THE LANCET Gastroenterology & Hepatology

Supplementary appendix 4

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplementary Materials

TABLE OF CONTENTS

- **Figure S1.** CONSORT Flow Chart of the HERO Study. DAA, direct-acting antivirals; HCV, hepatitis C virus; ITT, intention to treat; mDOT, modified directly observed therapy; mITT, modified intention to treat; PN, patient navigation; PP, per protocol; SVR, sustained virologic rate.
- Figure S2. Factors Associated with SVR in the ITT (Panel A) and PP (Panel B) Populations.
- Figure S3. Factors Associated with Adherence in the PP Population
- Figure S4. Factors Associated with Treatment Initiation in the ITT Population.
- **Figure S5.** Factors Associated with Treatment Completion in the ITT (Panel A), mITT (Panel B), and PP (Panel C) Populations.
- Figure S6. Proportion of Patients with Active Drug Use.
- **Figure S7.** Factors with Between-Subgroup Heterogeneous Intervention Effects on SVR in the ITT (Panel A), mITT (Panel B) and PP (Panel C) Populations
- **Figure S8.** Factors with Between-Subgroup Heterogeneous Intervention Effects on Adherence in the mITT (Panel A) and PP (Panel B) Populations
- Figure S9. Factors with Between-Subgroup Heterogeneous Intervention Effects on Treatment Initiation in the ITT Population
- **Figure S10.** Factors with Between-Subgroup Heterogeneous Intervention Effects on Treatment Completion in the ITT (Panel A), mITT (Panel B) and PP (Panel C) Populations
- Table S1. Baseline Characteristics of HERO Participants Among PP Sample.
- **Table S2.** Distribution of SAE by the study arms from N=219 participants (N=109 from mDOT and N=110 for PN)

List of Investigators

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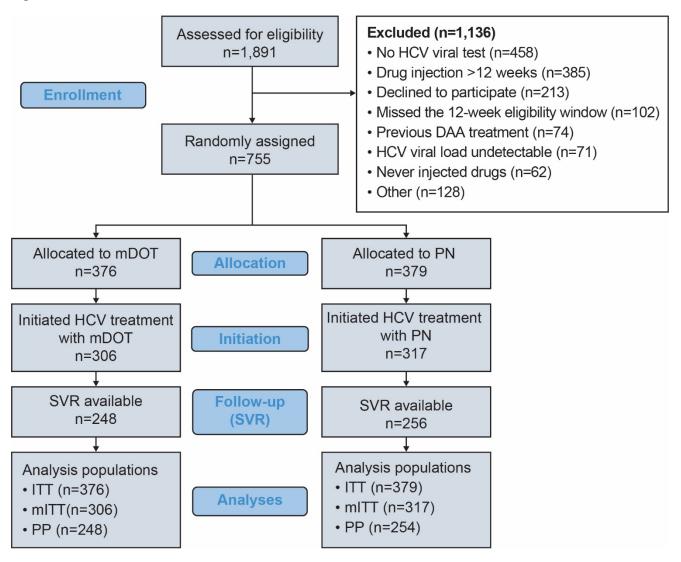
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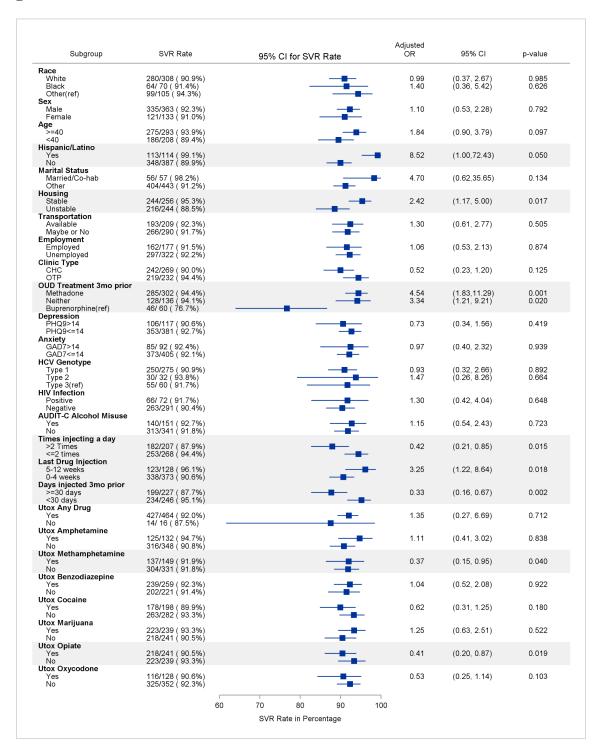
Figure S1. CONSORT Flow Chart.



DAA, direct-acting antivirals; HCV, hepatitis C virus; ITT, intention to treat; mDOT, modified directly observed therapy; mITT, modified intention to treat; PN, patient navigation; PP, per protocol; SVR, sustained virologic rate.

Figure S2. Factors Associated With SVR in the ITT (Panel A) and PP (Panel B) Populations.

Subgroup	SVR Rate	95% CI for SVR Rate	Adjusted OR	95% CI	p-value
Race White Black Other(ref)	281/476 (59.0%) 64/103 (62.1%) 99/151 (65.6%)		1.05 1.07	(0.67, 1.65) (0.59, 1.93)	0.815 0.826
Sex Male Female	335/528 (63.4%) 122/218 (56.0%)		1.35	(0.96, 1.89)	0.081
Age >=40 <40	275/421 (65.3%) 187/334 (56.0%)		1.29	(0.93, 1.80)	0.123
Hispanic/Latino Yes No	113/163 (69.3%) 349/592 (59.0%)		1.56	(0.94, 2.58)	0.087
Marital Status Married/Co-hab Other	56/ 90 (62.2%) 405/648 (62.5%)		1.02	(0.63, 1.64)	0.934
Housing Stable Unstable	244/339 (72.0%) 217/399 (54.4%)		2.26	(1.63, 3.14)	0.000
Transportation Available Maybe or No	194/302 (64.2%) 266/436 (61.0%)	-	1.39	(0.99, 1.97)	0.061
Employment Employed Unemployed	162/257 (63.0%) 298/480 (62.1%)	-	1.30	(0.93, 1.84)	0.129
Clinic Type CHC OTP	243/443 (54.9%) 219/312 (70.2%)		0.66	(0.47, 0.94)	0.021
OUD Treatment 3mo prior Methadone Neither Buprenorphine(ref)	285/399 (71.4%) 129/209 (61.7%) 46/107 (43.0%)		2.24 1.78	(1.39, 3.61) (1.07, 2.96)	0.001 0.026
Depression PHQ9>14 PHQ9<=14	106/171 (62.0%) 354/544 (65.1%)	-	0.87	(0.60, 1.26)	0.458
Anxiety GAD7>14 GAD7<=14	85/135 (63.0%) 374/578 (64.7%)	-	0.97	(0.65, 1.47)	0.901
HCV Genotype Type 1 Type 2 Type 3(ref)	250/368 (67.9%) 30/ 45 (66.7%) 55/ 94 (58.5%)		1.37 1.36	(0.83, 2.27) (0.61, 3.01)	0.214 0.451
HIV Infection Positive Negative	66/102 (64.7%) 263/421 (62.5%)	-	0.71	(0.41, 1.24)	0.225
AUDIT-C Alcohol Misuse Yes No	141/229 (61.6%) 313/477 (65.6%)		0.93	(0.66, 1.30)	0.657
Times injecting a day >2 Times <=2 times	182/325 (56.0%) 253/355 (71.3%)		0.59	(0.42, 0.82)	0.002
Last Drug Injection 5-12 weeks 0-4 weeks	123/182 (67.6%) 339/572 (59.3%)	-	1.63	(1.12, 2.37)	0.011
Days injected 3mo prior >=30 days <30 days	199/336 (59.2%) 234/344 (68.0%)		0.72	(0.51, 1.00)	0.047
Utox Any Drug Yes No	427/655 (65.2%) 15/ 27 (55.6%)		0.99	(0.43, 2.25)	0.975
Utox Amphetamine Yes No	125/193 (64.8%) 317/489 (64.8%)	#	0.84	(0.55, 1.28)	0.416
Utox Methamphetamine Yes No	137/218 (62.8%) 305/464 (65.7%)	-	0.62	(0.40, 0.96)	0.030
Utox Benzodiazepine Yes No	239/358 (66.8%) 203/324 (62.7%)		0.94	(0.67, 1.33)	0.736
Utox Cocaine Yes No Utox Marijuana	178/287 (62.0%) 264/394 (67.0%)		0.61	(0.43, 0.87)	0.006
Utox Marijuana Yes No Utox Opiato	223/337 (66.2%) 219/345 (63.5%)	#	0.98	(0.70, 1.38)	0.929
Utox Opiate Yes No	218/350 (62.3%) 224/332 (67.5%)	-	0.54	(0.38, 0.77)	0.001
Utox Oxycodone Yes No	116/182 (63.7%) 326/500 (65.2%)	-	0.75	(0.51, 1.10)	0.140
	;	30 40 50 60 70 80 90 SVR Rate in Percentage	100		



AUDIT-C, Alcohol Use Disorders Identification Test; CHC, community health centers; Co-hab, cohabitation; GAD7, general anxiety disorder 7-item; HCV, hepatitis C virus; ITT, intention to treat; OR, odds ratio; OTP, opioid treatment programs; OUD, opioid use disorder; PHQ-9, Patient Health Questionnaire-9; SVR, sustained virologic response; UTOX, urine toxicology screen.

Figure S3. Factors Associated With Adherence in the PP Population.

Subgroup	Estimates	95%Cl for Estimated Difference	Diff	95% CI	p-value
White vs. Other	(77.1 vs 74.8)	-	2.3	(-1.6, 6.2)	0.24
Black vs. Other	(74.9 vs 74.8)		0.0	(-5.4, 5.5)	0.989
Male vs. Female	(76.4 vs 74.7)		1.7	(-1.5, 4.9)	0.290
Age (>=40 vs. <40)	(77.9 vs 73.6)		4.3	(1.3, 7.2)	0.00
Hispanic/Latino (Yes vs. No)	(74.4 vs 76.6)		-2.3	(-6.4, 1.9)	0.28
Marrital Status (Married/Co-hab vs. Other)	(79.1 vs 75.6)	 	3.5	(-0.9, 7.9)	0.118
Housing (Stable vs. Unstable)	(75.5 vs 76.6)		-1.1	(-4.0, 1.7)	0.430
Transportation (Available vs. Maybe or No)	(76.6 vs 75.6)		1.0	(-2.1, 4.1)	0.522
Employment (Employed vs. Unemployed)	(78.4 vs 74.7)		3.7	(0.7, 6.6)	0.015
Clinic Type (CHC vs. OTP)	(74.3 vs 78.3)		-4.0	(-7.1, -0.9)	0.012
Cirrhosis (Yes vs. No)	(79.3 vs 75.8)		3.5	(-2.3, 9.2)	0.236
Methadone vs. Buprenorphine	(77.6 vs 72.7)		4.9	(0.2, 9.7)	0.043
Neither vs. Buprenorphine	(74.6 vs 72.7)		1.9	(-3.3, 7.0)	0.472
Depression (PHQ9 >14 vs. <=14)	(73.8 vs 76.8)		-3.1	(-6.3, 0.2)	0.069
Anxiety (GAD7 >14 vs. <=14)	(73.2 vs 76.7)		-3.5	(-7.1, 0.1)	0.054
HCV Genotype (Type 1 vs. Type 3)	(76.9 vs 78.2)		-1.3	(-5.6, 3.1)	0.566
HCV Genotype (Type 2 vs. Type 3)	(77.9 vs 78.2)		-0.3	(-6.9, 6.4)	0.940
HIV Infection (Yes vs. No)	(72.2 vs 76.7)		-4.5	(-9.3, 0.3)	0.067
AUDIT-C Alcohol Misuse (Yes vs. No)	(75.1 vs 76.4)		-1.4	(-4.4, 1.7)	0.373
Injecting drugs (>2 vs. <=2 Times a day)	(73.2 vs 78.4)		-5.2	(-8.1, -2.3)	0.000
Last Drug Injection (5-12 vs. 0-4 weeks)	(79.5 vs 74.8)		4.7	(1.5, 7.9)	0.004
Days injected 3mo prior (>=30 vs. <30)	(72.9 vs 78.8)		-5.9	(-8.8, -3.1)	0.000
Utox Any Drug (Yes vs. No)	(75.9 vs 76.6)		-0.6	(-9.0, 7.7)	0.88
Utox Amphetamine (Yes vs. No)	(69.1 vs 78.3)		-9.2	(-12.9, -5.6)	0.000
Utox Methamphetamine (Yes vs. No)	(69.3 vs 78.5)		-9.2	(-12.8, -5.5)	0.000
Utox Benzodiazepine (Yes vs. No)	(75.8 vs 76.1)		-0.3	(-3.2, 2.7)	0.848
Utox Cocaine (Yes vs. No)	(75.1 vs 76.5)		-1.4	(-4.4, 1.6)	0.36
Utox Marijuana (Yes vs. No)	(77.0 vs 75.0)	 -	2.0	(-0.9, 4.9)	0.169
Utox Opiate (Yes vs. No)	(74.1 vs 77.7)		-3.6	(-6.6, -0.7)	0.017
Utox Oxycodone (Yes vs. No)	(71.1 vs 77.8)		-6.8	(-10.0, -3.5)	0.000
		Poor Adherence Good Adherence -12 -8 -4 0 4 8 12			
		Estimated Difference			

AUDIT-C, Alcohol Use Disorders Identification Test; CHC, community health centers; Co-hab, cohabitation; diff, difference; GAD7, general anxiety disorder 7-item; HCV, hepatitis C virus; OR, odds ratio; OTP, opioid treatment programs; OUD, opioid use disorder; PHQ-9, Patient Health Questionnaire-9; SVR, sustained virologic response; UTOX, urine toxicology screen.

Figure S4. Factors Associated With Treatment Initiation in the ITT Population.

Subgroup	SVR Rate	95% CI for Treatment Initiation Rate	Adjusted OR	95% CI	p-value
Race White Black Other(ref)	397/476 (83.4%) 82/103 (79.6%) 122/151 (80.8%)	=	1.93 0.94	(1.10, 3.39) (0.46, 1.93)	0.022 0.867
Sex Male Female	445/528 (84.3%) 172/218 (78.9%)		1.39	(0.92, 2.11)	0.117
Age >=40 <40	348/421 (82.7%) 275/334 (82.3%)	_	0.83	(0.54, 1.26)	0.380
Hispanic/Latino Yes No	136/163 (83.4%) 487/592 (82.3%)		1.17	(0.62, 2.23)	0.627
Marital Status Married/Co-hab Other	72/ 90 (80.0%) 550/648 (84.9%)		0.75	(0.42, 1.33)	0.317
Housing Stable Unstable	299/339 (88.2%) 323/399 (81.0%)		1.90	(1.24, 2.92)	0.003
Transportation Available Maybe or No	261/302 (86.4%) 360/436 (82.6%)		1.52	(0.96, 2.40)	0.074
Employment Employed Unemployed	220/257 (85.6%) 401/480 (83.5%)	-	1.40	(0.89, 2.21)	0.147
Clinic Type CHC CHC OTP	350/443 (79.0%) 273/312 (87.5%)		0.66	(0.42, 1.04)	0.071
OUD Treatment 3mo prior Methadone Neither Buprenorphine(ref)	358/399 (89.7%) 177/209 (84.7%) 85/107 (79.4%)		1.53 1.31	(0.81, 2.86) (0.69, 2.48)	0.188 0.416
Depression PHQ9>14 PHQ9<=14	142/171 (83.0%) 478/544 (87.9%)		0.71	(0.44, 1.17)	0.179
Anxiety GAD7>14 GAD7<=14	114/135 (84.4%) 504/578 (87.2%)		0.90	(0.52, 1.56)	0.712
HCV Genotype Type 1 Type 2 Type 3(ref)	327/368 (88.9%) 41/ 45 (91.1%) 81/ 94 (86.2%)		1.05 1.49	(0.52, 2.13) (0.44, 5.09)	0.883 0.522
HIV Infection Positive Negative	85/102 (83.3%) 357/421 (84.8%)		0.50	(0.25, 1.00)	0.049
AUDIT-C Alcohol Misuse Yes No	190/229 (83.0%) 423/477 (88.7%)		0.66	(0.42, 1.04)	0.075
Times injecting a day >2 Times <=2 times	274/325 (84.3%) 316/355 (89.0%)		0.75	(0.47, 1.20)	0.226
Last Drug Injection 5-12 weeks 0-4 weeks	152/182 (83.5%) 471/572 (82.3%)		1.15	(0.72, 1.83)	0.555
Days injected 3mo prior >=30 days <30 days	286/336 (85.1%) 303/344 (88.1%)	<u></u>	0.82	(0.52, 1.30)	0.393
Utox Any Drug Yes No	571/655 (87.2%) 25/ 27 (92.6%)		0.38	(0.08, 1.69)	0.204
Utox Amphetamine Yes No	163/193 (84.5%) 433/489 (88.5%)	-	0.77	(0.44, 1.35)	0.358
Utox Methamphetamine Yes	186/218 (85.3%)		0.80	(0.45, 1.40)	0.433
No Utox Benzodiazepine Yes	410/464 (88.4%) 318/358 (88.8%)		1.10	(0.68, 1.80)	0.689
No Utox Cocaine Yes No	278/324 (85.8%) 251/287 (87.5%)	_ _	0.73	(0.44, 1.20)	0.219
Utox Marijuana Yes	344/394 (87.3%) 294/337 (87.2%)	-	0.95	(0.59, 1.54)	0.845
No Utox Opiate Yes	302/345 (87.5%) 302/350 (86.3%)	— 	0.66	(0.40, 1.09)	0.105
No Utox Oxycodone Yes No	294/332 (88.6%) 157/182 (86.3%) 439/500 (87.8%)	-	0.82	(0.48, 1.40)	0.469
		0 70 80 90 10	10		

AUDIT-C, Alcohol Use Disorders Identification Test; CHC, community health centers; Co-hab, cohabitation; GAD7, general anxiety disorder 7-item; HCV, hepatitis C virus; ITT, intention to treat; OR, odds ratio; OTP, opioid treatment programs; OUD, opioid use disorder; PHQ-9, Patient Health Questionnaire-9; SVR, sustained virologic response; UTOX, urine toxicology screen.

Figure S5. Factors Associated With Treatment Completion in the ITT (Panel A), mITT (Panel B), and PP (Panel C) Populations.

A

Subgroup	SVR Rate	95% CI for Treatment Completion Rate	Adjusted OR	95% CI	p-value
Race White Black Other(ref)	322/476 (67.6%) 68/103 (66.0%) 106/151 (70.2%)		1.14 1.00	(0.71, 1.81) (0.54, 1.84)	0.585 0.994
Sex Male Female	376/528 (71.2%) 134/218 (61.5%)		1.58	(1.12, 2.23)	0.009
Age >=40 <40	299/421 (71.0%) 216/334 (64.7%)		1.27	(0.90, 1.78)	0.170
Hispanic/Latino Yes No	119/163 (73.0%) 396/592 (66.9%)	-	1.50	(0.89, 2.55)	0.131
Marital Status Married/Co-hab Other	65/ 90 (72.2%) 449/648 (69.3%)		1.20	(0.73, 1.98)	0.475
Housing Stable Unstable	264/339 (77.9%) 250/399 (62.7%)		2.13	(1.51, 2.98)	0.000
Transportation Available Maybe or No	219/302 (72.5%) 294/436 (67.4%)		1.40	(0.97, 2.00)	0.069
Employment Employed Unemployed	189/257 (73.5%) 324/480 (67.5%)		1.57	(1.10, 2.26)	0.014
Clinic Type CHC OTP	278/443 (62.8%) 237/312 (76.0%)		0.65	(0.45, 0.94)	0.020
OUD Treatment 3mo prior Methadone Neither Buprenorphine(ref)	307/399 (76.9%) 141/209 (67.5%) 64/107 (59.8%)		1.59 1.16	(0.98, 2.59) (0.70, 1.94)	0.062 0.559
Depression PHQ9>14 PHQ9<=14	120/171 (70.2%) 392/544 (72.1%)		0.89	(0.60, 1.32)	0.567
Anxiety GAD7>14 GAD7<=14	95/135 (70.4%) 416/578 (72.0%)		0.94	(0.62, 1.44)	0.790
HCV Genotype Type 1 Type 2 Type 3(ref)	274/368 (74.5%) 34/ 45 (75.6%) 67/ 94 (71.3%)		1.04 1.16	(0.61, 1.77) (0.49, 2.72)	0.897 0.739
HIV Infection Positive Negative	68/102 (66.7%) 298/421 (70.8%)		0.52	(0.29, 0.91)	0.023
AUDIT-C Alcohol Misuse Yes No	155/229 (67.7%) 352/477 (73.8%)		0.80	(0.56, 1.14)	0.210
Times injecting a day >2 Times <=2 times	211/325 (64.9%) 277/355 (78.0%)		0.57	(0.40, 0.81)	0.002
Last Drug Injection 5-12 weeks 0-4 weeks	130/182 (71.4%) 385/572 (67.3%)	_	1.33	(0.91, 1.95)	0.145
Days injected 3mo prior >=30 days <30 days	234/336 (69.6%) 252/344 (73.3%)		0.87	(0.62, 1.22)	0.418
Utox Any Drug Yes No	472/655 (72.1%) 20/ 27 (74.1%)		0.63	(0.26, 1.56)	0.323
Utox Amphetamine Yes No	135/193 (69.9%) 357/489 (73.0%)		0.77	(0.49, 1.19)	0.239
Utox Methamphetamine Yes No	155/218 (71.1%) 337/464 (72.6%)	-	0.79	(0.51, 1.22)	0.281
Utox Benzodiazepine Yes No	260/358 (72.6%) 232/324 (71.6%)	#	0.89	(0.62, 1.26)	0.504
Utox Cocaine Yes No	206/287 (71.8%) 285/394 (72.3%)	=	0.79	(0.55, 1.14)	0.207
Utox Marijuana Yes No	243/337 (72.1%) 249/345 (72.2%)	-	0.91	(0.64, 1.29)	0.602
Utox Opiate Yes No	255/350 (72.9%) 237/332 (71.4%)	#	0.86	(0.60, 1.24)	0.421
Utox Oxycodone Yes No	128/182 (70.3%) 364/500 (72.8%)		0.77	(0.51, 1.14)	0.187
		50 60 70 80 90 10 Treatment Completion	0		

Subgroup	SVR Rate	95% CI for Treatment Completion Rate	Adjusted OR	95% CI	p-value
Race White Black Other(ref)	322/397 (81.1%) 68/ 82 (82.9%) 106/122 (86.9%)		0.63 1.02	(0.32, 1.26) (0.41, 2.52)	0.189 0.971
Sex Male Female	376/445 (84.5%) 134/172 (77.9%)		1.63	(1.04, 2.57)	0.035
Age >=40 <40	299/348 (85.9%) 216/275 (78.5%)		1.85	(1.18, 2.91)	0.008
Hispanic/Latino Yes No	119/136 (87.5%) 396/487 (81.3%)		1.86	(0.89, 3.90)	0.098
Marital Status Married/Co-hab Other	65/ 72 (90.3%) 449/550 (81.6%)	-	2.15	(0.95, 4.89)	0.067
Housing Stable Unstable	264/299 (88.3%) 250/323 (77.4%)	—	2.11	(1.34, 3.32)	0.001
Transportation Available Maybe or No	219/261 (83.9%) 294/360 (81.7%)		1.25	(0.78, 2.01)	0.359
Employment Employed Unemployed	189/220 (85.9%) 324/401 (80.8%)		1.64	(1.01, 2.65)	0.044
Clinic Type CHC OTP	278/350 (79.4%) 237/273 (86.8%)		0.69	(0.42, 1.12)	0.135
OUD Treatment 3mo prior Methadone Neither Buprenorphine(ref)	307/358 (85.8%) 141/177 (79.7%) 64/ 85 (75.3%)		1.50 1.01	(0.81, 2.79) (0.53, 1.95)	0.199 0.967
Depression PHQ9>14 PHQ9<=14	120/142 (84.5%) 392/478 (82.0%)		1.08	(0.64, 1.83)	0.761
Anxiety GAD7>14 GAD7<=14	95/114 (83.3%) 416/504 (82.5%)	-	0.97	(0.56, 1.69)	0.920
HCV Genotype Type 1 Type 2 Type 3(ref)	274/327 (83.8%) 34/ 41 (82.9%) 67/ 81 (82.7%)		1.06 1.00	(0.54, 2.07) (0.36, 2.79)	0.868 0.997
HIV Infection Positive Negative	68/ 85 (80.0%) 298/357 (83.5%)		0.63	(0.30, 1.31)	0.213
AUDIT-C Alcohol Misuse Yes No	155/190 (81.6%) 352/423 (83.2%)		0.95	(0.60, 1.50)	0.824
Times injecting a day >2 Times <=2 times	211/274 (77.0%) 277/316 (87.7%)		0.50	(0.32, 0.78)	0.003
Last Drug Injection 5-12 weeks 0-4 weeks	130/152 (85.5%) 385/471 (81.7%)	-	1.43	(0.84, 2.41)	0.185
Days injected 3mo prior >=30 days <30 days	234/286 (81.8%) 252/303 (83.2%)		0.92	(0.60, 1.42)	0.706
Utox Aný Drug Yes No	472/571 (82.7%) 20/ 25 (80.0%)		0.90	(0.32, 2.52)	0.839
Utox Amphetamine Yes No	135/163 (82.8%) 357/433 (82.4%)	-	0.78	(0.44, 1.40)	0.409
Utox Methamphetamine Yes No	155/186 (83.3%) 337/410 (82.2%)		0.79	(0.45, 1.41)	0.428
Utox Benzodiazepine Yes No	260/318 (81.8%) 232/278 (83.5%)	-	0.76	(0.49, 1.19)	0.234
Utox Cocaine Yes No	206/251 (82.1%) 285/344 (82.8%)	-	0.87	(0.55, 1.37)	0.552
Utox Marijuana Yes No	243/294 (82.7%) 249/302 (82.5%)	=	0.88	(0.57, 1.37)	0.580
Utox Opiate Yes No	255/302 (84.4%) 237/294 (80.6%)		1.05	(0.67, 1.66)	0.836
Utox Oxycodone Yes No	128/157 (81.5%) 364/439 (82.9%)	-	0.76	(0.46, 1.26)	0.291
		50 60 70 80 90 100)		

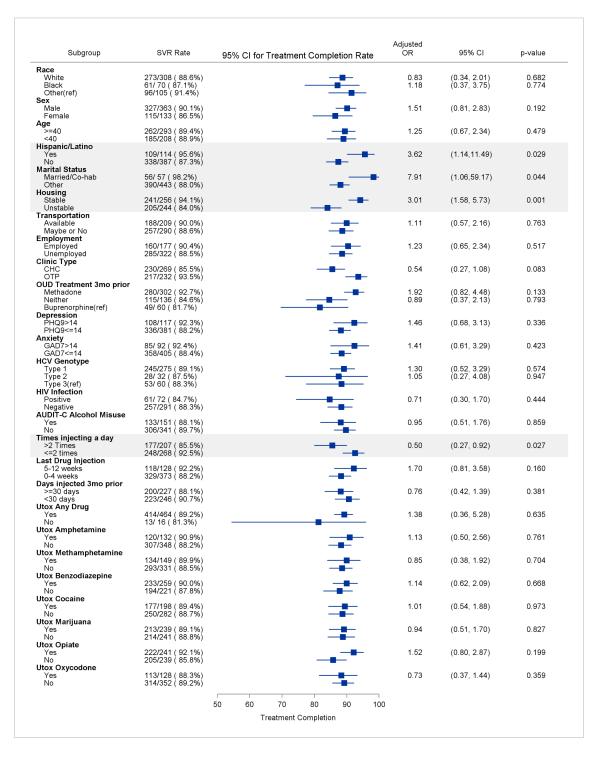


Figure S6. Proportion of Patients With Active Drug Use.

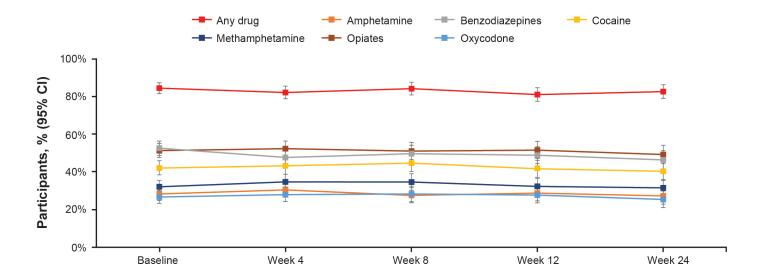
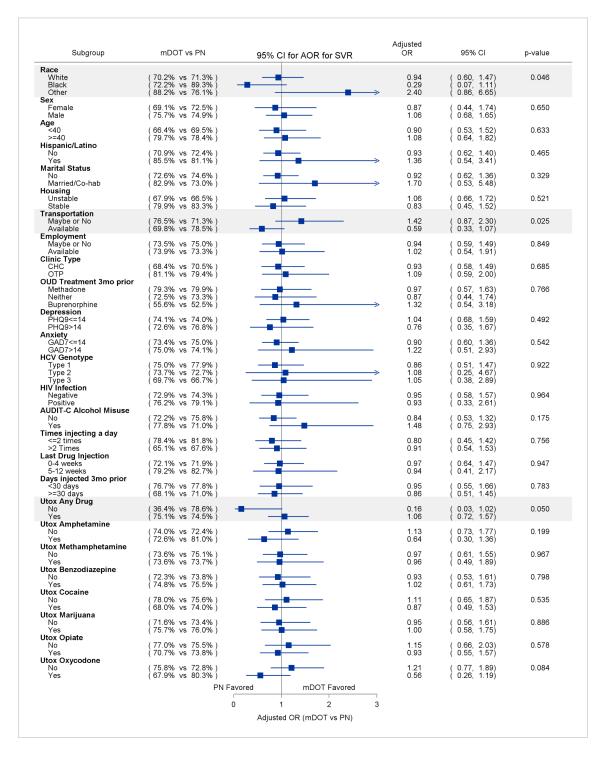
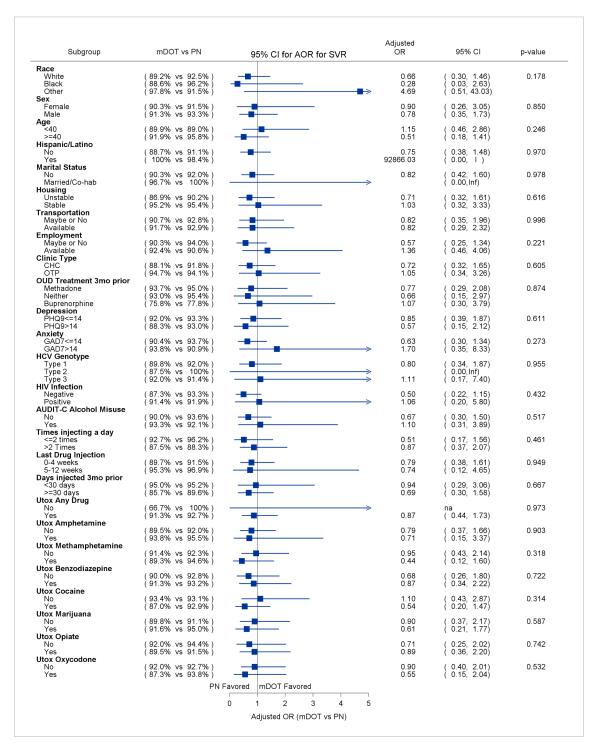


Figure S7. Factors With Between-Subgroup Heterogeneous Intervention Effects on SVR in the ITT (Panel A), mITT (Panel B), and PP (Panel C) Populations

A

Subgroup	mDOT vs PN	95% CI for AOR for SVR	OR	95% CI	p-value
Race White Black Other	(58.4% vs 59.6%) (59.1% vs 67.6%) (64.3% vs 66.7%)		0.96 0.71 0.89	(0.66, 1.42) (0.30, 1.67) (0.45, 1.77)	0.814
Sex Female Male	(51.4% vs 60.6%) (64.1% vs 62.8%)		0.74 1.04	(0.42, 1.29) (0.72, 1.51)	0.309
Age <40 >=40	(53.9% vs 58.0%) (64.9% vs 65.7%)		0.86 0.97	(0.55, 1.36) (0.64, 1.46)	0.705
Hispanic/Latino No Yes	(58.2% vs 59.7%) (67.1% vs 71.4%)		0.96 0.78	(0.69, 1.36) (0.40, 1.53)	0.583
Marital Status No Married/Co-hab	(60.7% vs 64.3%) (63.0% vs 61.4%)		0.87 1.05	(0.63, 1.21) (0.44, 2.53)	0.701
Housing Unstable Stable	(55.2% vs 53.6%) (67.2% vs 77.2%)	_	1.04 0.64	(0.69, 1.57) (0.39, 1.05)	0.135
Transportation Maybe or No Available	(62.0% vs 60.0%) (59.1% vs 69.3%)	-	1.14 0.61	(0.77, 1.70) (0.37, 1.01)	0.055
Employment Maybe or No Available	(59.7% vs 64.4%) (63.0% vs 63.1%)	-	0.83 0.99	(0.57, 1.22) (0.58, 1.69)	0.606
Clinic Type CHC OTP	(53.4% vs 56.4%) (69.9% vs 70.4%)		0.90 0.97	(0.61, 1.32) (0.59, 1.59)	0.821
OUD Treatment 3mo prior Methadone Neither Buprenorphine	(69.1% vs 73.7%) (62.9% vs 60.6%) (42.4% vs 43.8%)		0.80 1.02 1.06	(0.51, 1.24) (0.57, 1.81) (0.48, 2.33)	0.736
Depression PHQ9<=14 PHQ9>14	(63.7% vs 66.4%) (60.2% vs 63.9%)		0.92 0.78	(0.64, 1.33) (0.41, 1.49)	0.653
Anxiety GAD7<=14 GAD7>14 HCV Genotype	(62.4% vs 67.0%) (64.3% vs 61.5%)	-	0.79 1.30	(0.56, 1.13) (0.62, 2.72)	0.234
Type 1 Type 2 Type 3 HIV Infection	(66.5% vs 69.4%) (63.6% vs 69.6%) (59.0% vs 58.2%)		0.89 0.79 0.89	(0.56, 1.40) (0.21, 2.95) (0.37, 2.15)	0.986
Negative Positive AUDIT-C Alcohol Misuse	(60.8% vs 64.1%) (61.5% vs 68.0%)	-	0.93 0.75	(0.61, 1.41) (0.33, 1.72)	0.659
No Yes Times injecting a day	(63.5% vs 67.8%) (62.5% vs 60.7%)	-	0.81 1.17	(0.55, 1.21) (0.67, 2.04)	0.301
<=2 times >2 Times Last Drug Injection	(69.8% vs 72.8%) (53.2% vs 58.7%)	-	0.86 0.78	(0.54, 1.38) (0.49, 1.23)	0.761
0-4 weeks 5-12 weeks Days injected 3mo prior	(58.7% vs 59.8%) (64.2% vs 71.3%)	-	0.92 0.84	(0.65, 1.30) (0.44, 1.60)	0.804
<30 days >=30 days Utox Any Drug	(66.1% vs 70.0%) (57.8% vs 60.6%)	===	0.86 0.85	(0.54, 1.37) (0.54, 1.34)	0.979
No Yes Utox Amphetamine	(33.3% vs 73.3%) (64.7% vs 65.7%)	-	0.18 0.98	(0.03, 1.03) (0.70, 1.37)	0.061
No Yes Utox Methamphetamine	(63.9% vs 65.7%) (62.9% vs 66.7%)		0.96 0.82	(0.65, 1.42) (0.44, 1.51)	0.664
No Yes Utox Benzodiazepine	(63.8% vs 67.7%) (63.2% vs 62.5%)		0.86 1.02	(0.58, 1.29) (0.58, 1.81)	0.628
No Yes Utox Cocaine	(60.7% vs 64.6%) (66.3% vs 67.2%)		0.81 1.02	(0.51, 1.31) (0.65, 1.61)	0.502
No Yes Utox Marijuana	(67.4% vs 66.7%) (58.8% vs 65.5%)	_	1.01 0.83	(0.65, 1.57) (0.51, 1.37)	0.566
No Yes Utox Opiate	(62.4% vs 64.6%) (64.9% vs 67.5%)	===	0.93 0.90	(0.59, 1.47) (0.56, 1.44)	0.922
No Yes Utox Oxycodone	(65.8% vs 69.0%) (61.7% vs 62.9%)	-	0.92 0.97	(0.57, 1.50) (0.62, 1.51)	0.891
No Yes	(65.6% vs 64.8%) (58.5% vs 69.3%)		1.07 0.64	(0.72, 1.57) (0.34, 1.20)	0.175
	PN Fav 0	rored mDOT Favored	3		

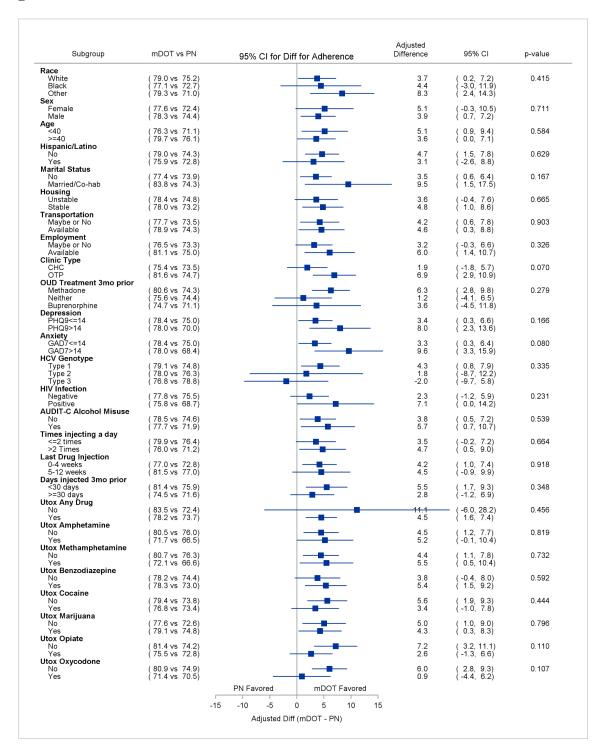




AOR, adjusted odds ratio; AUDIT-C, Alcohol Use Disorders Identification Test; CHC, community health centers; Co-hab, cohabitation; GAD7, general anxiety disorder 7-item; HCV, hepatitis C virus; ITT, intention to treat; mDOT, modified directly observed therapy; OR, odds ratio; OTP, opioid treatment programs; OUD, opioid use disorder; PHQ-9, Patient Health Questionnaire-9; PN, patient navigator; SVR, sustained virologic response; UTOX, urine toxicology screen.

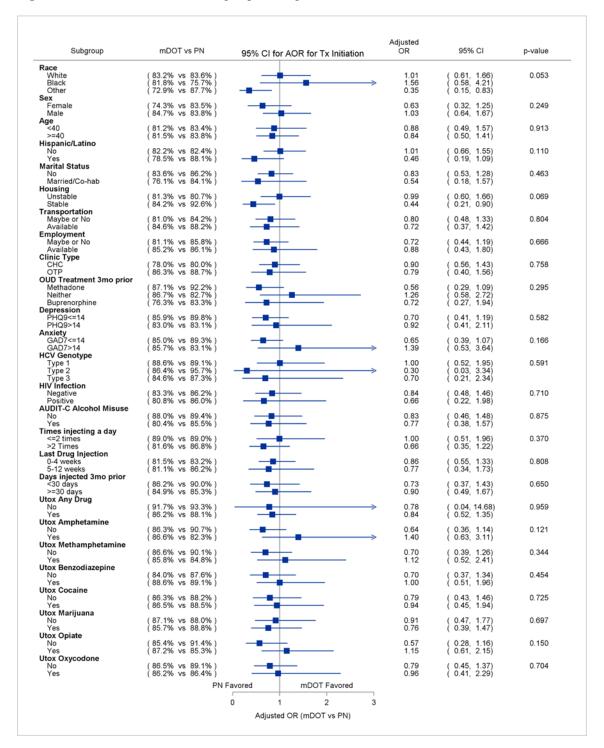
Figure S8. Factors With Between-Subgroup Heterogeneous Intervention Effects on Adherence in the mITT (Panel A) and PP (Panel B) Populations

A Adjusted Difference mDOT vs PN 95% CI Subgroup p-value 95% CI for Diff for Adherence Race White Black Other 76.5 vs 73.2) 75.1 vs 71.2) 78.6 vs 69.2) (-0.0, 6.7) (-3.6, 11.5) (3.4, 15.3) 0.218 3.3 3.9 9.4 Sex Female Male (75.0 vs 72.2) (76.4 vs 71.8) 2.8 4.6 0.549 (-2.4, 7.9) (1.4, 7.8) **Age** <40 (73.2 vs 69.0) (78.4 vs 74.5) 4.2 3.9 0.913 (0.1, 8.3) >=40 Hispanic/Latino No (76.6 vs 72.9) (74.5 vs 69.4) (0.7, 6.8) (-0.6, 10.9) 0.682 Yes Marital Status (75.4 vs 71.7) (81.1 vs 74.0) 3.6 7.1 0.411 (0.8, 6.5) (-0.6, 14.7) Married/Co-hab Housing
Unstable
Stable
Transportation
Maybe or No
Available (75.6 vs 72.0) (76.5 vs 72.0) 3.6 4.5 (-0.2, 7.4) (0.7, 8.3) 0.719 4.9 3.0 0.487 (76.1 vs 71.2) (75.9 vs 72.9) (1.4, 8.5) (-1.1, 7.1) Employment
Maybe or No
Available
Clinic Type 3.4 5.1 (-0.0, 6.7) (0.6, 9.7) (74.8 vs 71.4) (78.2 vs 73.0) 0.536 (73.3 vs 71.8) (79.6 vs 72.4) 1.5 7.2 0.034 OTP
OUD Treatment 3mo prior Methadone
Neither
Buprenorphine
Depression
PHQ9<=14
PHQ9>14 (78.3 vs 72.7) (73.3 vs 71.7) (74.0 vs 69.5) 5.6 1.6 4.5 0.430 (76.1 vs 72.3) (76.3 vs 70.6) 3.8 5.7 0.564 (0.8, 6.9) (0.1, 11.3) Anxiety
GAD7<=14
GAD7>14
HCV Genotype (76.1 vs 72.5) (76.6 vs 69.1) 3.5 7.5 (0.5, 6.5) (1.2, 13.8) 0.263 3AL
2V Geta
Type 1
Type 2
Type 3
HIV Infection
Negative
Cositive
T-C Al 4.6 3.4 -3.7 (77.7 vs 73.1) (75.6 vs 72.2) (72.4 vs 76.1) (1.1, 8.2) (-6.6, 13.4) (-10.9, 3.5) 0.123 (76.1 vs 73.4) (74.5 vs 67.8) 2.8 6.7 (-0.7, 6.2) (-0.4, 13.7) 0.322 AUDIT-C Alcohol Misuse (76.0 vs 73.0) (76.3 vs 69.4) 3.0 6.9 0.195 (-0.2, 6.3) (2.0, 11.7) Times injecting a day <=2 times (78.2 vs 75.0) (73.2 vs 69.1) 3.2 4.1 (-0.5, 6.8) (-0.0, 8.2) 0.733 >2 Times
Last Drug Injection
0-4 weeks
5-12 weeks
Days injected 3mo prior
<30 days
>=30 days
Vtox Any Drug
No
Yes 4.2 3.6 0.847 (74.9 vs 70.7) (79.5 vs 75.9) (1.1, 7.2) (-1.7, 8.9) (78.9 vs 74.9) (72.6 vs 68.8) 3.9 3.8 0.962 (0.1, 7.7) (-0.2, 7.8) (76.7 vs 75.1) (76.0 vs 71.7) 1.6 4.4 (-13.4, 16.6) (1.6, 7.2) 0.719 Yes Utox Amphetamine No 3.7 6.2 0.405 (78.1 vs 74.5) (70.2 vs 63.9) (0.5, 6.9) (1.1, 11.4) Utox Methamphetamine 3.5 6.1 (77.9 vs 74.5) (71.3 vs 65.2) (0.2, 6.7) (1.2, 11.0) 0.374 Yes Utox Benzodiazepine 2.7 5.6 0.288 (76.2 vs 73.5) (76.0 vs 70.3) (-1.4, 6.7) (1.9, 9.4) Utox Cocaine (76.9 vs 72.1) (74.9 vs 71.3) 4.8 3.6 (1.2, 8.5) (-0.6, 7.9) 0.668 Yes Utox Marijuana (75.4 vs 71.9) (76.8 vs 71.7) 3.5 5.1 0.565 (-0.4, 7.4) (1.2, 9.0) Yes Utox Opiate No Yes Utox Oxycodone (79.5 vs 73.0) (73.1 vs 70.3) 6.5 2.8 (2.6, 10.4) (-1.0, 6.6) 0.183 (78.0 vs 72.9) (71.2 vs 68.9) 0.367 No Yes (2.0, 8.3) (-3.0, 7.6) PN Favored mDOT Favored -15 -10 -5 10 15 0 5 Adjusted Diff (mDOT - PN)



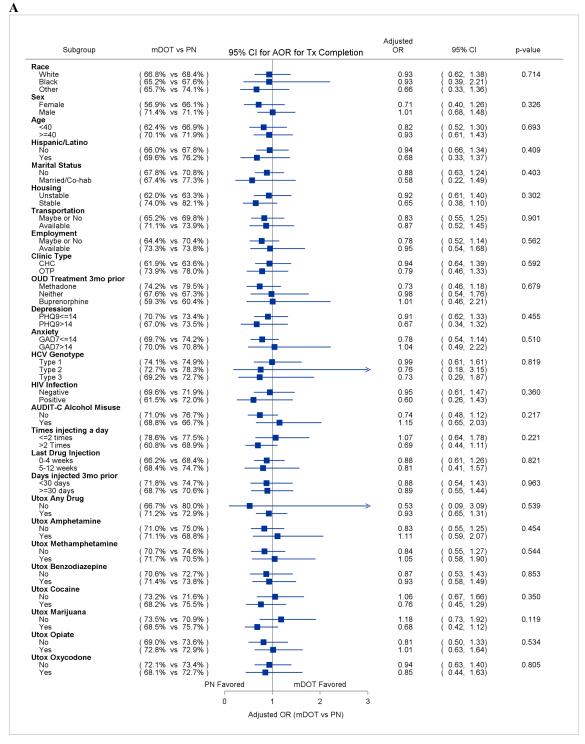
AOR, adjusted odds ratio; AUDIT-C, Alcohol Use Disorders Identification Test; CHC, community health centers; Co-hab, cohabitation; GAD7, general anxiety disorder 7-item; HCV, hepatitis C virus; ITT, intention to treat; mDOT, modified directly observed therapy; OR, odds ratio; OTP, opioid treatment programs; OUD, opioid use disorder; PHQ-9, Patient Health Questionnaire-9; PN, patient navigator; SVR, sustained virologic response; UTOX, urine toxicology screen.

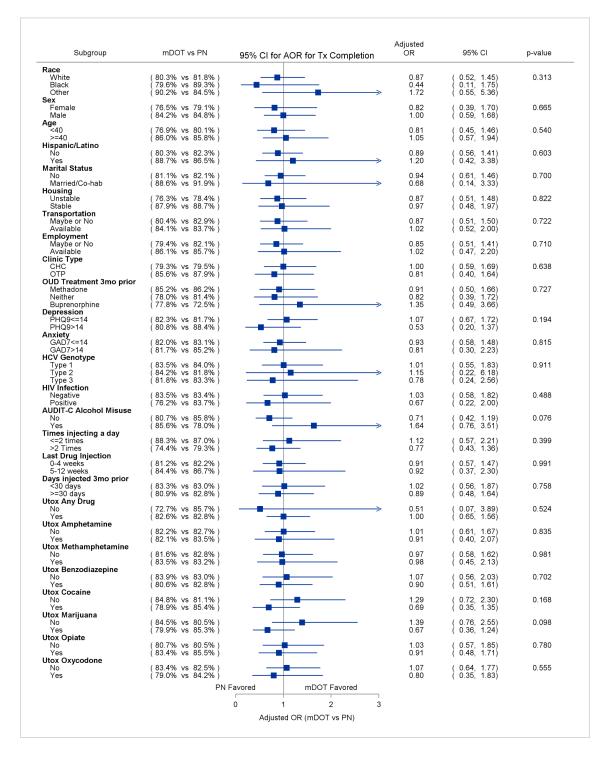
Figure S9. Factors With Between-Subgroup Heterogeneous Intervention Effects on Treatment Initiation in the ITT Population

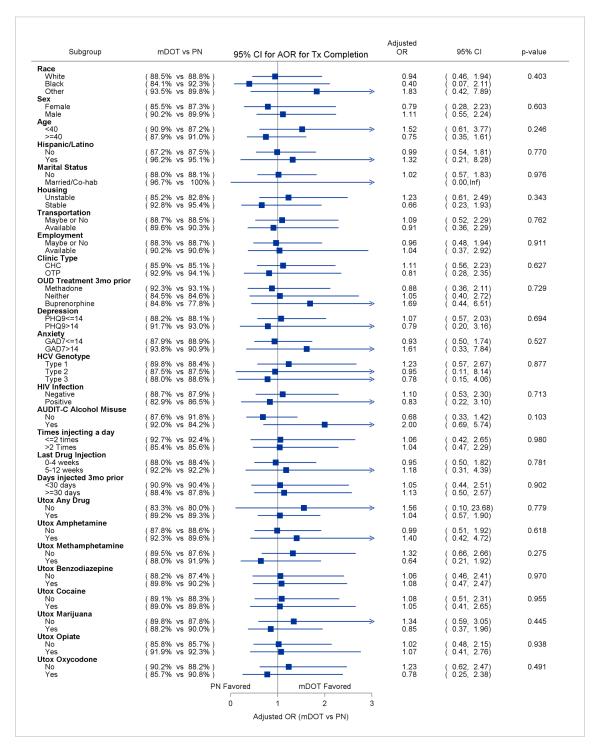


AOR, adjusted odds ratio; AUDIT-C, Alcohol Use Disorders Identification Test; CHC, community health centers; Co-hab, cohabitation; GAD7, general anxiety disorder 7-item; HCV, hepatitis C virus; ITT, intention to treat; mDOT, modified directly observed therapy; OR, odds ratio; OTP, opioid treatment programs; OUD, opioid use disorder; PHQ-9, Patient Health Questionnaire-9; PN, patient navigator; SVR, sustained virologic response; Tx, treatment; UTOX, urine toxicology screen.

Figure S10. Factors With Between-Subgroup Heterogeneous Intervention Effects on Treatment Completion in the ITT (Panel A), mITT (Panel B), and PP (Panel C) Populations







AOR, adjusted odds ratio; AUDIT-C, Alcohol Use Disorders Identification Test; CHC, community health centers; Co-hab, cohabitation; GAD7, general anxiety disorder 7-item; HCV, hepatitis C virus; ITT, intention to treat; mDOT, modified directly observed therapy; OR, odds ratio; OTP, opioid treatment programs; OUD, opioid use disorder; PHQ-9, Patient Health Questionnaire-9; PN, patient navigator; SVR, sustained virologic response; Tx, treatment; UTOX, urine toxicology screen.

 Table S1. Baseline Characteristics of HERO Participants Among PP Sample.

		Total	DOT	PN	
Characteristic	Category	$(N=501)^{a}$	(N=248) ^a	(N=253) a	P^{b}
Demographic Characterist	ics				
Gender, n (%)	Female	133 (26.5)	62 (25.0)	71 (28.1)	0.654
	Male	363 (72.5)	184 (74.2)	179 (70.8)	
	Transgender or gender non-	5 (1.0)	2 (0.8)	3 (1.2)	
	conforming				
Age	Mean (SD)	44.0 (11.5)	44.6 (11.7)	43.4 (11.3)	0.211
	Median (Q1, Q3)	42.6 (35.3, 53.7)	44.0 (35.7, 54.6)	41.6 (35.1, 51.1)	
Race, n (%)	White/Caucasian	308 (63.8)	148 (62.2)	160 (65.3)	0.037
Kacc, ii (70)	Black/African American	70 (14.5)	44 (18.5)	26 (10.6)	0.037
	Other	105 (21.7)	46 (19.3)	59 (24.1)	
Latino/Hispanic ethnicity,	Yes	114 (22.8)	53 (21.4)	61 (24.1)	0.465
n (%)	No	387 (77.2)	195 (78.6)	192 (75.9)	
Marital/	Single/separated/	438 (87.6)	215 (87.0)	223 (88.1)	0.795
cohabitation status, n (%)	divorced/widowed				
	Married/living together as	57 (11.4)	30 (12.1)	27 (10.7)	
	married				
	Other	5 (1.0)	2 (0.8)	3 (1.2)	
Education, n (%)	Less than HS	118 (23.6)	67 (27.1)	51 (20.2)	0.183
	HS diploma or GED	189 (37.8)	90 (36.4)	99 (39.1)	
	Some college or more	193 (38.6)	90 (36.4)	103 (40.7)	
Living situation ^c , n (%)	Shelter	34 (6.8)	20 (8.1)	14 (5.5)	0.741
Living situation, ii (%)					0.741
	Street/Outdoors	27 (5.4)	16 (6.5)	11 (4.3)	
	Someone else's apartment,	127 (25.4)	60 (24.3)	67 (26.5)	
	room, or house				
	Institution	37 (7.4)	17 (6.9)	20 (7.9)	
	Own/rent apartment, room,	256 (51.2)	125 (50.6)	131 (51.8)	
	or house				
	Other	19 (3.8)	9 (3.6)	10 (4.0)	
Availability of	Yes	209 (41.9)	96 (38.9)	113 (44.8)	0.414
transportation, n (%)	Maybe, if I can get a ride	26 (5.2)	16 (6.5)	10 (4.0)	
-	Maybe, if public	260 (52.1)	133 (53.8)	127 (50.4)	
	transportation is available	(-2)	(55.0)	(50)	
	No	4 (0.8)	2 (0.8)	2 (0.8)	
	Yes	177 (35.5)	92 (37.4)	85 (33.6)	0.375

		Total	DOT	PN	
Characteristic	Category	(N=501) ^a	(N=248) ^a	(N=253) a	P^{b}
Employed with a regular	No	322 (64.5)	154 (62.6)	168 (66.4)	
job or informal work ^d , n					
(%)					
Clinical Characteristics					
Clinical setting, n (%)	OTP	232 (46.3)	113 (45.6)	119 (47.0)	0.741
_	CHC	269 (53.7)	135 (54.4)	134 (53.0)	
Any medication for OUD	Buprenorphine				
in the past 3 months, n (%)	Yes	70 (14.1)	39 (15.8)	31 (12.4)	0.270
-	No	428 (85.9)	208 (84.2)	220 (87.6)	
	Methadone				
	Yes	302 (60.6)	143 (57.9)	159 (63.3)	0.213
-	No	196 (39.4)	104 (42.1)	92 (36.7)	
Depression PHQ-9	Mild (<10)	259 (52.0)	130 (52.6)	129 (51.4)	0.751
severity, n (%)	Moderate (10-14)	122 (24.5)	57 (23.1)	65 (25.9)	
	Moderately severe/severe	117 (23.5)	60 (24.3)	57 (22.7)	
	(>14)			, ,	
Anxiety GAD-7 severity, n	Mild (<10)	309 (62.2)	144 (58.5)	165 (65.7)	0.218
(%)	Moderate (10-14)	96 (19.3)	54 (22.0)	42 (16.7)	
-	Moderately severe/severe	92 (18.5)	48 (19.5)	44 (17.5)	
	(>14)	<i>72</i> (10.5)	10 (19.5)	11 (17.3)	
Genotype, n (%)	Type 1	275 (73.7)	137 (75.3)	138 (72.3)	0.714
Genotype, ii (70)	Type 2	32 (8.6)	16 (8.8)	16 (8.4)	0.714
_	Type 3	60 (16.1)	25 (13.7)	35 (18.3)	
-					
	Type 4	3 (0.8)	2 (1.1)	1 (0.5)	
	Mixed	3 (0.8)	2 (1.1)	1 (0.5)	1.000
HIV infection (positive), n	Yes	72 (19.8)	35 (19.8)	37 (19.9)	1.000
(%)	No	291 (80.2)	142 (80.2)	149 (80.1)	
Cirrhosis (positive), n (%)	Yes	31 (6.2)	16 (6.5)	15 (5.9)	0.808
	No	470 (93.8)	232 (93.5)	238 (94.1)	
Alcohol misuse ^e , n (%)	Yes	151 (30.7)	75 (30.6)	76 (30.8)	0.970
	No	341 (69.3)	170 (69.4)	171 (69.2)	
Last drug injection (within	0-4 weeks	373 (74.5)	184 (74.2)	189 (74.7)	0.640
3 months of screening), n	5-8 weeks	85 (17.0)	45 (18.1)	40 (15.8)	
(%)	9-12 weeks	43 (8.6)	19 (7.7)	24 (9.5)	
	Yes	475 (95.2)	233 (94.3)	242 (96.0)	0.375

		Total	DOT	PN	
Characteristic	Category	(N=501) a	(N=248) ^a	(N=253) a	P^{b}
Drug injection reported	No	24 (4.8)	14 (5.7)	10 (4.0)	
within 3 months of					
baseline f, n (%)					
Number of days injected	Mean (SD)	32.6 (30.5)	32.0 (29.1)	33.2 (31.8)	0.938
drugs in the past 3	Median (Q1, Q3)	24.0 (5.0, 60.0)	25.0 (6.0, 50.0)	21.0 (5.0, 60.0)	
months ^{f,g}					
Times injecting drugs a	Mean (SD)	2.9 (2.7)	2.8 (2.3)	3.0 (2.9)	0.305
day ^{f,h}	Median (Q1, Q3)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	
	≤2 times per day	268 (56.4%)	137 (58.8%)	131 (54.1%)	
	>2 times per day	207 (43.6%)	96 (41.2%)	111 (45.9%)	
Urine Drug Screen Results a	at Baseline Visiti, n (%)				II.
Any drugi	Yes	464 (96.7)	231 (97.5)	233 (95.9)	0.334
	No	16 (3.3)	6 (2.5)	10 (4.1)	
Amphetamine	Yes	132 (27.5)	65 (27.4)	67 (27.6)	0.972
	No	348 (72.5)	172 (72.6)	176 (72.4)	
Methamphetamine	Yes	149 (31.0)	75 (31.6)	74 (30.5)	0.778
	No	331 (69.0)	162 (68.4)	169 (69.5)	
Benzodiazepine	Yes	259 (54.0)	127 (53.6)	132 (54.3)	0.872
	No	221 (46.0)	110 (46.4)	111 (45.7)	
Cocaine	Yes	198 (41.3)	100 (42.2)	98 (40.3)	0.678
	No	282 (58.8)	137 (57.8)	145 (59.7)	
THC/cannabis	Yes	239 (49.8)	119 (50.2)	120 (49.4)	0.856
	No	241 (50.2)	118 (49.8)	123 (50.6)	
Opiate	Yes	241 (50.2)	124 (52.3)	117 (48.1)	0.361
	No	239 (49.8)	113 (47.7)	126 (51.9)	
Oxycodone	Yes	128 (26.7)	63 (26.6)	65 (26.7)	0.967
	No	352 (73.3)	174 (73.4)	178 (73.3)	

CHC denotes community health centers, DOT directly observed therapy, GAD-7 General Anxiety Disorder-7 scale, GED General Educational Development, HS high school, ITT intention-to-treat, mITT modified intention-to-treat, OTP opioid treatment program, OUD opioid use disorder, PHQ-9 Patient Health Questionnaire-9, PN patient navigation, PP per-protocol, THC tetrahydrocannabinol.

^aExtent of missing observations varies across the characteristics.

^bP values are based on Chi-square, Fisher exact, t, or Wilcoxon test comparing between DOT and PN groups among the mITT sample.

^cParticipants were asked: "In the last 3 months, where have you been living most of the time?" Answers included: shelter; street/outdoors; someone else's apartment, room, or house; institution (institution, hallway house, residential treatment facility/program); own/rent apartment, house, or room; other (dormitory/college residence, other, refused, don't know). ^dParticipants were asked: "In the last 3 months, what were your sources of income?" Employed was defined as including (a) a regular job and (b) informal work.

Based on the Alcohol Use Disorders Identification Test score: yes (alcohol misuse vs no). Note that

cutoffs are different for male and female participants.

^fPercentage calculated based upon the Behavioral Risk Assessment administered at baseline visit.

^gParticipants were asked: "In the past 3 months, on how many DAYS did you shoot up anything, including prescribed medications not intended to be injected?"

hParticipants were asked: "How many times a day did you usually inject on the days you injected?"

Percentages calculated based upon conducted urine drug screen at baseline visit.

^jPositive for any drug toxicology (including cannabis, barbituates, buprenorphine, and methadone).

Table S2 . Distribution of SAE by the study arms from N=219 participants (N=109 from mDOT and N=110 for PN)

Serious Adverse Event	Total N(%)	mDOT	PN
Death	35 (8.3%)	17 (7.8%)	18 (8.8%)
Life threatening	17 (4.0%)	6 (2.8%)	11 (5.4%)
Hospitalization	337 (80.1%)	176 (81.1%)	161 (78.9%)
Disability or permanent change	1 (0.2%)	0 (0.0%)	1 (0.5%)
Required intervention to prevent impairment/damage	2 (0.5%)	1 (0.5%)	1 (0.5%)
Other serious important medical event	29 (6.9%)	17 (7.8%)	12 (5.9%)
Total	421	217	204