

Supplementary Table 1: Characteristics of OTPs implementing RAPID HCV from OTP context questionnaire completed by OTP leadership

	Alabama	Baltimore 1	Baltimore 2	San Francisco	Toronto
Setting	Suburban	Urban	Urban	Urban	Urban
OUD treatment	Methadone/buprenorphine maintenance, individual and group counselling				
Other SUD treatment provided at site		Intensive outpatient treatment		Family addiction services	Alcohol use disorder treatment
Other services	Mental health	Health care coordination	Health care coordination	Primary care, Mental health	Benzodiazepine taper treatment
Client volume/month	380	800	544	450	290
HCV prevalence	40%	30%	43%	11%	40%
Clinical staffing	1 MD, 5 RN	2MD, 2 nurses,	1MD, 1 APP, 2 RN	1 MD, 6 RN	7 MD, 1 RN
Phlebotomy onsite	No	Yes	Yes	No	Yes
OTP funding	Private funding and grants	Grants, bundled insurance payments	Fee for service insurance payments	Insurance payments, health department	Ministry of health

Supplementary table 2: RAPID HCV implementation strategies

Strategy name	Strategy	Definition	Actor	Action	Action target	Dose
HCV treatment overview + overview of use of HCV treatment determination tool	Training	Training in HCV evaluation and treatment	HCV care specialist	90-minute session OTP clinical and implementation team staff were invited to attend	OTP clinicians providing care	Once
HCV overview and availability of HCV treatment at OTP	Training	Broad overview of HCV for OTP staff	HCV care specialist/ Research team	Brief information session with OTP staff	All OTP staff	As needed
Peer mentor training	Training	Training to support communication with intervention participants on HCV treatment initiation, adherence and reinfection prevention	Research team staff	Facilitation of 5-module training and post-training evaluation Monthly retraining as needed	OTP clients previously treated for HCV identified by OTP staff as potential peer mentors	At baseline and monthly retraining in specific areas as needed
Access to local HCV specialist support	Local technical assistance	HCV specialist available to OTP staff to guide local HCV test and treatment program implementation and consult as needed for HCV treatment	HCV care specialist	HCV specialist available to OTP staff including regular scheduled check-ins at some sites	OTP clinicians	Continuous

#Peer support	*Patient engagement	An OTP client with lived experience of HCV trained to provide peer support for HCV treatment initiation and adherence support	Peer mentor	Facilitates HCV treatment initiation and adherence	RAPID HCV intervention arm participants	Weekly
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Peers were compensated \$50 for each training completed. Peers had to complete training and score 80% or higher on a post-training assessment prior to performing peer support functions. Peers were supervised in their peer-support roles by site-based research staff. Peer supervisors provided monthly refresher training using components of the initial training, reviewed weekly logs of patient contacts and helped to troubleshoot any issues arising for peers in their peer mentor role

*Peers were expected to engage participants in the RAPID HCV arm at least weekly, either by phone or in-person, providing support based on the stage of participant HCV care engagement. Peers were paid \$20 for each documented weekly interaction per participant supported.

Supplementary Table 3: Factors associated with A. treatment initiation among treatment-eligible and B. sustained virologic response among treatment initiators

A. Factors associated with treatment initiation				
	Referral arm n/N (% [95% CI])	p-value	RAPID HCV arm n/N (% [95% CI])	p-value
Characteristic				
Biological Sex				
Male	9/37 (24 [14-39])		33/36 (92 [79-97])	
Female	3/19 (16 [5-39])	0.461	26/30 (87 [69-95])	0.511
Race				
White/Caucasian only	7/34 (21 [8-44])		34/37 (92 [8-100])	
Black/African only	5/20 (25 [11-47])		21/25 (84 [14-99])	
Others and Multiracial	0/2 (0.0)	0.701	4/4 (100)	0.476
Hispanic	1/3 (33 [3-89])	0.605	2/3 (67 [11-97])	0.191
Education Level				
Less than HS	7/26 (27 [14-45])		21/25 (84 [63-94])	
HS/GED	3/18 (17 [6-40])		20/23 (87 [67-96])	
Some College or Higher	2/12 (17 [5-46])	0.647	18/18 (100)	0.218
Employment Status (Prior 3 years)				
Full Time/Part Time	3/12 (25 [7-60])		16/17 (94 [1-100])	
Retired/Disability	3/14 (21 [6-56])		23/24 (96 [0-100])	
Unemployed	5/28 (18 [7-39])	0.736	18/23 (78 [52-92])	0.211
Marital Status				
Married or committed Relationship	3/18 (17 [5-42])		23/26 (89 [67-97])	
Single, separated, divorced or widowed	9/38 (24 [13-39])	0.550	35/39 (90 [77-96])	0.929
Homeless in last 6 months	2/17 (12 [3-34])	0.227	20/21 (95 [68-100])	0.280
Food insecurity in the past 12 months§§	5/34 (15 [7-30])	0.127	40/41 (98 [84-100])	0.006
Hazardous Alcohol Use¶	0/4 (0)	0.247	8/9 (89 [44-99])	0.752
Clinical Characteristics				
Depression Severity (PHQ-8 ≥ 10)	4/25 (16 [6-36])	0.340	26/28 (93 [76-98])	0.412
Anxiety Severity (GAD-7 ≥ 10)	5/24 (21 [8-45])	0.775	22/24 (92 [73-98])	0.650
Treatment for Drug Use				
Any medication for opioid use disorder	11/46 (24 [10-48])	0.431	50/55 (91 [80-96])	0.655
Methadone	10/42 (24 [12-41])	0.959	48/52 (92 [82-97])	0.133
Drug use characteristics				

Injection drug use reported in the past 30 days**	3/13 (23 [6-57])	0.900	18/21 (86 [65-95])	0.507
Urine drug screen results at baseline visit ‡				
Any drug§	8/43 (19 [9-33])	0.349	37/42 (88 [73-95])	0.650
Study site				
Baltimore 1	8/25 (32 [16-53])		30/34 (88 [73-95])	
Baltimore 2	1/9 (11 [1-57])		12/14 (86 [43-98])	
San Francisco	0/7 (0.0)		5/5 (100)	
Alabama	2/7 (29 [7-66])		5/5 (100)	
Toronto	1/8 (13 [1-63])	0.316	7/8 (88 [40-99])	0.833
Country				
USA	11/48(23 [13-36])		52/58 (90[80-95])	
Canada	1/8 (13 [2-58])	0.506	7/8 (88 [38-99])	0.853
B. Factors associated with SVR among treatment initiators				
Characteristic				
Biological Sex				
Male	5/11 (46 [20-74])		21/33 (64 [45-79])	
Female	3/3 (100)	0.091	19/26 (73 [53-87])	0.441
Race				
White/Caucasian only	4/9 (44 [16-78])		21/34 (62 [45-76])	
Black/African only	4/5 (80 [31-97])		15/21 (71 [45-88])	
Others and Multiracial		0.198	4/4 (100)	0.273
Hispanic	1/1 (100)	0.369	1/2 (50 [5-95])	0.584
Education Level				
Less than HS	5/7 (71 [16-97])		10/21 (48 [23-73])	
HS/GED	2/5 (40 [8-84])		15/20 (75 [14-98])	
Some College or Higher	1/2 (50 [4-96])	0.542	15/18 (83 [58-95])	0.041
Employment Status (Prior 3 years)				
Full Time/Part Time	1/5 (20 [0-97])		13/16 (81 [35-97])	
Retired/Disability	2/3 (67 [7-98])		15/23 (65 [11-97])	
Unemployed	4/5 (80 [14-99])	0.191	12/18 (67 [39-86])	0.315
Marital Status				
Married or committed Relationship	2/5 (40 [8-84])		17/23 (74 [41-92])	
Single, separated, divorced or widowed	6/9 (67 [33-89])	0.334	23/35 (66 [50-79])	0.277
Homeless in last 6 months	1/2 (50 [5-95])	0.715	12/20 (60 [39-78])	0.254

Food insecurity in the past 12 months§§	4/6 (67 [24-93])	0.533	27/40 (68 [45-84])	0.254
Hazardous Alcohol Use			6/8 (75 [34-95])	0.519
Clinical Characteristics				
Depression Severity (PHQ-8 $\geq$ 10)	3/4 (75 [20-97])	0.506	16/26 (62 [42-78])	0.270
Anxiety Severity (GAD-7 $\geq$ 10)	4/5 (80 [22-98])	0.277	13/22 (59 [38-77])	0.270
Treatment for Drug Use				
Methadone	7/11 (64 [17-94])	0.217	35/48 (73 [59-84])	0.392
Drug use characteristics				
Injection drug use reported in the past 30 days	1/4 (25 [3-81])	0.071	12/18 (67 [39-86])	0.902
Urine drug screen results at baseline visit ‡				
Any drug§	5/10 (50 [21-79])	0.393	26/37 (70 [53-83])	0.598
Study site				
Baltimore 1	6/8 (75 [5-100])		20/30 (67 [13-96])	
Baltimore 2	1/1 (100)		10/12 (83 [1-100])	
San Francisco	-----		5/5 (100)	
Alabama	1/3 (33 [3-91])		2/5 (40 [9-83])	
Toronto	0/2 (0.0)	0.161	3/7 (43 [8-87])	0.112
Country				
USA	8/12 (67 [29-91])		37/52 (71 [60-81])	
Toronto	0/2 (0)		3/7 (43 [10-84])	

Footnotes: Variable distributions are reported as n (% of total non-missing responses) unless otherwise specified. *Extent of missing observations varies across the characteristics

§§ Food insecurity risk was assessed at baseline using a 2-item validated tool: The Hunger Vital Sign. Patients were considered at risk if they reported a response other than “never” to either question on the tool (worry about running out of food or having insufficient food in the prior 12 months)

P-value : chi square of proportions

95% CI robust confidence intervals

Abbreviations: ITT=intention-to-treat. mITT=modified intention-to-treat. PHQ-9=Patient Health Questionnaire-9, OTP=Opioid Treatment Program, MOUD=Medication for Opioid Use Disorder,

Supplementary Table 4: Characteristics of participants who initiated HCV treatment and did not achieve SVR

	Age	Birth Sex	Race	Education	Homeless	Food insecure	Injection drug use	Any substance in toxicology	Completed treatment	Sample for SVR HCV RNA	Site	Study Arm
1	49.5	Male	Black/African	HS/GED	Yes	Yes	No	Yes	No	No	Baltimore 1	Referral
2	39.5	Male	White/Caucasian	College or Higher	No	No	Yes	No	Yes	No	Alabama	Referral
3	56	Male	White/Caucasian	less than HS	No	No	Yes	Yes	No	No	Toronto	Referral
4	60.3	Male	White/Caucasian	less than HS	No	No	No	Yes	No	Yes	Baltimore 1	Referral
5	40.4	Male	White/Caucasian	HS/GED	.	No		Yes	Yes	No	Toronto	Referral
6	38.4	Male	White/Caucasian	HS/GED	No	Yes	Yes	Yes	Yes	No	Alabama	Referral
7	28.6	Female	White/Caucasian	HS/GED	No	No	No	No	Yes	Yes	Alabama	RAPID HCV
8	49.9	Female	Black/African	less than HS	No	Yes	No	No	No	Yes	Baltimore 1	RAPID HCV
9	34.5	Male	White/Caucasian	less than HS	No	Yes	Yes	Yes	No	Yes	Toronto	RAPID HCV
10.	50.5	Male	White/Caucasian	less than HS	No	Yes	No	Yes	Yes	No	Toronto	RAPID HCV
11	48.9	Female	White/Caucasian	College or Higher	No	No	No	No	Yes	No	Alabama	RAPID HCV
12	50.4	Male	White/Caucasian	less than HS	No	Yes	Yes	Yes	Yes	Yes	Baltimore 1	RAPID HCV
13	36.8	Male	White/Caucasian	HS/GED	Yes	Yes	No	Yes	No	Yes	Toronto	RAPID HCV
14	61.6	Male	Black/African	less than HS	No	Yes	No	Yes	Yes	Yes	Baltimore 1	RAPID HCV
15	52	Female	White/Caucasian	less than HS	Yes	Yes	No	No	Yes	No	Baltimore 1	RAPID HCV
16	36.6	Female	White/Caucasian	less than HS	Yes	Yes	Yes	No	Yes	No	Baltimore 1	RAPID HCV
17	48.1	Male	White/Caucasian	less than HS	Yes	No	No	Yes	Yes	No	Baltimore 1	RAPID HCV
18	59.8	Male	Black/African	less than HS	Yes	Yes	No	Yes	No	Yes	Baltimore 1	RAPID HCV
19	45.6	Male	White/Caucasian	College or Higher	.	Yes	Yes	No	Yes	No	Alabama	RAPID HCV
20	43.7	Female	White/Caucasian	HS/GED	Yes	Yes	Yes	Yes	No	Yes	Baltimore 1	RAPID HCV
21	64.5	Female	Black/African	less than HS	No	No	No	Yes	Yes	Yes	Baltimore 2	RAPID HCV
22	50	Male	White/Caucasian	HS/GED	Yes	No	Yes	Yes	No	No	Toronto	RAPID HCV
23	43.5	Male	Black/African	College or Higher	No	Yes	No	Yes	No	Yes	Baltimore 1	RAPID HCV
24	50.7	Male	White/Caucasian	HS/GED	Yes	Yes	No	No	Yes	No	Baltimore 1	RAPID HCV
25	64.5	Male	Black/African	less than HS	No	No	No	No	Yes	Yes	Baltimore 2	RAPID HCV

Supplementary Table 5: Acceptability, Appropriateness and Feasibility of HCV treatment integration scores pre and post implementation

Study site	Mean Scores					
	AIM		IAM		FIM	
	Pre	Post	Pre	Post	Pre	Post
OTP 1	5	4.8	4.5	4.5	4	3.7*
OTP 2	5	4.8	5	5	4.3	3.5
OTP 3	5	n/a	5	n/a	4.3	n/a
OTP 4	5	4.3	5	5	5	4.5
OTP 5	5	5	5	5	5*	5*
Mean score	5	4.7	4.9	4.9	4.5	4.2

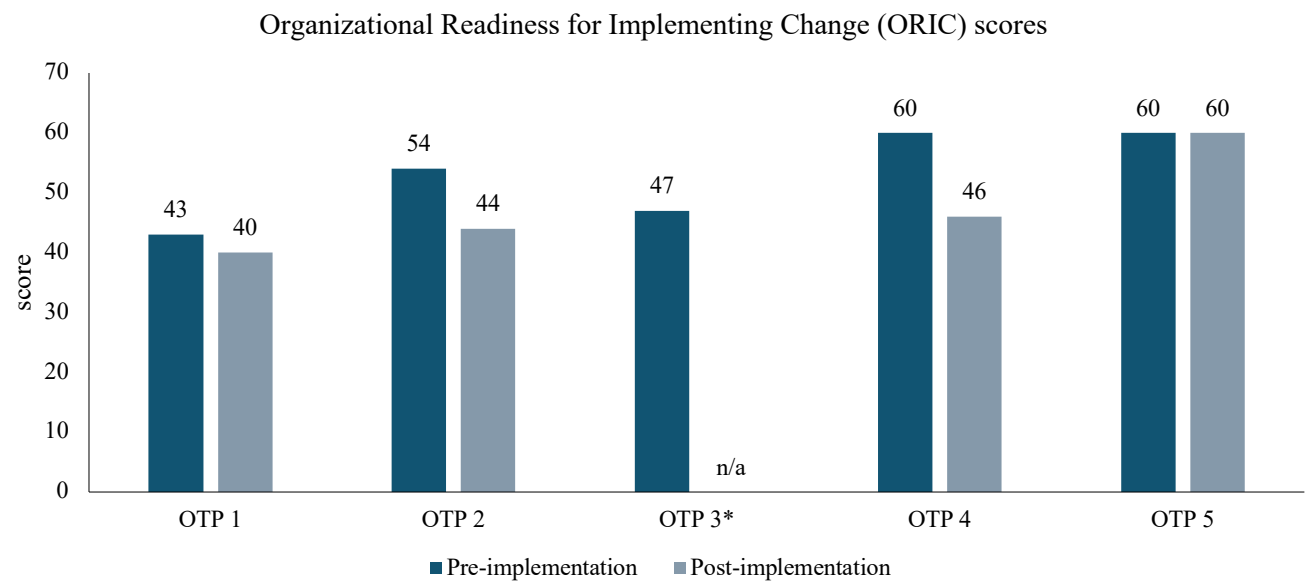
Footnotes: AIM: acceptability of intervention measure, IAM: intervention appropriateness measure, FIM: feasibility of intervention measure. *Only 3 of the 4 items on the FIM questionnaire were completed and used to calculate mean scores; n/a = not available, one (1) site did not complete a post-implementation survey.

SUPPLEMENTARY Figure A1: Organizational Readiness for Implementing Change OTP survey responses

Organizational Readiness ²¹		OTP 1		OTP 2		OTP 3		OTP 4		OTP 5		Average score
		Pre	Post	Pre	Post			Pre	Post	Pre	Post	
1	People who work here feel confident that the organization can get people invested in implementing on-site HCV treatment.											4.3
2	People who work here are committed to implementing on-site HCV treatment.											4.4
3	People who work here feel confident that they can keep track of progress in implementing on-site HCV treatment.											4.3
4	People who work here will do whatever it takes to implement on-site HCV treatment											4
5	People who work here feel confident that the organization can support people as they adjust to on-site HCV treatment.											4.3
6	People who work here want to implement on-site HCV treatment.											4.3
7	People who work here feel confident that they can keep the momentum going in implementing on-site HCV treatment.											3.9
8	People who work here feel confident that they can handle the challenges that may arise in implementing on-site HCV treatment.											4
9	People who work here are determined to implement on site HCV treatment.											4.3
10	People who work here feel confident they can coordinate tasks so that implementation of on-site HCV treatment goes smoothly.											4.1
11	People who work here are motivated to implement on-site HCV treatment.											4.3
12	People who work here feel confident that they can manage the politics of implementing on-site HCV treatment.											4
	Change Commitment (Resolve) ORIC Subdomain	4	3.2	4.8	3.8	4.2		5	4.6	5	5	
	Change Efficacy (Belief in Capacity) ORIC subdomain	3.3	3.5	4.3	3.7	3.7		5	4.6	5	5	

Completely disagree (1)	Disagree (2)	Neither agree nor disagree (3)	Agree (4)	Completely agree (5)	
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SUPPLEMENTARY Figure A2: Organizational Readiness for Implementing Change OTP pre and post-implementation scores



Footnotes: n/a = not available, one (1) site did not complete a post-implementation survey; ORIC scores ranges from 12 - 60.

Appendix B: Study inclusion and exclusion criteria

Inclusion criteria: Participants must meet all of the following inclusion criteria to be eligible for participation

1. Ability and willingness of participant to provide written informed consent
2. Men and women age ≥ 18 to ≤ 70 years at study entry
3. HCV antibody positive/Detectable HCV RNA
4. HCV treatment naïve (no prior treatment with an approved or investigational oral DAA therapy)
5. Negative pregnancy test at screening or at the day of treatment initiation (females of childbearing potential only)
6. If co-infection with Human Immunodeficiency Virus (HIV) is documented, the subject must be anti-retroviral treatment (ART) naïve with CD4 T cell count >500 cells/mm³ OR on a stable ART regimen (containing only permissible ART – Raltegravir; dolutegravir; Rilpivirine; Elvitegravir/cobicistat; Tenofovir disoproxil fumarate; Tenofovir alafenamide; Emtricitabine; Lamivudine and/or Abacavir, bictegravir)

Exclusion criteria: Subjects who meet any of the following exclusion criteria are not to be enrolled in this study

1. Women who are pregnant or breastfeeding, or considering becoming pregnant during the study and for 30 days after the last dose of study drug
2. Known allergy/sensitivity or any hypersensitivity to components of study drugs or their formulation
3. Current or history of decompensated liver disease (including but not limited to encephalopathy, variceal bleeding, or ascites) prior to study entry
4. History of hepatocellular carcinoma (HCC)
5. Any history of active Hepatitis B or positive HBsAg test
6. Platelet count $< 150,000/\text{mm}^3$
7. HCV RNA undetectable
8. History of clinically significant abnormalities or co-morbidities that make the subject an unsuitable candidate for this study, in the opinion of the investigator.
9. Women of childbearing potential that are not practicing at least one specified method of birth control that is effective from Study Day 1 through at least 30 days after the last dose of study drug.

10. Subject is currently taking any of the following prohibited medications:
11. Red yeast rice (monacolin K), St. John's Wort
12. Carbamazepine, Dabigatran, efavirenz, phenytoin, pentobarbital, phenobarbital, primidone, rifabutin, rifampin
13. Subject is not able or willing to safely discontinue the prohibited medications or supplements listed below at least 14 days prior to the first dose of GLE/PIB:
14. Some HMG-CoA reductase inhibitors (including atorvastatin, lovastatin, or simvastatin) should not be taken with the study drug. Subjects receiving these statins should either (a) switch to pravastatin or rosuvastatin at least 14 days or 10 half-lives (whichever is longer) prior to the first dose of study drug or (b) may interrupt statin therapy throughout the treatment period beginning at least 14 days or 10 half-lives (whichever is longer) prior to the first dose of study drug and until 14 days after the last dose of study drug, based on investigator's judgment. If switching to or continuing pravastatin or rosuvastatin, it is recommended to reduce the pravastatin dose by 50% or limit the rosuvastatin dose to 5 mg QD when taking with the study drug.
15. Astemizole, cisapride, terfenadine
16. Ethinyl estradiol

Appendix C: Schedule of events (all participants)

	Recruitment Screen	Day 0	Treatment Day 1	Treatment Week 4	End of Treatment -0d/+30d	Post-Treatment Week 12 -14d/+30d	Post-Treatment Week 24 -14d/+30d	Post-Treatment Week 36 -14d/+30d	Early D/C Visit
Eligibility Review ^a	X	X							
Vital Signs ^b		X							
Demographics		X							
Medical History		X							
Concomitant Medications ^c		X			X				
Randomization		X							
Referral to HCV Treatment (SOC Arm Only)		X							
AE/SAE Collection ^d			→	→	→				
Laboratory Testing									
HBsAg		X							
Pregnancy Test ^e		X							
CBC ^f		X							
HCV RNA ^g		X			X	X		X	X
CMP		X			X	X			X
Urine Toxicology Screen		X			X	X	X	X	
Dried Blood Spot		X			X	X	X	X	X
Surveys/Questionnaires									
Study Survey		X			X	X	X	X	
PRO/QOL Measures		X			X	X	X	X	
Intervention Arm Only									
Peer Contact ^h		X	→ X	→X	→X	→X			X
Study Drug Dispensation ⁱ			X	X					

^aIncluding documentation of HCV infection (antibody) and treatment history.

^bIncluding height, weight, temperature, pulse, respiratory rate, and blood pressure.

^cAll medication (including supplements and over-the-counter) will be collected.

^dAE/SAE collection starts with initiation of DAAs, continues through 30 days after last DAA dose.

^eFor all participants of childbearing potential. Urine or serum test.

^fWith or without differential.

^gCLIA certified.

^hPeer contact to occur weekly and as needed between visits until SVR 12. Contact can be in-person, via phone, or video.

ⁱStudy drug can be dispensed in smaller amounts more frequently if participant is unable to maintain 4-week supply at home.

Appendix D: Schedule of events (participants who do not start HCV treatment by week 12 after randomization in either arm)

For participants who have not initiated treatment by Week 12 after randomization, complete the following.

	Week 12 after randomization -14d/+30d	Week 24 after randomization -14d/+30d	Week 36 after randomization -14d/+30d	Week 56 after randomization -14d/+30d
Laboratory Testing				
Urine Toxicology Screen	X	X	X	X
Dried Blood Spot	X	X	X	X
HCV RNA ^e		X		X
Surveys/Questionnaires				
Study Survey	X	X	X	X
PRO/QOL Measures	X	X	X	X
Rescreen for SOC Participants to Rollover to Intervention Arm				
Eligibility Review		X		
Vital Signs ^a		X		
Concomitant Medications ^b		X		
HBsAg		X		
Pregnancy Test ^c		X		
CBC ^d		X		
CMP		X		
Peer Contact ^f		→		

^aIncluding height, weight, temperature, pulse, respiratory rate, and blood pressure.

^bAll medication (including supplements and over-the-counter) will be collected.

^cFor all participants of childbearing potential. Urine or serum test.

^dWith or without differential.

^eCLIA certified.

^fParticipant will meet with peer on date of rescreen. If participant is still eligible for rollover to Intervention Arm after rescreening labs result, peer contact to occur weekly and as needed between visits until SVR 12. Contact can be in-person, via phone, or video.