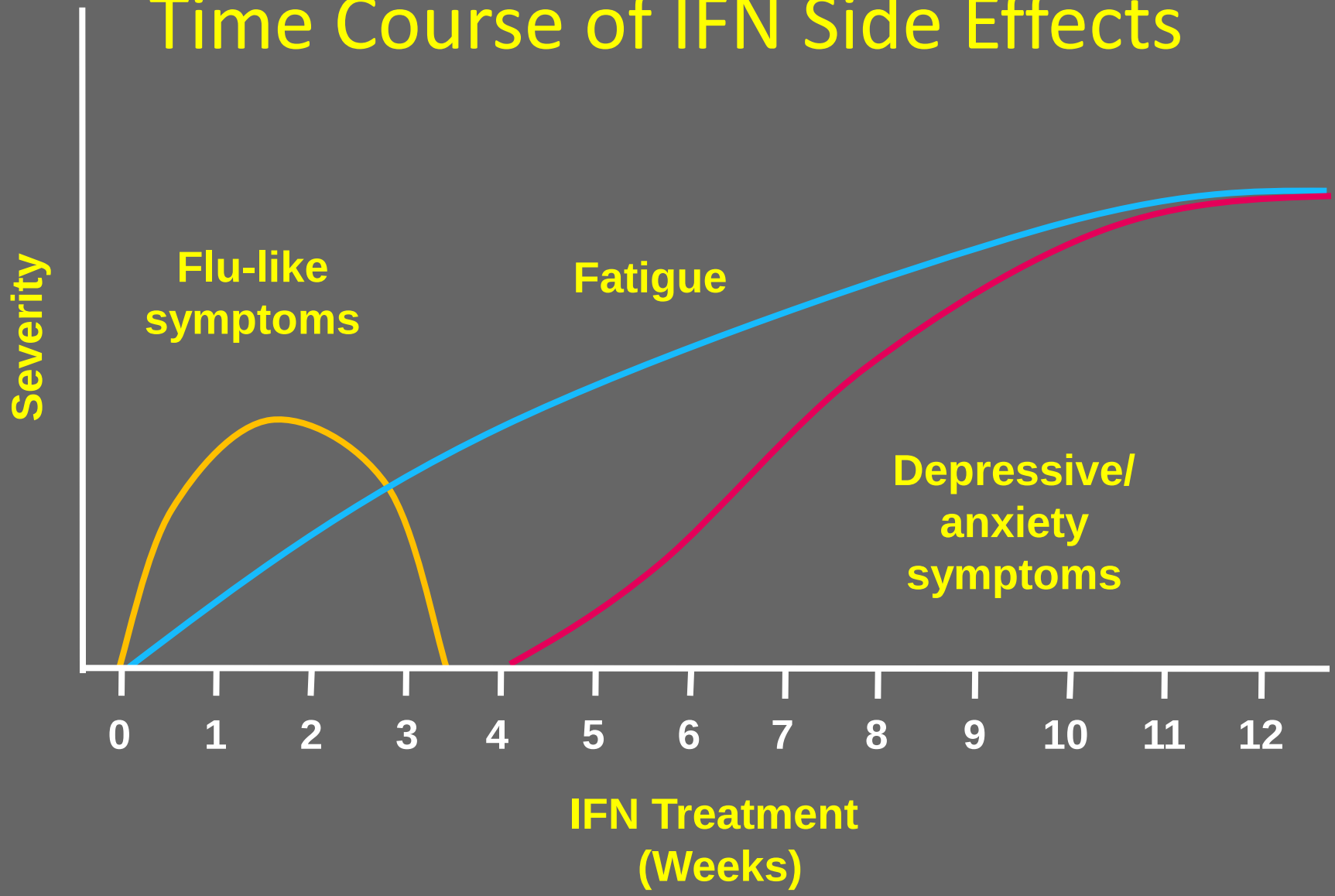
Neuro-psychiatric Context

There are higher rates of psychiatric and substance use disorders and cognitive impairment (risk factors for non-adherence) in persons with chronic HCV infection than in the general population.

HCV treatment causes neuro-psychiatric symptoms (depression, anxiety, emotional lability, irritability, insomnia) in a high percentage of treated patients.

HCV treatment side effects often result in early treatment discontinuation which reduces rates of cure.

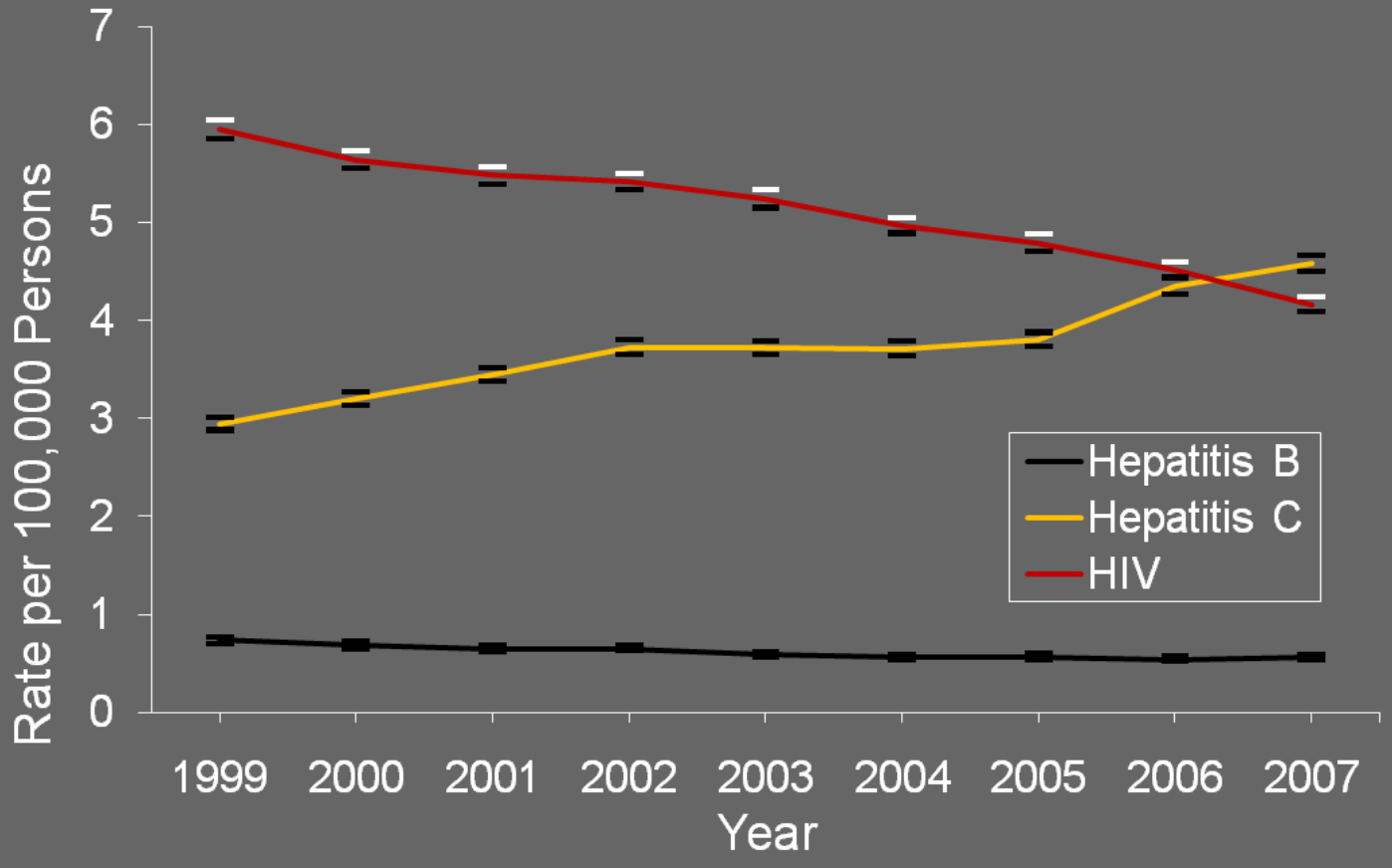
Time Course of IFN Side Effects



Boceprevir Adverse Event Data Presented to FDA Pooled Phase 2 and Phase 3 trials

Adverse Events	Boceprevir-containing Arm N=1548	P-R Control Arm N=547
Neuro-psychiatric AEs:		
Suicidal Ideation	1 %	< 1 %
Homicidal ideation	< 1%	0 %
Anxiety	19%	15%
Depression	29%	26%
Insomnia	48%	41%
Most common AEs:		
Fatigue	57%	57%
Anemia	49%	29%
Nausea	45%	40%
Headache	44%	43%

Age-Adjusted Rates of Mortality Associated with Hepatitis B, Hepatitis C, and HIV United States, 1999 – 2007



Ly et al. Annals of Int Med 2012

HIV/HCV-co-infection

- HIV/HCV-co-infected patients have twice the risk of developing cirrhosis and a six-fold increased risk of liver failure compared to those with HCV alone
- *Graham et al. Clin Infect Dis 2001; Vachon & Dieterich Clin Liver Dis 2011; Thein et al. AIDS 2008)*

- End-stage liver disease is now a leading cause of mortality in HIV-infected persons as a result of high rates of untreated chronic HCV-co-infection
- *Bica et al. Clin Inf Dis 2001, Rosenthal et al. J Viral Hep 2007, Weber et al. Arch Int Med 2006, Salmon-Ceron et al. J Hep 2009, Branch et al. Clin Inf Dis 2012*

- HCV can be cured and the effectiveness of HCV treatment has dramatically increased with the DAAs: SVR12 45% vs. 74% with telaprevir *Dieterich et al. CROI 2012*

HIV/HCV-co-infection

- The uptake of HCV treatment in HIV/HCV-co-infected patients remains unacceptably low - estimated at 10%
  Mehta et al. AIDS 2005, Mehta et al. AIDS 2006, Butt et al. Alim Pharm Ther 2006, Osilla et al. AIDS Pat Care & STDs 2011

- Progress in developing effective behavioral interventions to successfully engage and retain HIV-co-infected patients in HCV care has not kept pace with the rapid pharmacologic advances made in HCV treatment

- There are multiple barriers to HCV treatment initiation at patient, provider, and structural levels

Patient level barriers to HCV treatment initiation in HIV/HCV-co-infected patients

- Adequate knowledge about HCV disease course, HCV treatment, and relationship to HIV infection

  Fleming et al. Clin Inf Dis 2005, McLaren et al Can J Gastro 2008

- Low motivation for HCV treatment

  Mehta et al. AIDS 2005, Wagner et al. AIDS Pat Care STDs 2009, Osilla et al. AIDS Pat Care STDs 2009

- Negative and/or incorrect attitudes and beliefs regarding HCV infection and treatment

  Osilla et al. AIDS Pat Care STDS 2011, Salmon-Ceron et al. BMC Health Serv Res 2012

- Low perceived self-efficacy to tolerate HCV treatment side effects and obtain adequate support during treatment

  Bova et al. J Assoc Nurses AIDS Care 2010, Ogawa & Bova, Subst Use Misuse 2009

Provider Barriers: Low Rates of Referral/Treatment of HCV

Providers are hesitant to refer and treat HCV in patients for many reasons:

- Current/History of depression/psychiatric illness
- Current/History of Substance use problems
- Cognitive impairment
- Suspected poor adherence
- High burden of treatment side effects
- Perceived low likelihood of treatment success

Structural Barriers

- Poor access to HCV testing (49% tested for HCV in Miami cohort of 15,000 HIV+ patients in care, *Deeb et al. CROI 2012*).
- Provider inexperience in treating HCV
- Lack of collaborative relationships across disciplines (HIV primary care provider, liver specialist, psychiatrist/psychologist)
- Inadequate insurance coverage for HCV treatment

Wagner & Ryan, AIDS, 2005; Wagner et al. AIDS Patient Care STDs 2009

Differences between HCV and HIV: Implications for Intervention

- Goal of HCV treatment is cure; whereas cure is not (yet) possible in HIV
- HCV treatment is time-limited; whereas HIV treatment is life-long
- If patient is adherent, HIV treatment works *whereas* this is not necessarily the case with HCV treatment
- HCV treatment is not accompanied by a 'Lazarus effect'; to the contrary

Cost of HCV medication alone

- 48 weeks PEG-IFN + RBV = $30,000
- 12 weeks telaprevir = $49,200 (12 wk course) OR
- 48 weeks boceprevir = $48,400 (28-48 wk course)
- Total Medication Cost = $80,000

- Cost-effectiveness of behavioral interventions to promote treatment readiness and adherence
  Garcia-Retortillo et al., AASLD 2011, Poster 938

Continuum of Care for Persons Chronically infected with HCV

- Awareness of HCV infection
- Linkage to and engagement in HCV Care
- Preparation for HCV Treatment
- HCV Treatment (Adherence)

Prevalence and Patient Awareness of Medical Comorbidities in an Urban AIDS Clinic

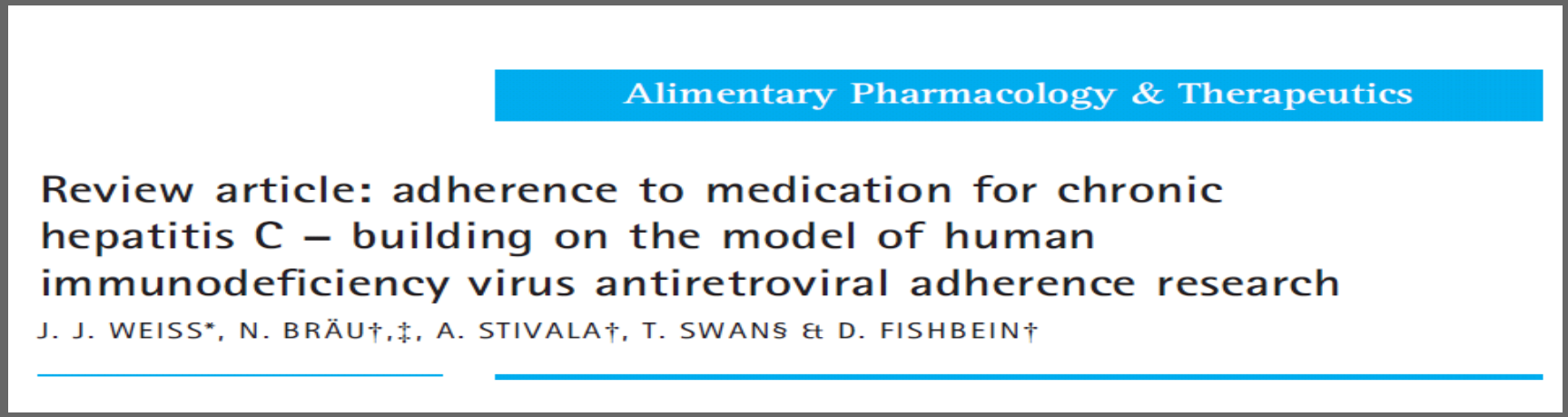
- All patients attending the Mount Sinai HIV outpatient clinic during the summer of 2005 were invited to participate.
- 200 subjects were recruited and asked whether they had each of 15 medical conditions and if so, whether they were getting treated and taking medication for it.
- Demographic information and permission to access medical records were obtained.
- Subsequently, their medical charts were independently reviewed by a physician to determine concordance between patient self-report and chart documentation.

Weiss et al. (2010) AIDS Patient Care & STDs, 24, 39-48

HIV+ Patients Awareness of chronic HCV infection

- 102/200 (51%) of HIV+ patients in HIV care chronically infected with HCV – chart documentation
- 68/102 (67%) were aware of HCV infection
- 19/102 said they were not infected
- 15/102 said they did not know

1/3 of HIV+ patients in HIV care with chronic HCV infection could not correctly report this



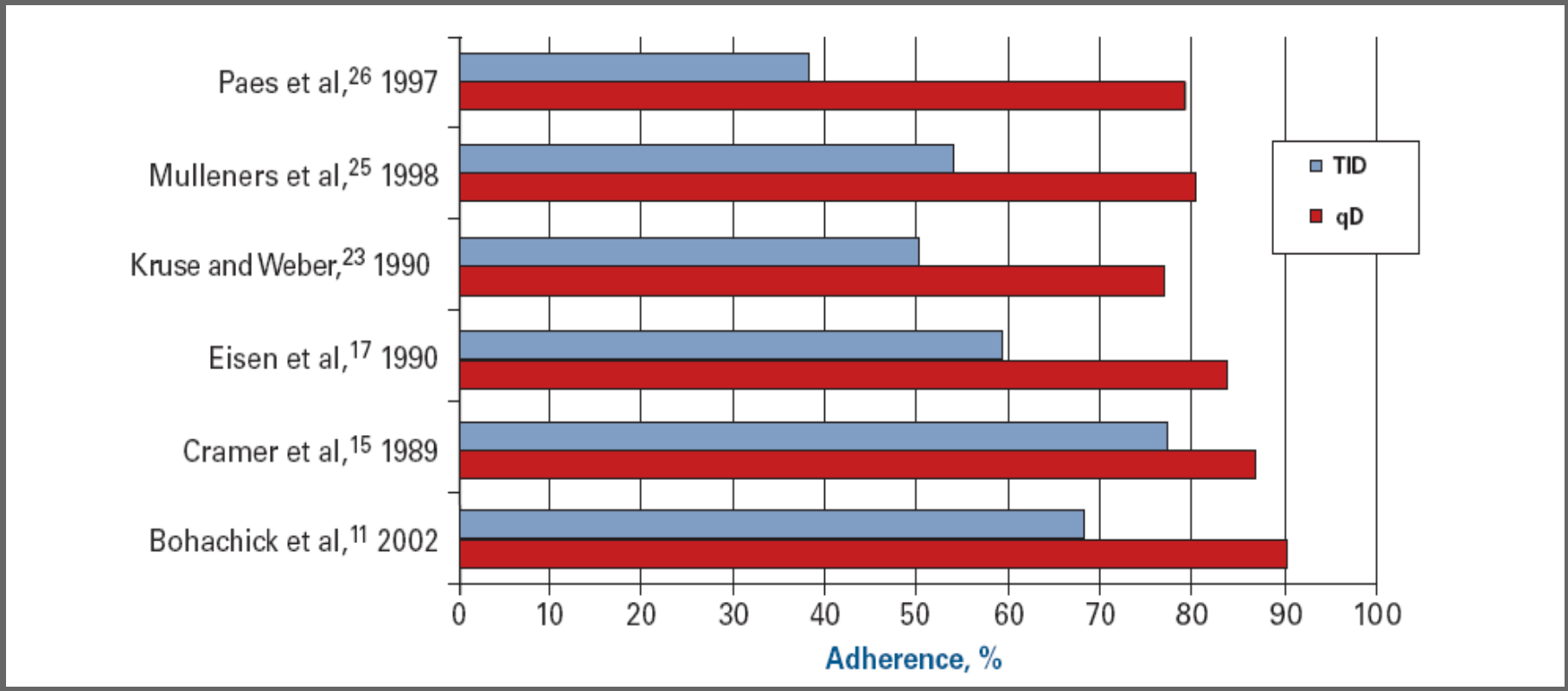
HCV medication adherence is even more critical in the DAA era:

- Risk of development of resistance
- Increased regimen complexity (pill burden, dosing frequency, dietary requirement)
- Increased side effects

- HCV Adherence - Definitional Confusion

Adherence decreases as dosing frequency increases

Systematic Review 1986-2007 – 20 studies
Prospective design, Chronic Disease, MEMS adherence assessment



Saini et al. (2009) Effect of Medication Dosing Frequency on Adherence in Chronic Diseases. Am J Man Care, 15, E22-E33.

Dose and Dose Interval Adherence to TID regimens Assessed With MEMS

Condition	Number of Participants on TID Regimen	Dose Adherence (Mean ± SD)	Dose Interval Adherence (Mean ± SD)
HIV	59	85.7%*	45%*
Heart disease	68	66 ± 29%	46 ± 31%
Epilepsy	36	80 ± 18%	40 ± 19%
Diabetes	15	65.8 ± 30.1%	5.3 ± 5.3%
Heart failure	26	88.9 ± 13.9%	52.6 ± 27.7%

*Only median available

Weiss J, et al. J Hepatol 2012

Lower SVR Rates were observed in RESPOND-2 previous treatment failure patients who adhered to the dosing interval < 60% of the time

Table 4. SVR by adherence of BOC to TID 7-9-hour dosing interval†

a. All patients in previously untreated (SPRINT-2) and previous-treatment-failure (RESPOND-2) patients

Adherence, %	SVR, n/N (%)		
	BOC RGT	BOC/PR48	Combined BOC arms
SPRINT-2	**n=368**	**n=366**	**n=734**
<60	45/73 (61.6)	39/58 (67.2)	84/131 (64.1)
60 to <70	22/31 (71.0)	25/30 (83.3)	47/61 (77.0)
70 to <80	26/41 (63.4)	23/30 (76.7)	49/71 (69.0)
≥80	77/103 (74.8)	73/115 (63.5)	150/218 (68.8)
RESPOND-2	**n=162**	**n=161**	**n=323**
<60	12/25 (48.0)	15/30 (50.0)	27/55 (49.1)
60 to <70	13/20 (65.0)	10/13 (76.9)	23/33 (69.7)
70 to <80	2/20 (60.0)	13/18 (72.2)	25/38 (65.8)
≥80	43/62 (69.4)	47/66 (71.2)	90/128 (70.3)

Gordon et al. 2011. EASL Poster: Adherence To Assigned Dosing Regimen and Sustained Virologic Response Among Hepatitis C-Genotype 1 Previously Untreated and Peginterferon/Ribavirin Treatment-Failure Patients Treated With Boceprevir Plus Peginterferon Alfa-2b/Ribavirin

New concepts introduced to HCV treatment with DAAs

- No dose reductions with DAAs
- TID (every 7-9 hours) with food
- Increased pill burden
- DDIs with ARVs and other medications
- Risk of resistance
- Increased side effects
- Increased focus on virologic response
- Increased rate of cure

The Decision to Treat HCV

- Age
- Stage of liver disease
- HCV genotype, IL28B gene
- Prior response to treatment (side effects, adherence, and virologic outcome)
- Control of other co-morbid illnesses
- Psychosocial readiness

Parallel Work-ups

- Medical work-up for Hepatitis C treatment is usually a lengthy process that involves assessment, referral for further evaluation, and intervention to improve medical condition prior to HCV treatment initiation.
- A psychosocial work-up should occur in parallel to the medical work-up being conducted.
- Identifying psychosocial factors that could potentially interfere with treatment adherence prior to treatment initiation can result in delivery of interventions to improve these areas of functioning prior to treatment.
- The parallel psychosocial work-up also provides support for patients to complete the medical work-up.

Research from HCV mono-infection

- Providing treatment for psychiatric and substance use disorders increases rates of HCV treatment initiation
- *Knott et al. Am J Gastro 2006, Evon et al. 2011*

- Patients who are receiving treatment for mental health and substance use disorders do as well on treatment as those without these disorders when adequate treatment and support is provided
- *Bruggmann et al. J Viral Hep 2008, Robaeys et al. Eur J Gastro Hep 2006, Grebely et al. Int J Drug Pol 2007, Schaefer et al. Hep 2007, Jakiche et al. Am J Gastro 2007*

Several studies find that IDUs (including active users) can do 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).

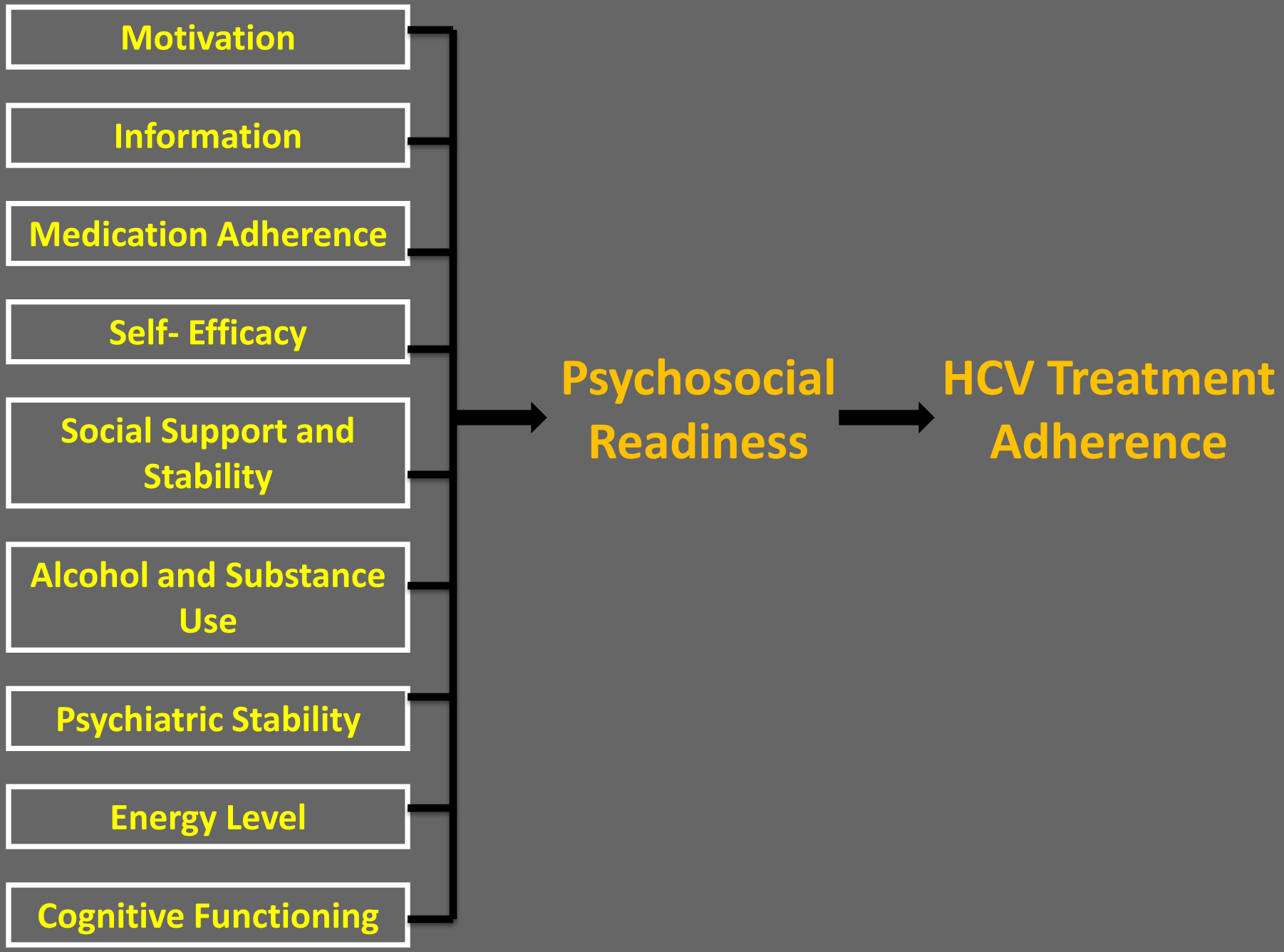
Robaeys et al. (2006) Eur J Gastroenterol Hepatol (Benelux)
Bruggmann et al. (2008) J Viral Hepatitis (Switzerland)
Grebely et al. (2010) Eur J Gastroenterol Hepatol (Vancouver)

PREP-C

- Psychosocial Readiness Evaluation and Preparation for hepatitis C treatment (PREP-C) is a clinical interview that healthcare providers from diverse disciplines can be trained to administer
- It provides an assessment of a patient's psychosocial readiness to begin HCV treatment and identifies domains of functioning which require intervention to improve treatment readiness

PREP-C

- Background
  - Developed in response to lack of guidelines and screening tools to meet clinicians' needs for assessing patient's preparedness to begin chronic HCV therapy
- Description
  - Clinical interview (30 – 45 minutes)
  - Assessment of 9 areas of psychosocial functioning
- Implementation
  - Used over last 2 years to evaluate chronic HCV patients
  - Continually revised over this period


Motivation
Information
Medication Adherence
Self- Efficacy
Social Support and Stability
Alcohol and Substance Use
Psychiatric Stability
Energy Level
Cognitive Functioning
Psychosocial Readiness
HCV Treatment Adherence

PREP-C

Psychosocial Readiness Evaluation and Preparation for hepatitis C treatment

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- Psychosocial
- Readiness
- Evaluation and
- Preparation for hepatitis
- C treatment

WELCOME

A brief, friendly introduction to what PREP-C is. As this is for the general public, we don't want to be too technical here. Brevi vel toto est iunior anno. Utor permisso, caudaeque pilos ut equinae paulatim vello unum, demo etiam unum. Si meliora dies, ut vina, poemata reddit, scire velim, chartis perficit quotus pretium quotus arroget annus. Scriptor abhinc eddit misso annos centum qui decidit, inter perfectos veteresque referri debet an inter vilis atque perfectos novos? Excludat iurgia finis. "Est etus atque probus, centum qui perficit annos." Quid, qui deperiitnihis perfectos uno mense vel anno?

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PREP-C Pilot Data

PREP-C was administered to 50 patients in 2011 being evaluated for HCV treatment at primary-care based liver clinic and HIV Clinic.

The patients were 50% male; 46% Hispanic, 42% black, 12% white; 30% HIV-co-infected.

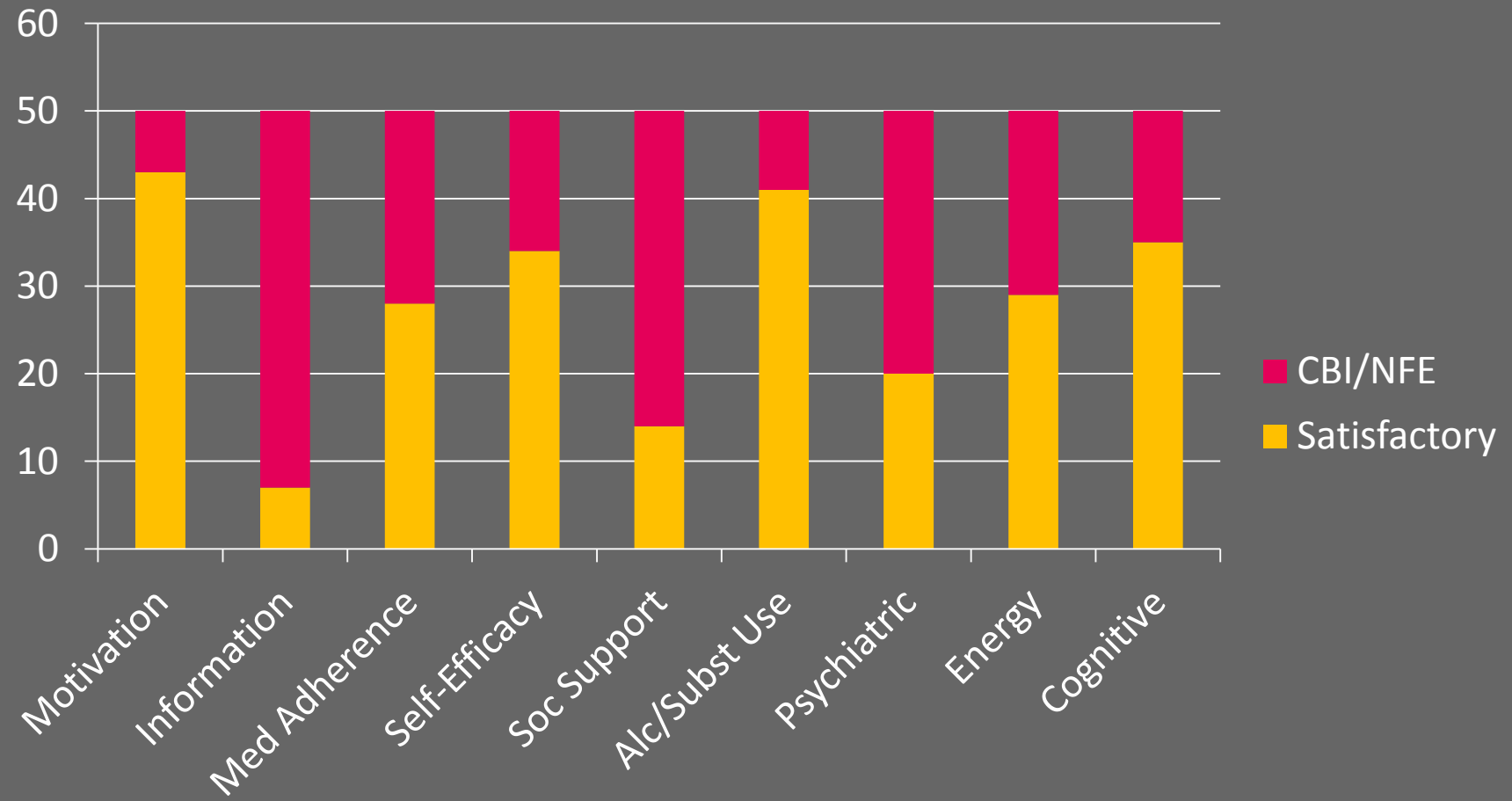
A clinically derived scoring algorithm was used to rate the completed interviews on each of the 9 domains.

The median number of domains on which patients received a rating of 'Satisfactory' is 5 (range = 1-8).

The number of domains rated 'Satisfactory' did not differ by sex, race/ethnicity, or by HIV-co-infection status.

Weiss et al. Poster 79354 presented at Second International Conference on Viral Hepatitis New York, March 2012

PREP-C Category Scores (n=50)



21/50 patients (42%) began HCV treatment within 6 months of PREP-C

Variable	% Beginning HCV Treatment in 6 months	P value – Fisher's Exact Test
Male	44%	
Female	40%	1.0
HIV-positive	40%	
HIV-negative	43%	1.0
Black	38%	
Hispanic	43%	
White	50%	0.86

21/50 patients (42%) began HCV treatment within 6 months of PREP-C

Variable	% Beginning HCV Treatment in 6 months	P value – Fisher's Exact Test
Motivation - Satisfactory	47%	
Motivation - CBI/NFE	14%	0.22
Information - Satisfactory	71%	
Information – CBI/NFE	37%	0.12
Med Adh - Satisfactory	50%	
Med Adh – CBI/NFE	32%	0.25
Self-efficacy - Satisfactory	53%	
Self-efficacy – CBI/NFE	19%	0.03
Soc Support - Satisfactory	36%	
Soc Support – CBI/NFE	44%	0.75

21/50 patients (42%) began HCV treatment within 6 months of PREP-C

Variable	% Beginning HCV Treatment in 6 months	P value – Fisher's Exact Test
Alcohol and Substance Use - Satisfactory	41%	
Alcohol and Substance Use - CBI/NFE	44%	1.0
Psychiatric - Satisfactory	30%	
Psychiatric – CBI/NFE	50%	0.24
Energy - Satisfactory	41%	
Energy – CBI/NFE	43%	1.0
Cognitive - Satisfactory	46%	
Cognitive – CBI/NFE	33%	0.54

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 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

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- Sue Marcus, PhD
- Alicia Stivala, NP

www.PrepC.org

July 28, 2012 - World Hepatitis Day

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PREP-C

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