HCV TREATMENT ELIGIBILITY

Jesse Powell PA-C
Director, Community Collaboration on Viral Hepatitis ECHO
Director, Gastroenterology and Liver clinic
Hennepin Healthcare

AASLD guidelines

Goal of Treatment	
RECOMMENDED	RATING
The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.	I, A

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING
Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.	I, A

Benefits of treatment

- Clinical benefit of cure
  - *Stop fibrosis*
  - *Decrease HCC*
- Reduced transmission

Fibrosis improvement following HCV treatment

- **Impact of Pegylated interferon Alfa-2b and Ribavirin on Liver Fibrosis in Patients With Chronic Hepatis C[1]**
- 4 randomized trials
  - *4493 naïve patients*
    - 3010 had paired biopsies (mean 20 months between biopsies)
    - At baseline
      - *2243 no significant fibrosis (75%)*
    - Overall response
      - *Fibrosis stage improved in 20%, stable in 65% and worsened in 15%*
      - *Most changes were the difference in 1 stage*
      - *Those who achieved SVR – less frequently experienced worsening of fibrosis (7%) compared with 17% for relapsers and 21% for non responders*

Patient with cirrhosis

- 153 patients with cirrhosis at time of first biopsy
  - *75 patients (49%) had reversal of cirrhosis*
    - 1/3 were sustained responders
    - 23 – stage 3
    - 26 - stage 2
    - 23 stage 1
    - 3 – no fibrosis

Reduction in HCC development

Table 2. **GRADE Evidence Profile for Association of SVR Versus Nonresponse to Treatment With the Development of HCC Among HCV-Infected Persons**

Outcome	Quality Assessment		Summary of Findings						
	Participants (Studies), *n*	Overall Quality of Evidence	Study Event Rates, *n/N (%)*		Relative Effect (95% CI)	Anticipated Absolute Effects			
			Failed or No Treatment	Viral Eradication		Risk With Failed or No Treatment		Absolute Effect With Viral Eradication (95% CI)	
						All Stages of Fibrosis, per Year	Advanced Fibrosis, per Year*	All Stages of Fibrosis, per Year	Advanced Fibrosis, per Year*
HCC among HCV-infected persons at all fibrosis stages; follow-up, 3.0–8.2 y	25 906 (12)	Moderate†	990/16 312 (6.1)	145/9185 (1.6)	Adjusted HR, 0.24 (0.18–0.31)	17 HCCs per 1000 persons	33 HCCs per 1000 persons	14 fewer HCCs per 1000 persons (12 to 15 fewer)	23 fewer HCCs per 1000 persons (18 to 26 fewer)

GRADE = Grading of Recommendations Assessment, Development and Evaluation; HCC = hepatocellular carcinoma; HCV = hepatitis C virus; HR = hazard ratio; SVR = sustained virologic response.

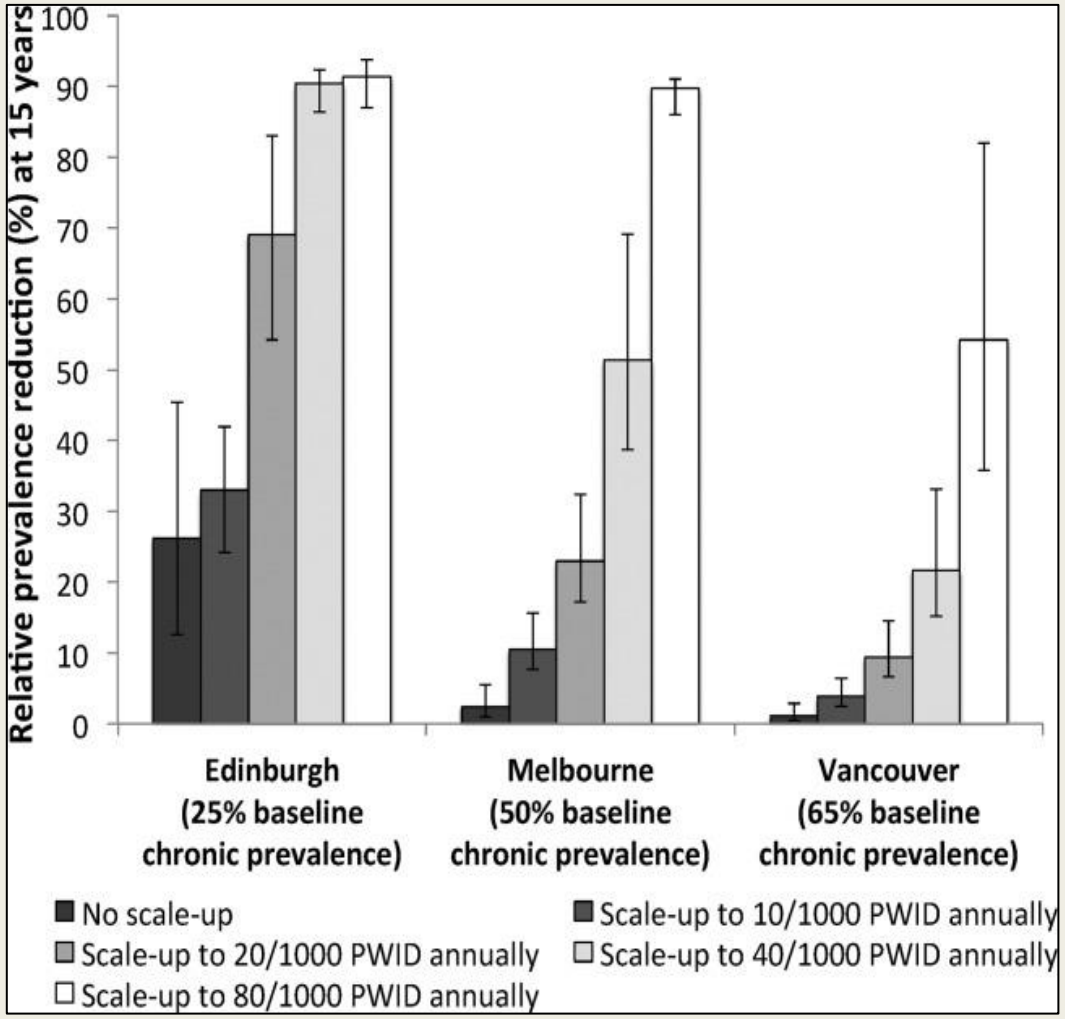
* Separate analysis of studies that reported event rates in patients with cirrhosis (HR, 0.23 [95% CI, 0.16 to 0.35]).

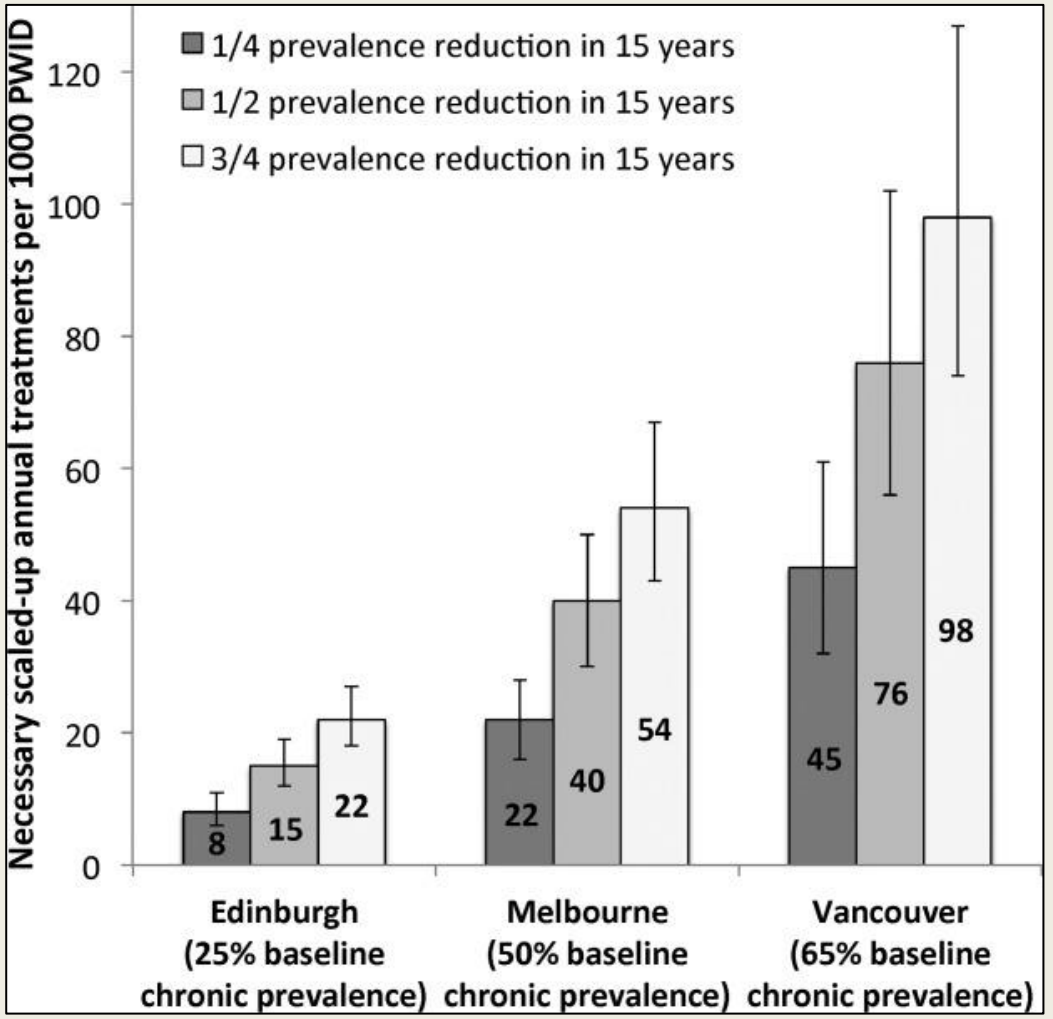
† Rated up because of large relative risk effect. Most studies controlled for baseline liver disease severity (for example, presence of cirrhosis) and other important confounders, such as hepatitis B virus infection.

Active drug use

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 including intranasal naloxone, needle/syringe service programs, medications for opioid use disorder, and other 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

Case for scaling up care in PWID





Real world

- **Falade-Nwulia et al.**
  - *830 PWID*
    - 418 with pos HCV Ab and 364 (63.7%) had detectable RNA
    - Mean age 49
    - 27% female (1140)
    - 57% non-Hispanic black (239)
    - 53% (223) income <5,000
    - 6% (25) employed
    - 83% (347) lifetime homelessness
    - 91 % (382) incarceration ever
    - 76.5% (313) reported having a PCP they saw for general health problems
    - 84% (349) reported sharing a needle at least once

HCV care continuum among PWID

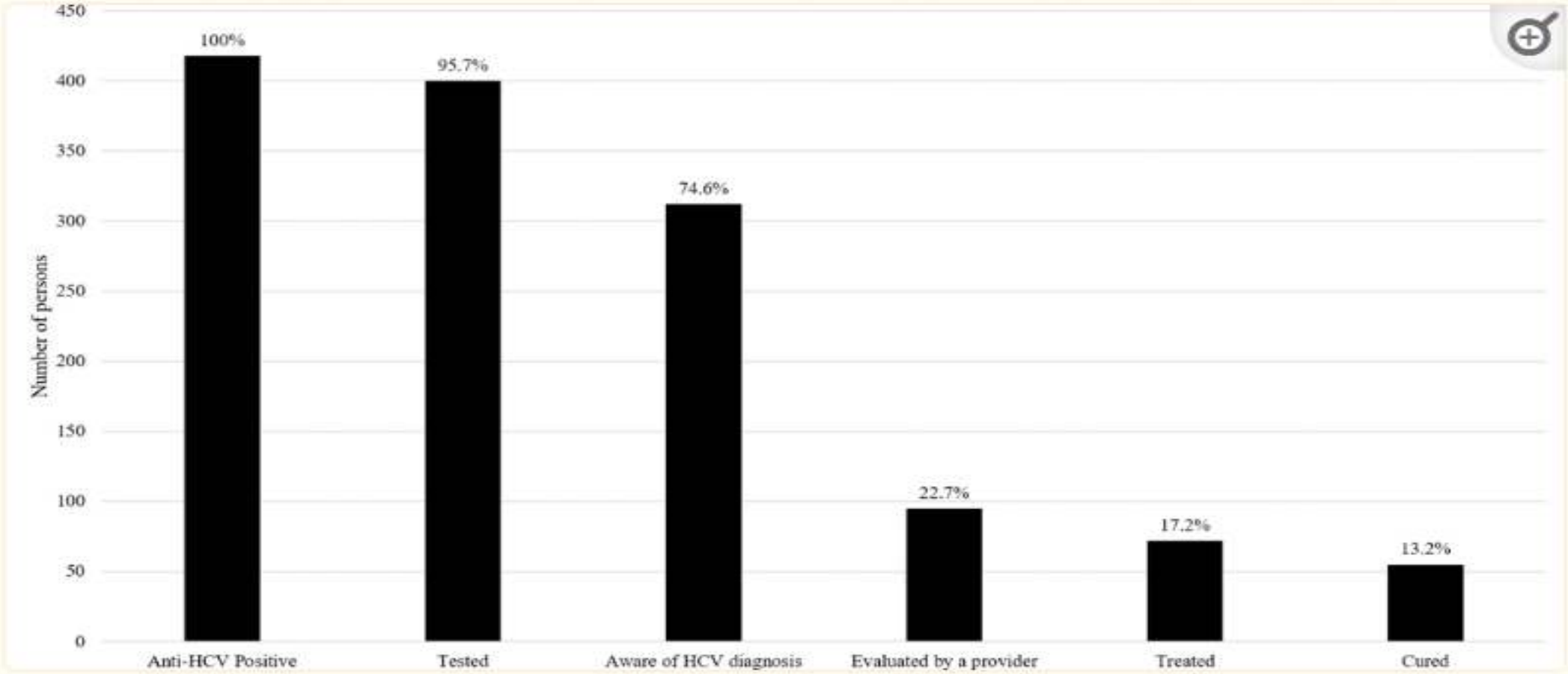


Figure 1:

HCV Care Contiuum for 418 PWID with HCV from a Community-based Cohort in Baltimore, MD

Direct-acting antiviral treatment for chronic hepatitis C in people who use drugs in a real-world setting

Kanellos Rafail Koustenis[a], Olga Anagnostou[a], Hariklia Kranidioti[a], Sofia Vasileiadi[a], Pinelopi Antonakaki[a], Evangelia Koutli[a], Paris Pantsas[a], Melanie Deutsch[a], Spilios Manolakopoulos[a,b]

Medical School of National and Kapodistrian University of Athens, Hippokration General Hospital; Medical School of National and Kapodistrian University of Athens, Laiko General Hospital, Athens, Greece

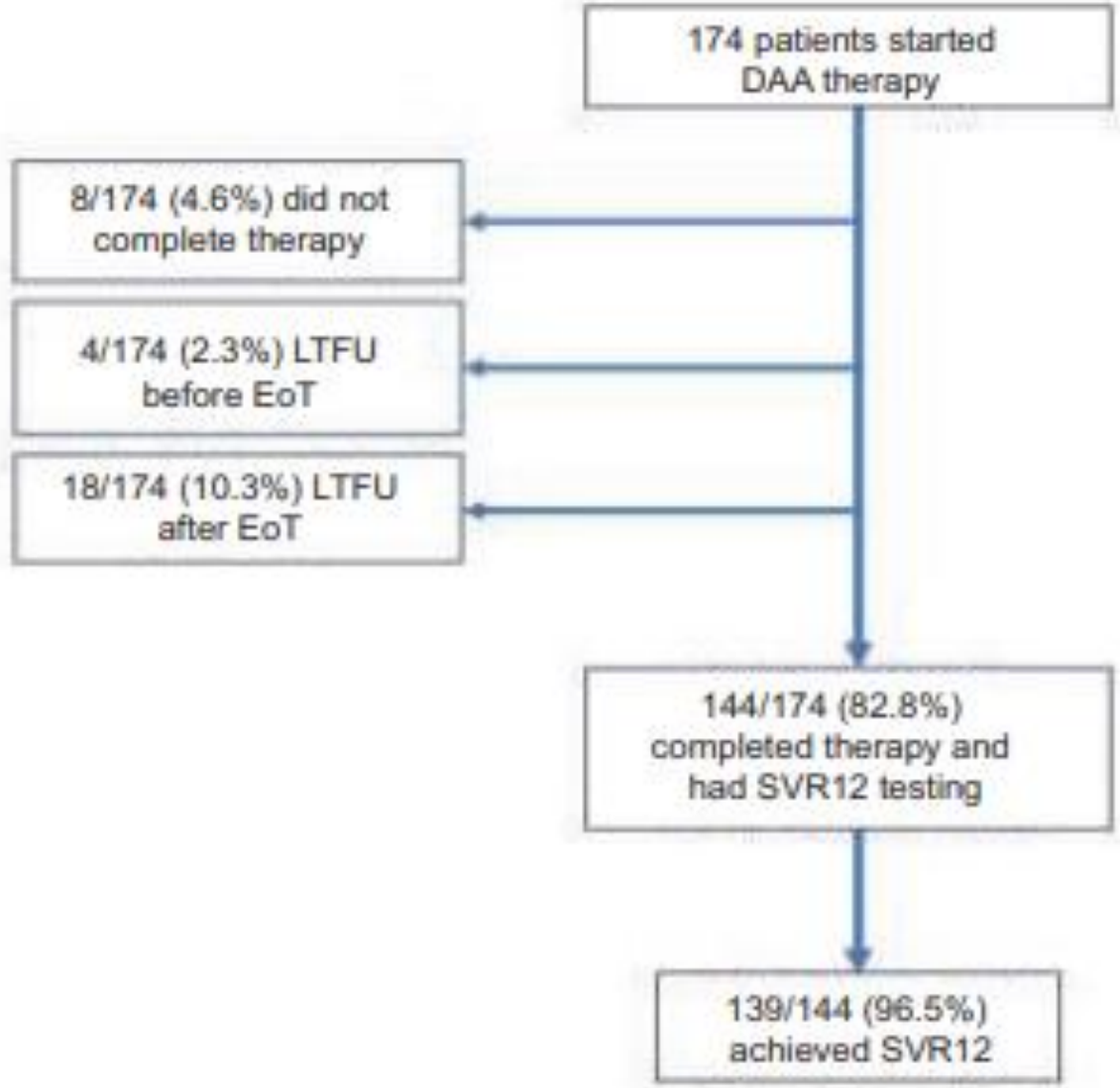


Figure 1 Patients' flowchart
DAA, direct-acting antiviral; LTFU, lost to follow up; EoT, end of treatment; SVR12, sustained virological response 12 weeks after treatment completion

Active alcohol use

- Alcohol is a significant co-factor in the progression to cirrhosis and liver cancer
- No specific guidelines/recommendations from AASLD
- Alcohol does not impact SVR rates with current DAA regimens but is a significant barrier to treatment

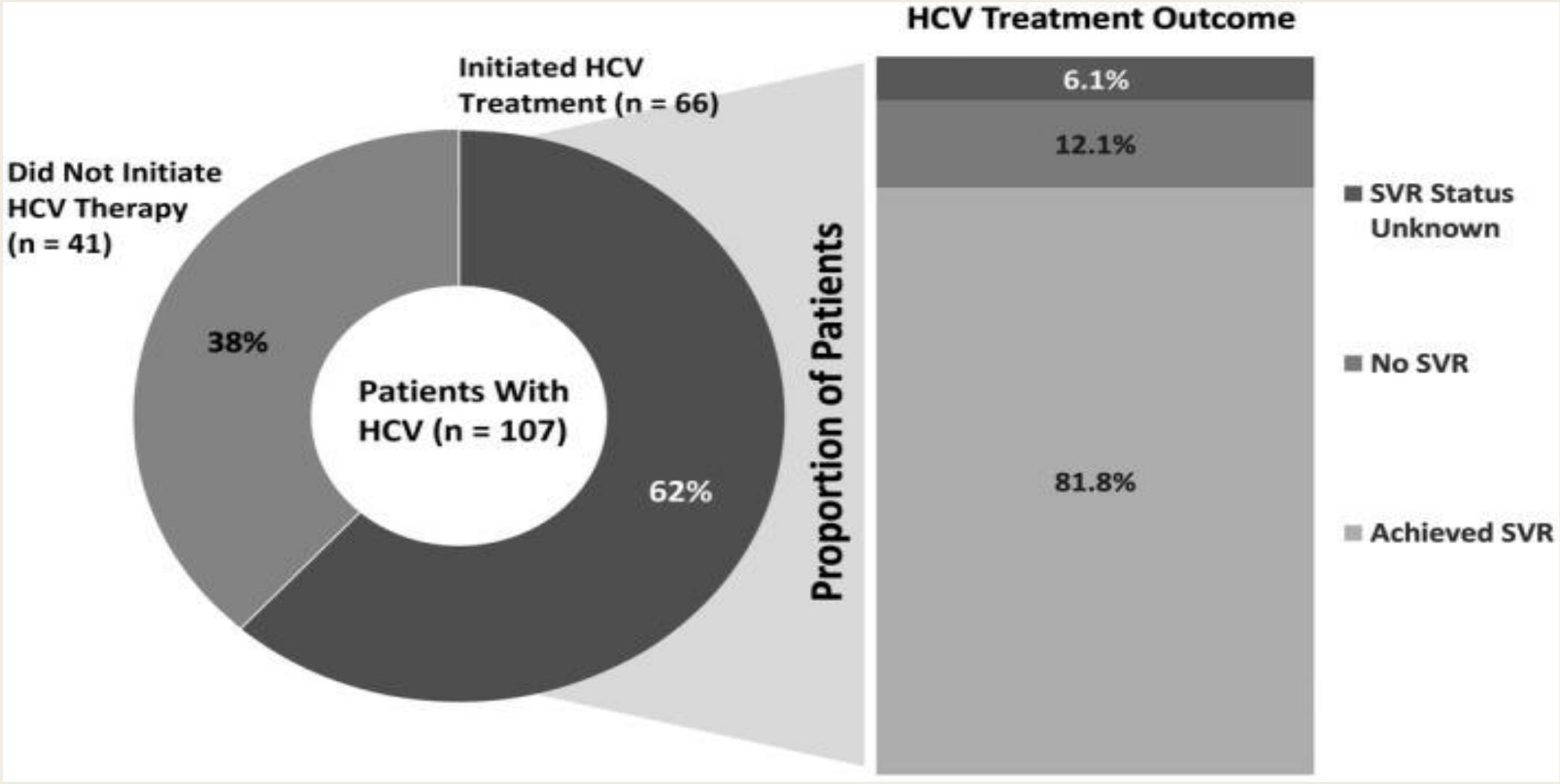
Unhoused individuals

- Amanda Noska's study on homeless vet's in 2015
- Unhoused and housed vets were equally as likely to have a PCP
- Unhoused vets were less likely to have received treatment for HCV
- Both unhoused and housed vets achieved similar SVR rates (67.9% and 73.5%)

Engagement in the HCV care cascade among homeless and nonhomeless veterans with chronic HCV infection in VHA care, United States, 2015[a]

Steps in the HCV Care Cascade	Homeless Veterans With HCV Infection[b]			Nonhomeless Veterans With HCV Infection		
	No.	%	Engaged in Prior Step of Care Cascade, %	No.	%	Engaged in Prior Step of Care Cascade, %
Estimated No. of veterans with HCV infection[c]	32 449	100.0		188 156	100.0	
Diagnosed with chronic HCV[d]	29 063	89.6		144 964	77.0	
Linked to HCV care[e]	25 786	79.5	88.7	136 169	72.4	93.9
Received HCV antiviral therapy[f]	7421	22.9	28.8	58 321	31.0	42.8
Achieved SVR[g]	5041	15.5	67.9	42 878	22.8	73.5

Our study on unhoused in Minneapolis



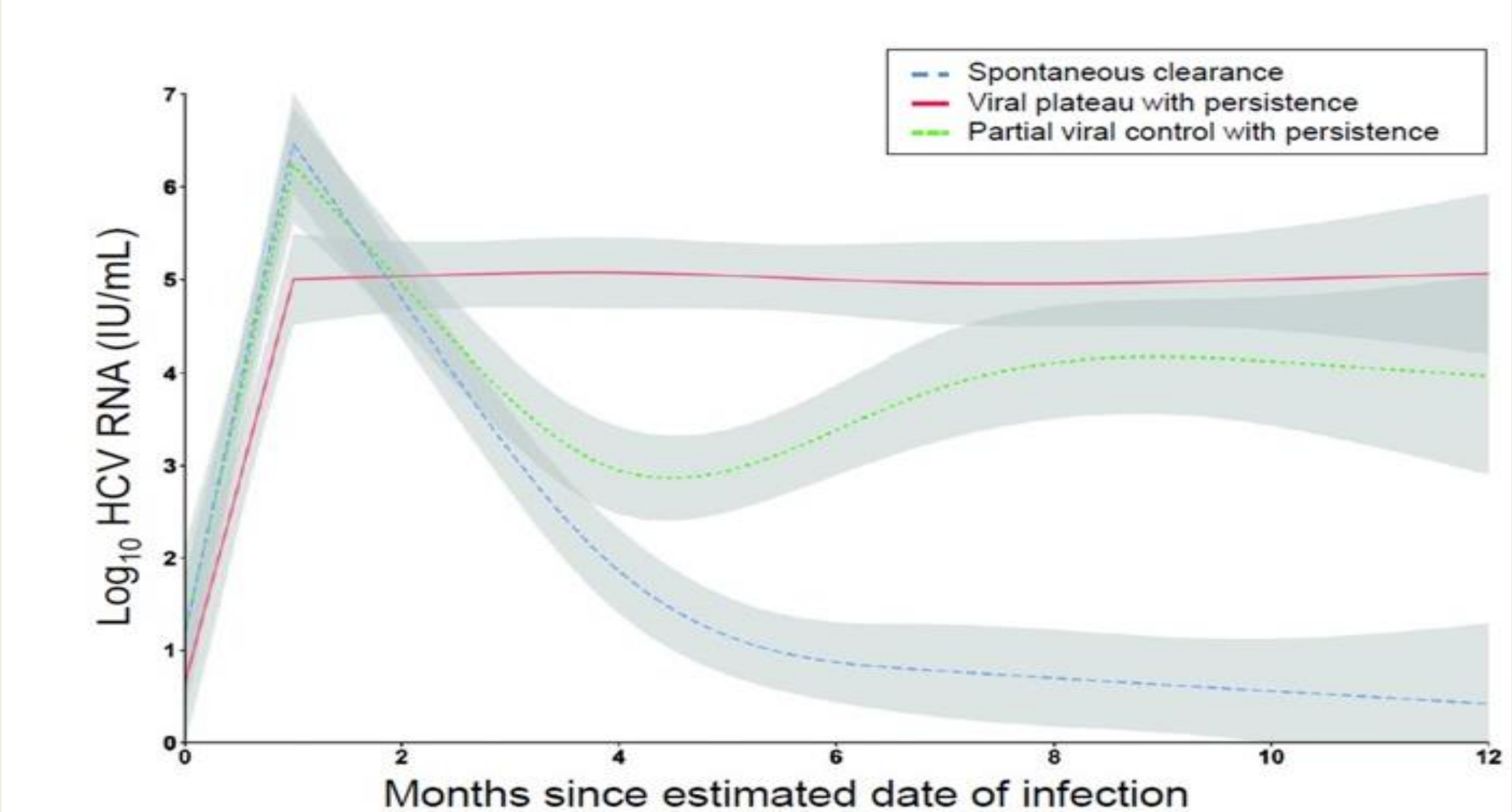
Acute infection

Recommendations for Medical Management and Monitoring of Acute HCV Infection	
RECOMMENDED	RATING
After the initial diagnosis of acute HCV with viremia (defined as quantifiable RNA), HCV treatment should be initiated without awaiting spontaneous resolution.	I, B
Counseling is recommended for patients with acute HCV infection to avoid hepatotoxic insults, including hepatotoxic drugs (eg, acetaminophen) and alcohol consumption, and to reduce the risk of HCV transmission to others.	I, C
Referral to an addiction medicine specialist is recommended for patients with acute HCV infection related to substance use.	I, B

Acute infection

- **Spontaneous clearance**
  - *Acute infection is defined as the first 6 months of infection*
    - Spontaneous clearance usually occurs within the first 12 weeks of infection
      - *Insurance often require documented 6 months of infection*
      - *Can occur up to a year later*
  - ***Between 14-50% will clear spontaneously***
  - ***Factors that might favor this:***
    - Being symptomatic
    - Younger age
    - Female
    - GT 1
    - Chronic or resolved HBV infection
  - *Patients are more likely to have clearance upon reinfection*

Rapid HCV replication during acute infection



Case for open access to treatment

- **Dutch study on HCV among MSM with HIV**
  - *Unrestricted access to HCV treatment*
    - 2014 -93 acute cases of HCV were diagnosed
    - 2016 -49 cases were diagnosed
    - 51% decrease in acute cases
    - Proportion of the population with HCV dropped from 4.2% to 1.5%
  - *Cases of syphilis and gonorrhea increase substantially in 2016*

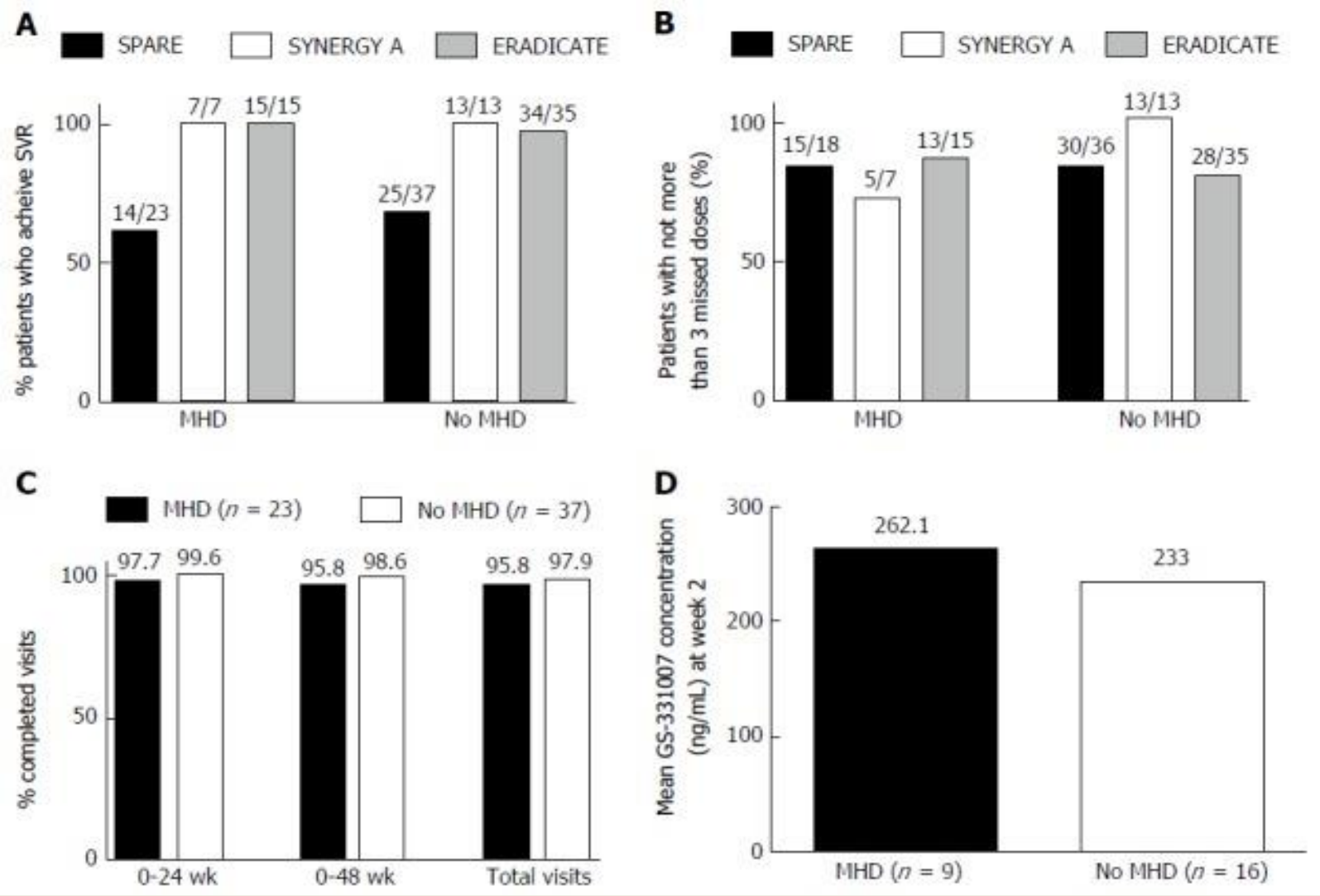
Mental health

- **Interferon era**
  - *Worries about exacerbations of underlying mental health conditions*
- **Current regimens**
  - *No contraindications to treatment*
  - *Some minor medication interactions*
    - Antipsychotics/anticonvulsants

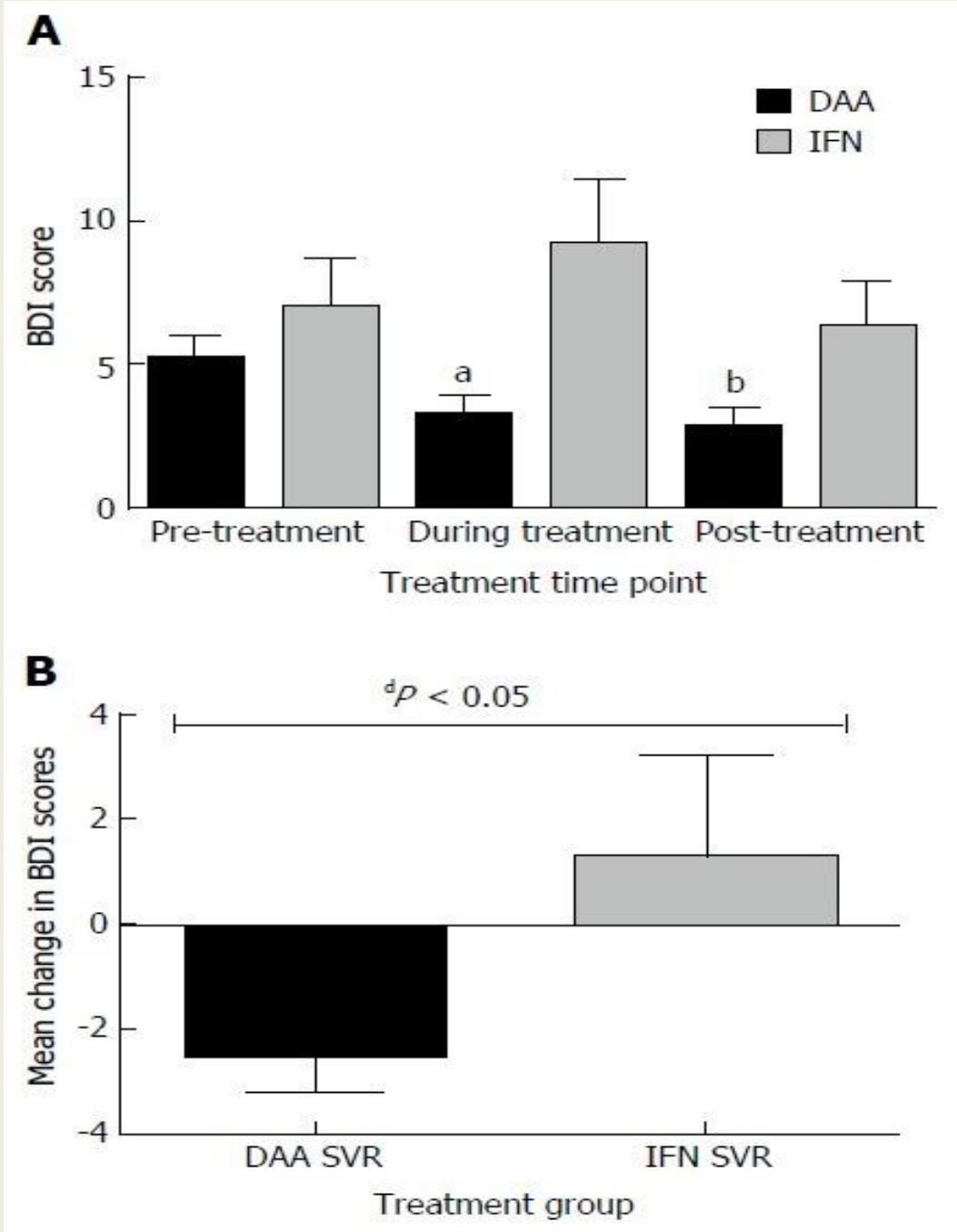
Safe and effective sofosbuvir-based therapy in patients with mental disease and hepatitis C virus infection

- Study looking at 5 clinical trials
  - *SPARE trial: sof/RBV*
  - *SYNERGY-A trial: ledipasvir and sofosbuvir*
  - *ERADICATE trial: ledipasvir and sofosbuvir*
  - *PIFNPK trial: INF/RBV*
  - *ALBIN trial: INF/RBV*
- AIMS
  - *Impact of baseline MHD on SVR and adherence to sof based regimens*
  - *Characterize the changes in BECK's Depression Inventory (BDI) scores among patients with (HIV/HCV) treated with sof based regimen (ERADICATE trial) and INF containing regimens.*

SVR and adherence rates



Changes in BDI score



References

- Poynard T, McHutchison J, Manns M, Trepo C, Lindsay K, Goodman Z, Ling MH, Albrecht J. Impact of pegylated interferon alfa-2b and ribavirin on liver fibrosis in patients with chronic hepatitis C. Gastroenterology. 2002 May;122(5):1303-13. doi: 10.1053/gast.2002.33023. PMID: 11984517.
- Morgan RL, Baack B, Smith BD, Yartel A, Pitasi M, Falck-Ytter Y. Eradication of hepatitis C virus infection and the development of hepatocellular carcinoma: a meta-analysis of observational studies. Ann Intern Med. 2013 Mar 5;158(5 Pt 1):329-37. doi: 10.7326/0003-4819-158-5-201303050-00005. PMID: 23460056.
- Martin NK, Vickerman P, Grebely J, Hellard M, Hutchinson SJ, Lima VD, Foster GR, Dillon JF, Goldberg DJ, Dore GJ, Hickman M. Hepatitis C virus treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals. Hepatology. 2013 Nov;58(5):1598-609. doi: 10.1002/hep.26431. Epub 2013 Aug 26. PMID: 23553643; PMCID: PMC3933734.
- Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, Vickerman P. Combination interventions to prevent HCV transmission among people who inject drugs: modeling the impact of antiviral treatment, needle and syringe programs, and opiate substitution therapy. Clin Infect Dis. 2013 Aug;57 Suppl 2(Suppl 2):S39-45. doi: 10.1093/cid/cit296. Erratum in: Clin Infect Dis. 2014 Apr;58(8):1203. PMID: 23884064; PMCID: PMC3722076.
- Falade-Nwulia O, Gicquelais RE, Astemborski J, McCormick SD, Kirk G, Sulkowski M, Thomas DL, Mehta SH. Hepatitis C treatment uptake among people who inject drugs in the oral direct-acting antiviral era. Liver Int. 2020 Oct;40(10):2407-2416. doi: 10.1111/liv.14634. PMID: 32770638; PMCID: PMC7706292.
- Koustenis KR, Anagnostou O, Kranidioti H, Vasileiadi S, Antonakaki P, Koutli E, Pantsas P, Deutsch M, Manolakopoulos S. Direct-acting antiviral treatment for chronic hepatitis C in people who use drugs in a real-world setting. Ann Gastroenterol. 2020 Mar-Apr;33(2):195-201. doi: 10.20524/aog.2020.0449. Epub 2020 Jan 20. PMID: 32127741; PMCID: PMC7049240.
- Ia Okwor C, Petrosyan Y, Lee C, Cooper C. History of alcohol use does not predict HCV direct acting antiviral treatment outcomes. J Assoc Med Microbiol Infect Dis Can. 2022 Sep 27;7(3):233-241. doi: 10.3138/jammi-2021-0037. PMID: 36337601; PMCID: PMC9629724.
- Noska AJ, Belperio PS, Loomis TP, O'Toole TP, Backus LI. Engagement in the Hepatitis C Care Cascade Among Homeless Veterans, 2015. Public Health Rep. 2017 Mar/Apr;132(2):136-139. doi: 10.1177/0033354916689610. Epub 2017 Jan 30. PMID: 28135425; PMCID: PMC5349485.
- Khalili M, Powell J, Park HH, Bush D, Naugle J, Ricco M, Magee C, Braimoh G, Zevin B, Fokuo JK, Masson CL. Shelter-Based Integrated Model Is Effective in Scaling Up Hepatitis C Testing and Treatment in Persons Experiencing Homelessness. Hepatol Commun. 2022 Jan;6(1):50-64. doi: 10.1002/hep4.1791. Epub 2021 Oct 10. PMID: 34628726; PMCID: PMC8710795.
- Boerekamps A, van den Berk GE, Lauw FN, Leyten EM, van Kasteren ME, van Eeden A, Posthouwer D, Claassen MA, Dofferhoff AS, Verhagen DWM, Bierman WF, Lettinga KD, Kroon FP, Delsing CE, Groeneveld PH, Soetekouw R, Peters EJ, Hullegie SJ, Popping S, van de Vijver DAMC, Boucher CA, Arends JE, Rijnders BJ. Declining Hepatitis C Virus (HCV) Incidence in Dutch Human Immunodeficiency Virus-Positive Men Who Have Sex With Men After Unrestricted Access to HCV Therapy. Clin Infect Dis. 2018 Apr 17;66(9):1360-1365. doi: 10.1093/cid/cix1007. PMID: 29186320.
- Hajarizadeh B, Grady B, Page K, Kim AY, McGovern BH, Cox AL, Rice TM, Sacks-Davis R, Bruneau J, Morris M, Amin J, Schinkel J, Applegate T, Maher L, Hellard M, Lloyd AR, Prins M, Dore GJ, Grebely J; InC3 Study Group. Patterns of hepatitis C virus RNA levels during acute infection: the InC3 study. PLoS One. 2015 Apr 2;10(4):e0122232. doi: 10.1371/journal.pone.0122232. PMID: 25837807; PMCID: PMC4383375.
- Tang LS, Masur J, Sims Z, Nelson A, Osinusi A, Kohli A, Kattakuzhy S, Polis M, Kottilil S. Safe and effective sofosbuvir-based therapy in patients with mental health disease on hepatitis C virus treatment. World J Hepatol. 2016 Nov 8;8(31):1318-1326. doi: 10.4254/wjh.v8.i31.1318. PMID: 27872683; PMCID: PMC5099584.