

SUBSTANCE USE AND INJECTING BEHAVIORS
DURING AND AFTER HEPATITIS C
TREATMENT AMONG PERSONS WHO INJECT
DRUGS

Kimberly Page, Ph.D., MPH

This project was led by Dr. Judith Tsui, MD, MPH at University of Washington for
The HERO Study Team

DISCLOSURES

- Site PI for Patient Centered Outcomes Research Institute (PCORI) funded study (HERO Study) that used HCV medications donated by Gilead.
- Research/views presented do not represent NIH/NIDA

HCV ELIMINATION

- Elimination of HCV is now a global and national priority (WHO goal for global elimination by 2030)
- Achieving cure among persons who inject drugs (PWID) is essential to achieve elimination (“treatment as prevention”)
- Guidelines now recommend universal screening and treatment indicated for **all persons with chronic infection**
- Treatment of HCV among active PWID is increasing
- Little research describe injecting behaviors during treatment and impact on likelihood of cure

INJECTING BEHAVIORS AMONG PERSONS WITH HCV

- Globally, it is estimated that 24% (95% CI: 21-27%) of PWID engage in receptive needle/syringe sharing in the past month.¹
- Counseling patients not to share injecting equipment is standard care for patients who are diagnosed with HCV, yet prior studies have not clearly demonstrated that this impacts sharing behaviors.²⁻³
- Avoiding sharing behaviors during/after HCV treatment is necessary to avoid re-exposure that would jeopardize achieving cure and re-infection after cure.

1. Tran LT, Peacock A, College S, et al. International Journal of Drug Policy 2020
2. Tsui JI, Vittinghoff E, Hahn JA, et al. Drug and Alcohol Dependence 2009
3. Spelman T, Morris MD, Zang G, et al. J Epidemiol Community Health 2015

GENERAL RESEARCH QUESTIONS

- Do PWID modify their injecting behaviors to avoid re-exposure during DAA treatment? If so, are those changes in behavior sustained over time?
- Does sharing of injecting equipment during treatment jeopardize cure?

SPECIFIC AIMS

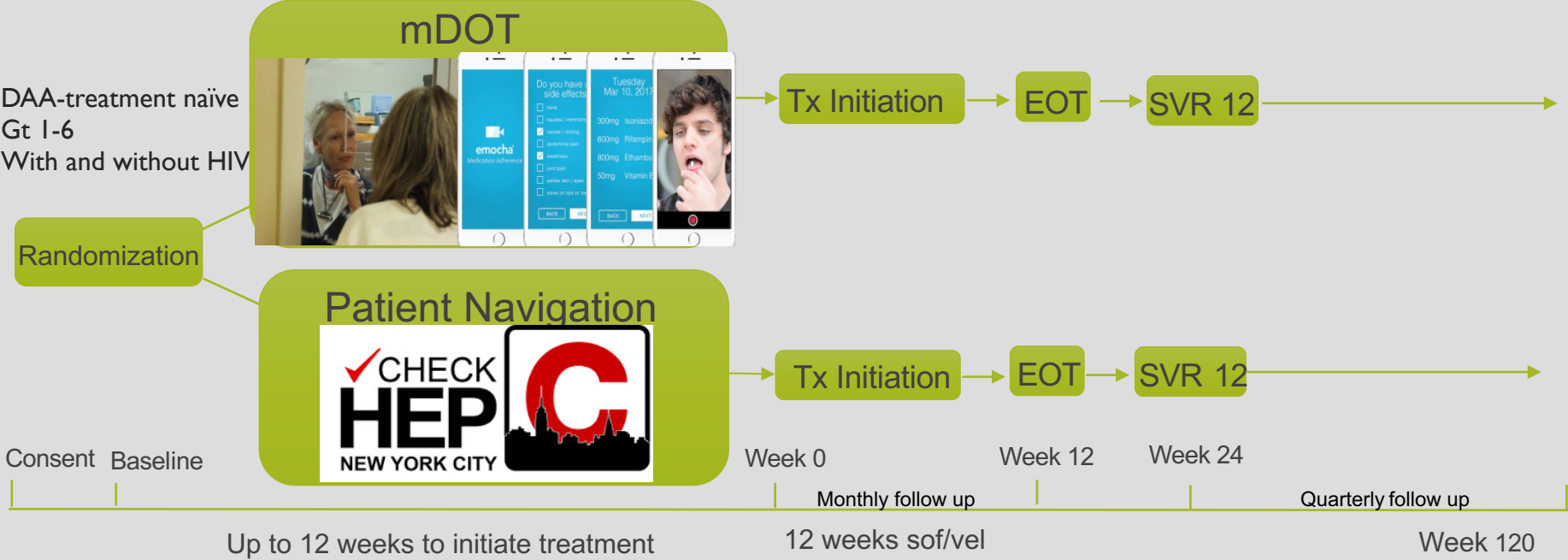
- **Aim 1:** Define injection practices of PWID before, during and after HCV treatment with DAAs.
- **Aim 2:** Examine whether sharing injecting equipment during treatment is associated with not achieving sustained virologic response (SVR), i.e., cure.

STUDY DESIGN AND SAMPLE



- Observational cohort study: secondary analysis of the “Hepatitis C Real Options” (HERO) study, a pragmatic clinical effectiveness study testing models of delivery of care for treating HCV among PWID
- Participants recruited from sites in 8 states across the U.S. (MA, RI, NY, MD, WV, NM, CA, WA); community health centers and opioid treatment programs
- Inclusion criteria: 1) age ≥ 18 years; 2) injected drugs within 3 months; 3) HCV-infected and no prior treatment with DAAs
- Study sample further restricted to participants who initiated treatment and had SVR data (“Per Protocol”)

Overall Study Design



Litwin AH, Jost J, Wagner K, Heo M, Karasz A, Feinberg J, Kim AY, Lum PJ, Mehta SH, Taylor LE, Tsui JI, Pericot-Valverde I, Page K; HERO Study Group. Rationale and design of a randomized pragmatic trial of patient-centered models of hepatitis C treatment for people who inject drugs: The HERO study. *Contemp Clin Trials* 2019

Litwin AH, Lum PJ, Taylor LE, Mehta SH, et al. A Multi-Site Randomized Pragmatic Trial of Patient-Centered Models of Hepatitis C Treatment for People Who Inject Drugs: The HERO Study. Oral presentation at The Liver Meeting Digital Experience: American Association for the Study of Liver Disease (AASLD), November 16, 2020



STUDY MEASURES: INJECTION RISK

- Injection frequency (days in the past month, episodes per day)
- Substances injected in the past 3 months: Speedballs, Goofballs, Methamphetamine, Cocaine, Crack
- Receptive sharing behaviors: syringes, cookers, cottons,
- Backloading
- Re-use of one's own equipment

MAIN OUTCOMES

- Sustained Virologic Response (SVR)/cure: defined as HCV RNA level below the limit of quantitation (≤ 15 IU/mL) at least 12 weeks following treatment completion.
- Time window for determination of SVR set between 70- and 365-days post-end of treatment

STATISTICAL ANALYSIS – AIM I

- To compare trends in injecting behaviors during the treatment period to post-treatment period, performed logistic regression with Generalized Estimating Equations (GEE) with a linear spline to test difference in slopes before and after EOT.

STATISTICAL ANALYSIS – AIM 2

- Multivariate logistic regression models used to explore associations between sharing behaviors during treatment (assessed at EOT visit) and relative odds for achieving SVR.
 - If EOT data missing, utilized data from week 4 visit; if week 4 missing, utilized data from baseline visit.
- Models were a priori adjusted for site, randomization arm, age, gender, HIV status, and homelessness.
- **Primary hypothesis:** reporting any sharing injecting equipment during treatment will be associated with higher relative odds of not achieving SVR/cure.

Figure 1: Injection Risk Behaviors from Baseline to 60 Weeks Post DAA Treatment (N=501)

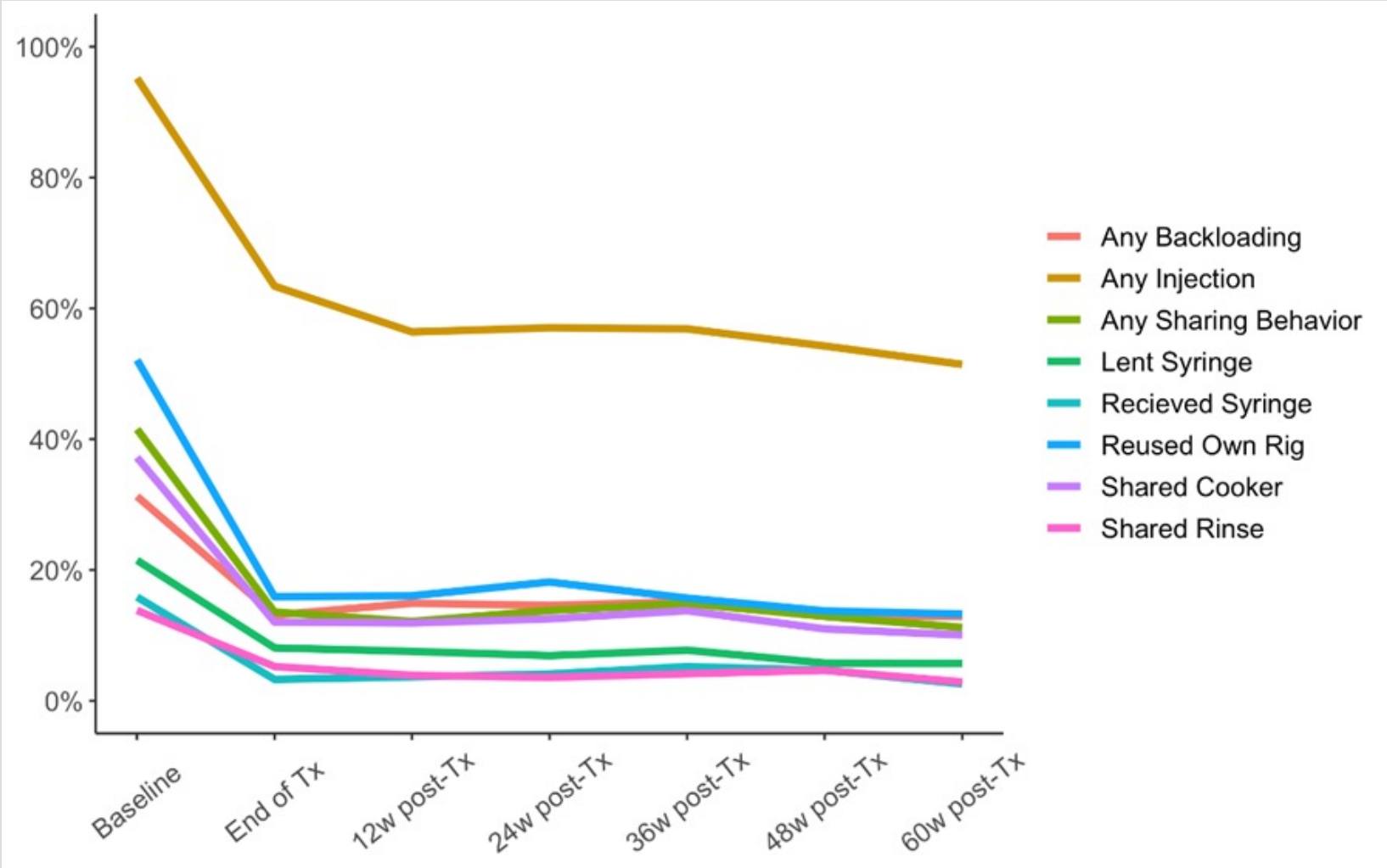


Figure 2: Positive Urine Drug Toxicology Before, During and After Treatment (N=501)

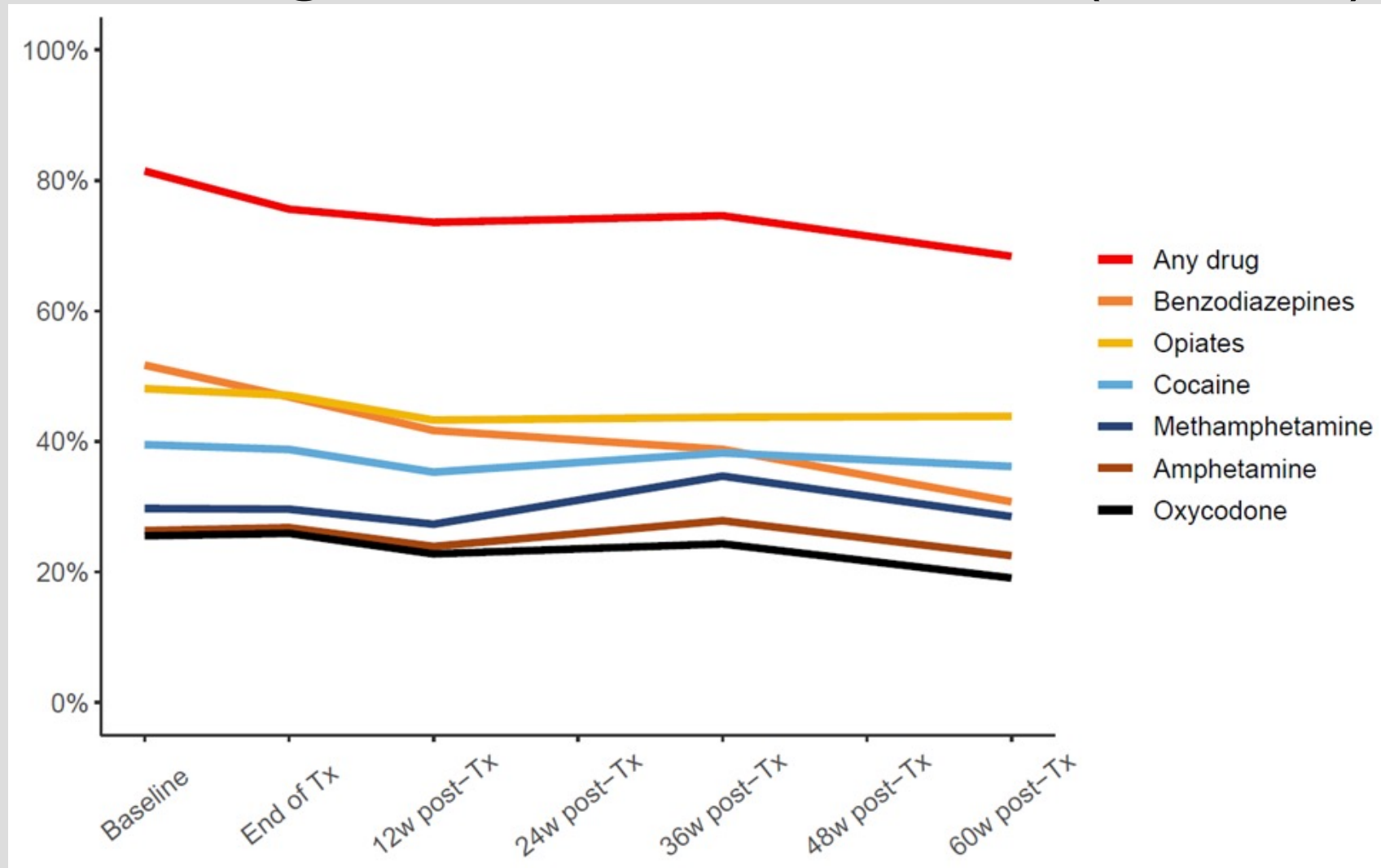


Figure 3: Sharing of Injection Drug Use Equipment from Baseline to 60 Weeks Post-Treatment by SVR Result (N=501)

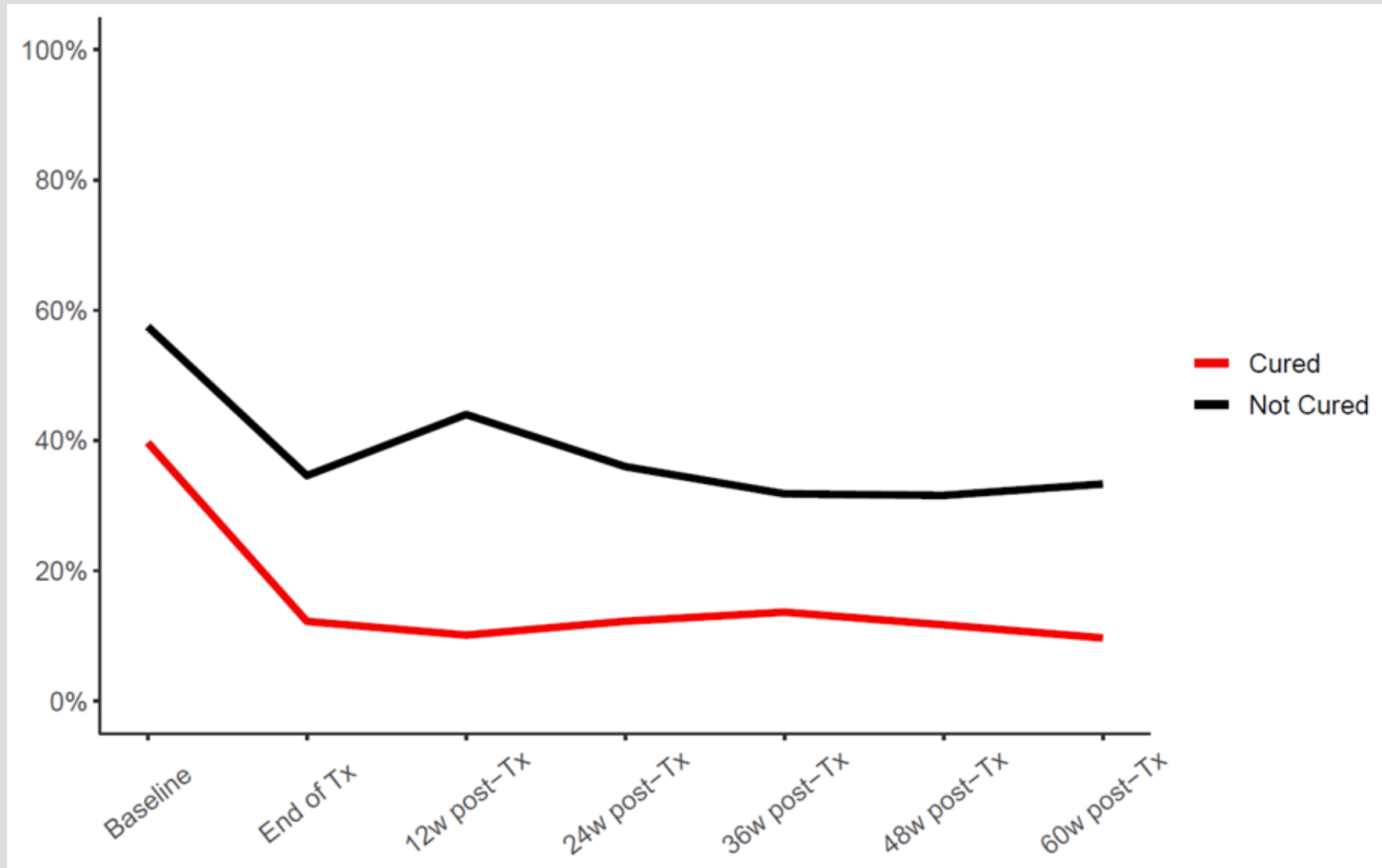


TABLE I: CHARACTERISTICS OF PARTICIPANTS WHO DO AND DO NOT REPORT SHARING INJECTING EQUIPMENT DURING DAA TREATMENT

	Sharing injection equipment	No sharing injection equipment	Total	p-value ¹
	n=79	n=422	N=501	
Gender				0.67
Female	24 (30.4%)	109 (25.8%)	133 (26.6%)	
Male	54 (68.4%)	309 (73.2%)	363 (72.5%)	
Transgender or Gender Non-conforming	1 (1.3%)	4 (1.0%)	5 (1.0%)	
Age Mean (SD)	40.8 (11.0)	44.6 (11.5)	44.0 (11.5)	<0.01
Race				
White/Caucasian	48 (60.8%)	260 (61.6%)	308(61.5%)	0.93
Black/African American	11 (13.9%)	59 (14.0%)	70 (14.0%)	
Other	18 (22.8%)	87 (20.6%)	105 (21.0%)	
Missing	2 (2.5%)	16 (3.8%)	18 (3.6%)	
Latino/Hispanic Ethnicity	14 (17.7%)	100 (23.7%)	114 (22.8%)	0.31
Education				0.71
Less than high school	16 (20.2%)	102 (24.2%)	118 (23.6%)	
HS diploma or GED	30 (38.0%)	159 (37.7%)	189 (37.7%)	
Some college or more	33 (41.8%)	160 (37.9%)	193 (38.5%)	
Missing	0 (0.0%)	1 (0.2%)	1 (0.2%)	

¹Chi-squared test for categorical or t-test for means

TABLE I (CONT'D): CHARACTERISTICS OF PARTICIPANTS WHO DO AND DO NOT REPORT SHARING INJECTING EQUIPMENT DURING DAA TREATMENT

	Sharing injection equipment	No sharing injection equipment	Total	P-value
	n=79	n=422	N=501	
Homeless/unstably housed ¹	48 (60.8%)	196 (46.4%)	244 (48.7%)	0.03
Employed with a regular job or informal work ²	22 (27.8%)	155 (36.7%)	177 (35.3%)	0.16
History jail/prison	72 (91.1%)	358 (84.8%)	430 (85.8%)	0.43
Years injecting drugs (Mean/SD)	13.1 (11.1)	13.6 (11.5)	13.5 (11.4)	0.71
Any medication for OUD in the past 3 months ³	61 (77.2%)	301 (71.3%)	362 (72.3%)	0.34
Methadone only	51 (64.6%)	241 (57.1%)	292 (58.3%)	<0.01
Buprenorphine only	6 (7.6%)	54 (12.8%)	60 (12.0%)	
Methadone and Buprenorphine	4 (5.1%)	6 (1.4%)	10 (2.0%)	
HIV infection (positive)	12 (15.2%)	60 (14.2%)	72 (14.4%)	0.97

¹Defined as living on the street/outdoors; in someone else's apartment, room or house; in an institution; or in an other living situation.

²Sources of income in the past 3 months; Employed includes a) regular job and b) informal work;

³OAT, opioid agonist therapy (methadone or buprenorphine) last 30 days;

Table 2: GEE Linear Spline Model Analysis for Estimating and Testing Odds-Ratios of Injection Drug Use Practices comparing in treatment period to post-treatment period

	Odds Ratio (OR) per one-week difference				P-value ¹
	In treatment period (Baseline-EOT/Wk12)		Post-treatment period (EOT – 60 weeks post EOT)		
Injection Behavior	OR	95% CI	OR	95% CI	
Reused Own Rig	0.87	(0.85, 0.89)	1.00	(0.99, 1.00)	<.001
Shared Cooker	0.89	(0.87, 0.91)	1.00	(0.99, 1.00)	<.001
Any Backloading	0.92	(0.90, 0.94)	1.00	(0.99, 1.00)	<.001
Shared Rinse	0.91	(0.88, 0.94)	0.99	(0.99, 1.00)	<.001
Lent Syringe	0.91	(0.89, 0.93)	0.99	(0.99, 1.00)	<.001
Received Syringe	0.88	(0.85, 0.91)	1.00	(0.99, 1.01)	<.001
Any injecting	0.81	(0.78, 0.84)	0.99	(0.99, 1.00)	<.001
Any sharing behavior	0.88	(0.86, 0.90)	1.00	(0.99, 1.00)	<.001

¹ Test for difference in odds-ratios between the in-treatment and the post-treatment periods.

Table 3: Injection Risk Behaviors During Treatment¹ and Relative Odds of Not Achieving SVR I2/Cure: Results from Logistic Regression Models

	Unadjusted Models		Adjusted Models ²	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Any Receptive Sharing of Cookers, Rinses, or Needles/Syringes	4.76 (2.38, 9.38)	< 0.01	4.83 (2.26, 10.28)	< 0.01
Any Injecting	1.94 (0.94, 4.41)	0.09	2.40 (1.10, 5.77)	0.04
Any Sharing of Cooker	4.34 (2.12, 8.65)	< 0.01	4.20 (1.92, 9.06)	< 0.01
Any Backloading	3.35 (1.59, 6.75)	< 0.01	4.93 (2.02, 12.11)	< 0.01
Any Sharing of Rinses	4.44 (1.65, 10.80)	<0.01	4.41 (1.46, 12.47)	<0.01
Any Receipt of Needles/Syringes	2.90 (0.80, 8.34)	0.07	1.85 (0.46, 5.98)	0.34
Any Lending of Needles/Syringes	2.23 (0.86, 5.11)	0.07	1.81 (0.63, 4.66)	0.24
Any Re-use of One's Own Needles/Syringes	2.95 (1.46, 5.79)	<0.01	2.37 (1.11, 4.92)	0.02
Any Methamphetamine Injection	1.45 (0.69, 2.89)	0.30	2.59 (1.03, 6.47)	0.04

¹ Self-report of behaviors over the past 3 months reported at the End-of-Treatment (Visit 4, week 12 since treatment initiation) visit. If data missing for that visit, reported behaviors for the past 3 months at Visit 2 (week 4) were used (n=34). If data missing for that visit, reported behaviors for the past 3 months at Baseline were used (n= 8).

² Adjusted for study arm, site, age, gender, HIV positive status, and homelessness at baseline.

STUDY STRENGTHS/LIMITATIONS

- Large study of HCV treatment among PWID in “real-world” setting with information on injection drug use behaviors captured over time
- Recall bias and social desirability bias may influence responses
- Missing data (sample restricted “Per Protocol”)
 - Sensitivity analyses with “ITT” sample provides similar results
- Results do not differentiate between treatment failures and early reinfection

CONCLUSIONS

- PWID appear to be adopting safer injecting behaviors during and after DAA treatment for HCV.
- As such, treatment of HCV among PWID may lead to other health benefits related to safer drug use practices.

CONCLUSIONS

- Any receptive sharing of injecting equipment is associated with not achieving cure for HCV among PWID treated with DAAs.
- Also, reuse of one's own equipment is also associated with not being cured → providers should be aware and counsel appropriately.
- Providing access to sterile injecting equipment is essential to achieving HCV cure among active PWID who are treated with DAAs.

Acknowledgements



The **HERO Research Group** includes the primary investigator (PI) and co-investigators from each of the 9 sites, PIs from the CDC and the NYC DOH, statisticians and key staff (eg, project directors, patient representatives), and key stakeholders. The HERO study sites are Clemson University and Prisma Health, Albert Einstein College of Medicine/Montefiore Medical Center, University of Rhode Island, Johns Hopkins Bloomberg School of Public Health, Massachusetts General Hospital, University of California–San Francisco, University of New Mexico, University of Washington, and West Virginia University. Research reported in this presentation was supported through Patient-Centered Outcomes Research Institute (**PCORI**) **Award HPC-1503-28122** with additional support from Gilead Sciences, Quest Diagnostics, Monogram Biosciences, and OraSure Technologies.

The opinions presented in this work are solely the responsibility of the authors and do not necessarily represent the views of PCORI, its board of governors, or its methodology committee.

Alain H. Litwin, MD, MS, MPH
Judith Feinberg, MD
Arthur Y. Kim, MD
Paula J. Lum, MD, MPH
Shruti H. Mehta, PhD, MPH
Brianna L. Norton, DO, MPH
Kimberly A. Page, PhD, MPH
Lynn E. Taylor, MD, FAASLD
Judith I. Tsui, MD, MPH



CO-AUTHORS

- Paula J. Lum
- Lynn E. Taylor
- Shruti H. Mehta
- Judith Feinberg
- Arthur Y. Kim
- Brianna L. Norton
- Jiajing Niu
- Moonseong Heo
- Julia Arnsten
- Irene Pericot-Valverde
- Aurielle Thomas
- Kendra L. Blalock
- Andrea C. Radick
- Christina Murray-Krezan
- Kimberly A. Page
- Alain Litwin (PI)
- HERO Research Group

QUESTIONS?

THANK YOU!