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The PREVAIL Study: Intensive Models of HCV Care for People Who Inject Drugs

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INHSU, 2017
Jersey City, New Jersey
September 7, 2017

Disclosures

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Intensive Models of HCV Care for People Who Inject Drugs

Advisory Board / Research Grants

- Gilead Sciences
- Merck Pharmaceuticals

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Introduction

- Majority of new and existing cases of HCV occur among people who inject drugs (PWID).
- Many PWID are denied HCV treatment.
- Directly observed therapy (DOT) vs. self-administered treatment is associated with increased adherence to HCV medications among PWID in IFN-era.
  - unknown whether DOT improves SVR
- Group treatment: effective model of care in IFN-era
- In the DAA-era, It's unknown whether intensive models of care (DOT or group treatment) are better than self-administered treatment for improving adherence, treatment completion, and SVR among PWID.

Grebely 2007, Bonkovsky 2008, Litwin 2011, Stein 2012, Barua 2015

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RCT: Intensive Models of HCV Care for Injection Drug Users – The PREVAIL Study (R01 DA034086)

- Randomize 150 genotype-1 patients to one of three models of on-site care
  - Individual (self-administered treatment)
  - Directly Observed Treatment
  - Group Treatment
- Outcomes: Adherence, Treatment completion, SVR12
  - Adherence measured by electronic blister packs and self-report (Visual Analog Scale)
- What factors are associated with adherence and SVR12?
  - Is drug use associated with decreased adherence and SVR12?

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Methods: Overview

- All subjects received HCV treatment on-site within opiate agonist treatment program
  - All Genotype 1 patients
  - Randomization
    - Blocking: Variable 3 – 6 block size
    - Stratification: IL28B, HIV status, and cirrhosis
  - HCV regimens administered as per AASLD/IDSA guidelines between 10/29/2013 – 5/23/2016

Regimen	Duration	Start Date
TVR/PEG/RBV	24 – 48 weeks	10/29/2013
SOF/RBV ± PEG	12 – 24 weeks	12/10/2013
SOF + SMV	12 – 24 weeks	8/1/2014
SOF + LDV	8 – 24 weeks	11/1/2014

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Randomized, controlled trial

- Individual arm (control arm): subjects self-administer all HCV medications.
- DOT arm: subjects receive observed oral doses by nursing staff at same time as receive methadone or buprenorphine. Weekly directly administered IFN injections (if applicable).
- Group arm: subjects attend weekly treatment group. Weekly directly administered IFN injections (if applicable).

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Eligibility Criteria

Inclusion criteria

- HCV genotype 1
- Age 18 or older
- English or Spanish speaking
- Willing to receive HCV treatment on-site at opiate agonist treatment program
- Receiving methadone/buprenorphine at medication window at least once per week

Exclusion criteria

- Decompensated cirrhosis
- Unable to provide informed consent
- Pregnant or breast-feeding
- Hypersensitivity to any HCV medication

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Directly Observed Treatment (DOT)

Litwin et al, BMC ID 2011

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Group Treatment in Action

Stein, Soloway, Litwin J Substance Abuse Treatment 2014

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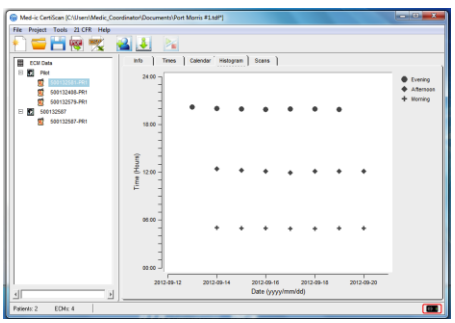
Electronic Blister Packs



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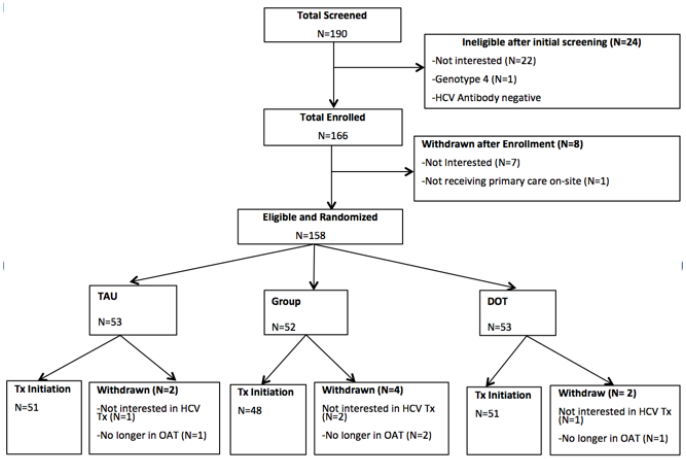
Study Flow Diagram



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Demographics

Characteristic	Individual (n=51)	Group (n=48)	DOT (n=51)	Total (n=150)
	n (%)	n (%)	n (%)	n (%)
Age (years)	51.0 (10.3)	51.2 (10.6)	51.4 (10.3)	51.2 (10.6)
Male	32 (62.8)	32 (66.7)	33 (64.7)	97 (64.7)
Race/ethnicity				
Latino	29 (56.9)	24 (50.0)	31 (60.8)	84 (56.0)
African-American	13 (27.5)	13 (27.1)	13 (25.5)	40 (26.7)
Caucasian	3 (5.9)	5 (10.4)	4 (7.8)	12 (8.0)
Other	5 (9.8)	6 (12.5)	3 (5.9)	14 (9.3)
Not high school graduate	23 (45.1)	21 (43.8)	20 (39.2)	64 (42.7)
Married (living with partner)	35 (68.6)	27 (56.3)	33 (64.7)	95 (63.3)
Homeless	15 (29.4)	10 (20.8)	9 (17.7)	34 (22.7)
Unemployed	41 (80.4)	38 (79.2)	41 (80.4)	122 (81.3)

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Drug Use Characteristics

Characteristic	Individual (n=51)	Group (n=48)	DOT (n=51)	Total (n=150)
Drug use – 6 months				
Any drug	30 (58.2)	34 (70.8)	34 (66.7)	98 (65.3)
Other opiates	21 (41.2)	26 (54.2)	23 (45.1)	70 (46.7)
Cocaine	24 (47.1)	23 (47.9)	24 (47.1)	71 (47.3)
Benzodiazepines	13 (25.5)	15 (31.3)	15 (29.4)	43 (28.7)
Urine drug screen at baseline				
Any drug	28 (54.9)	24 (50.0)	25 (49.0)	77 (51.3)
Opiates/oxycodone	11 (21.6)	14 (29.2)	12 (23.5)	37 (24.7)
Cocaine	16 (31.4)	11 (22.9)	17 (33.3)	44 (29.3)
Benzodiazepines	10 (19.6)	4 (8.30)	9 (17.7)	23 (15.3)
Amphetamines	0 (0)	0 (0)	0 (0)	0 (0)
Injection drug use	35 (68.6)	40 (83.3)	38 (74.5)	113 (75.3)
Current tobacco	44 (86.3)	39 (81.2)	43 (84.3)	126 (84.0)
Opiate agonist treatment				
Methadone	49 (96.1)	47 (97.9)	51 (100)	147 (98.0)
Buprenorphine	2 (3.9)	1 (2.1)	0 (0)	3 (2.0)
Weekly pick up schedule				
1-3	14 (27.5)	12 (25.0)	6 (11.8)	32 (21.3)
4-6	37 (72.6)	36 (75.0)	45 (88.2)	118 (78.7)

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Medical and Psychiatric Comorbidities

Characteristic	Individual (n=51)	Group (n=48)	DOT (n=51)	Total (n=150)
	n (%)	n (%)	n (%)	n (%)
Psychiatric comorbidities				
Any	25 (49.0)	22 (45.8)	20 (39.2)	67 (44.7)
Major depressive episode	12 (23.5)	15 (31.2)	11 (21.6)	38 (25.3)
Generalized anxiety disorder	10 (19.6)	10 (20.8)	8 (15.7)	28 (18.7)
Psychotic disorder	20 (39.2)	17 (35.4)	12 (23.5)	49 (32.7)
Current manic episode	4 (7.8)	6 (12.5)	1 (2.0)	11 (7.3)
Depression (PHQ-9)				
None or mild	31 (60.1)	33 (68.8)	33 (64.7)	97 (64.7)
Moderate or severe	20 (39.2)	15 (31.2)	18 (35.2)	53 (35.3)
HIV/HCV Co-infected	9 (17.7)	6 (12.5)	6 (11.8)	21 (14.0)
Alcohol to intoxication (last 30 days)	12 (23.5)	11 (22.9)	13 (25.5)	36 (24.0)

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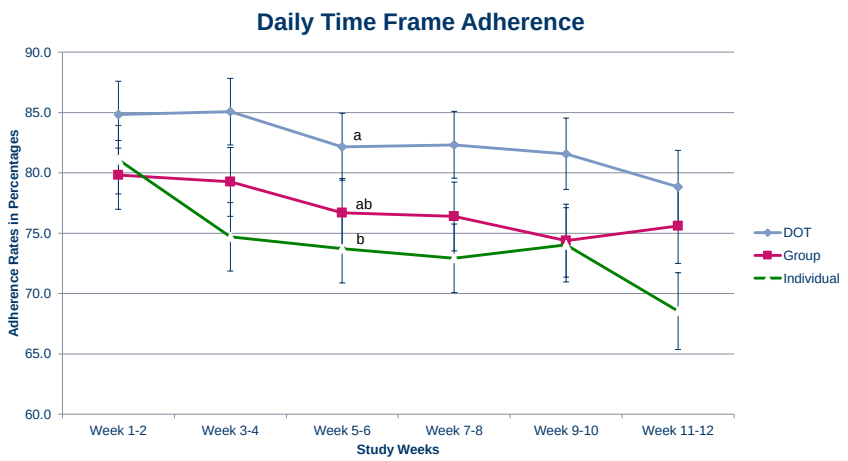
HCV and Treatment Characteristics

Characteristic	Individual (n=51)	Group (n=48)	DOT (n=51)	Total (n=150)
Baseline HCV viral load >2,000,000 IU/ml	24 (47.1)	24 (50.0)	22 (43.1)	70 (46.7)
HCV Subtype 1a 1b	44 (86.3) 7 (13.7)	41 (85.4) 7 (14.6)	43 (84.3) 8 (15.7)	128 (85.3) 22 (14.7)
IL28B C/C T/C T/T	13 (25.5) 27 (52.9) 11 (21.6)	11 (22.9) 26 (54.2) 11 (22.9)	9 (17.7) 26 (50.1) 16 (31.4)	33 (22.0) 79 (52.7) 38 (25.3)
Cirrhosis	10 (19.6)	16 (33.3)	15 (29.4)	41 (27.3)
Treatment-experienced	6 (11.8)	6 (12.5)	4 (7.8)	16 (10.7)
DAA Regimen SOF/LDV SOF/SMV SOF/RBV SOF/RBV/PEG TVR/RBV/PEG	 35 (68.6) 4 (7.8) 5 (9.8) 7 (13.7) 0 (0)	 38 (79.2) 2 (4.2) 3 (6.3) 3 (6.3) 2 (4.2)	 31 (60.8) 5 (9.8) 9 (17.7) 5 (9.8) 1 (2.0)	 104 (69.3) 11 (7.3) 17 (11.3) 15 (10.0) 3 (2.0)
Combination DAAs	39 (76.5)	40 (83.3)	36 (70.6)	115 (76.7)

Adherence higher in DOT vs. Individual (p=0.007)



Overall adherence: DOT (82.8%) vs. Group (77.5%) vs. Individual (74.4%)

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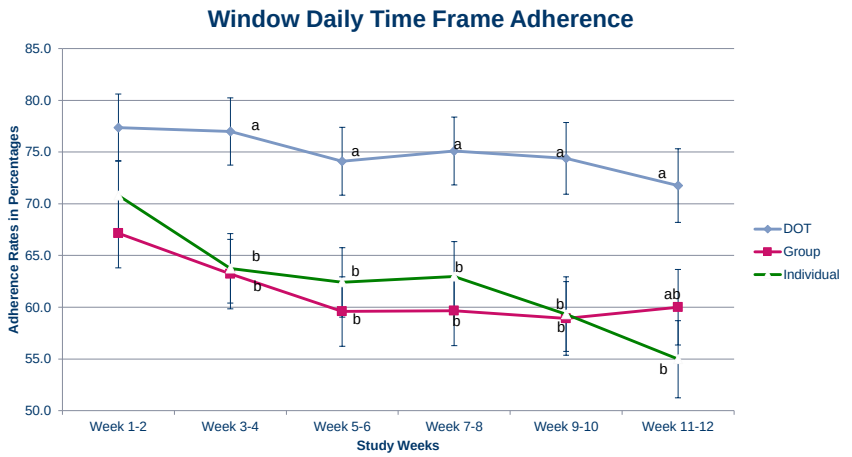
Adherence higher in DOT vs. both Individual (p=0.0008) and Group (p=0.0003)



Overall adherence: DOT (75.0%) vs. Group (61.4%) vs. Individual (62.4%)

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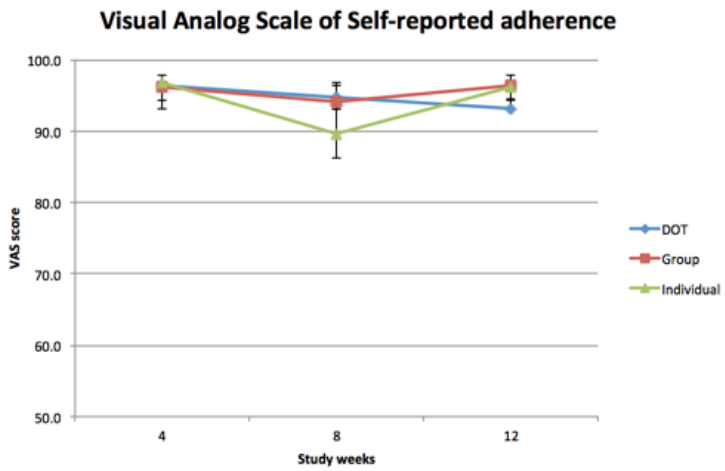
Adherence high in all 3 arms
Self report – Visual Analog Scale (p=0.85)



Overall adherence: DOT (94.8%) vs. Group (95.5%) vs. Individual (94.2%)

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Treatment completion high in all 3 arms (p=0.81)

Study Arm	Completion (≥ 80%)	Reasons for discontinuation
DOT	98.0% (50/51)	Viral non-response (n=1)
Group	95.8% (46/48)	Viral non-response (n=1) Deceased (n=1)
Individual	96.1% (49/51)	Side Effects- vomiting and dyspepsia (n=1) Deceased (n=1)
Total	**96.7% (145/150**) (95% CI 92% - 99%)	

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SVR12 high in all 3 arms (p=0.24)

Study Arm	ETR	SVR12
DOT	98.0% (50/51)	98.0% (50/51)
Group	93.8% (45/48)	93.8% (45/48)
Individual	96.1% (49/51)	90.2% (46/51)
Total	**96.0% (144/150)** (95% CI 92% - 99%)	**94.0% (141/150)** (95% CI 89% - 97%)

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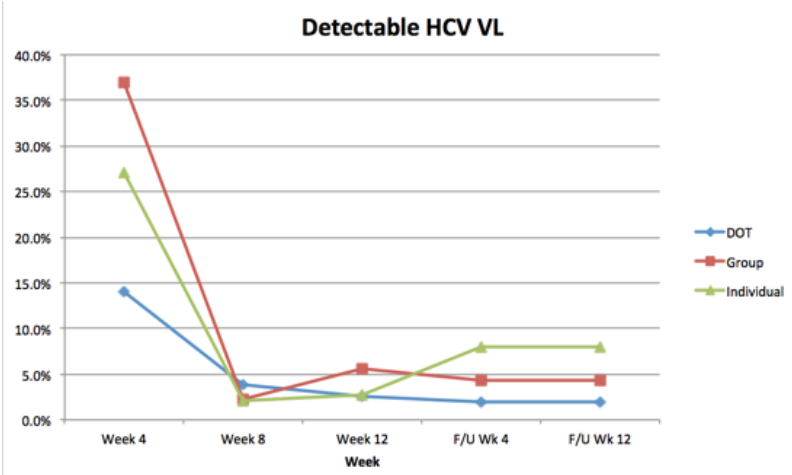
Detectable HCV viral loads significantly different among the 3 arms over time (p=0.035)



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Adherence associated with SVR12

Adherence Measure	10% ↑ in adherence - OR SVR12	P value
Daily adherence	1.62 (95% CI 1.12 – 2.34)	p=0.01
Daily window adherence	1.82 (95% CI 1.20 – 2.75)	p=0.005

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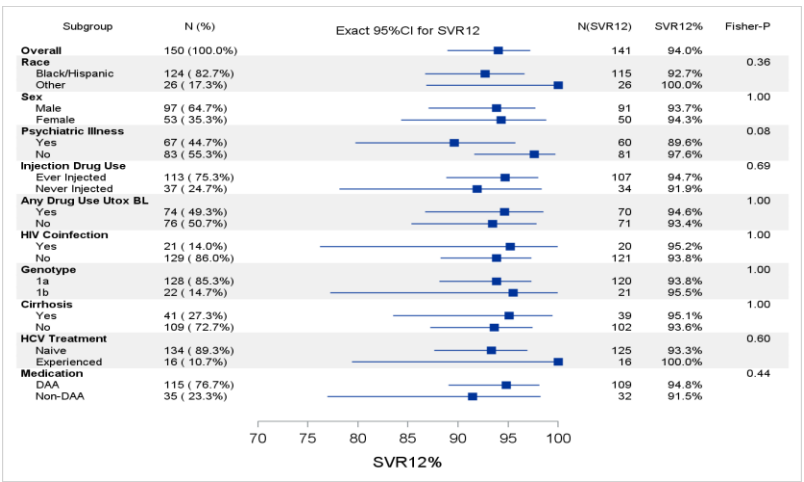
Factors associated with SVR12



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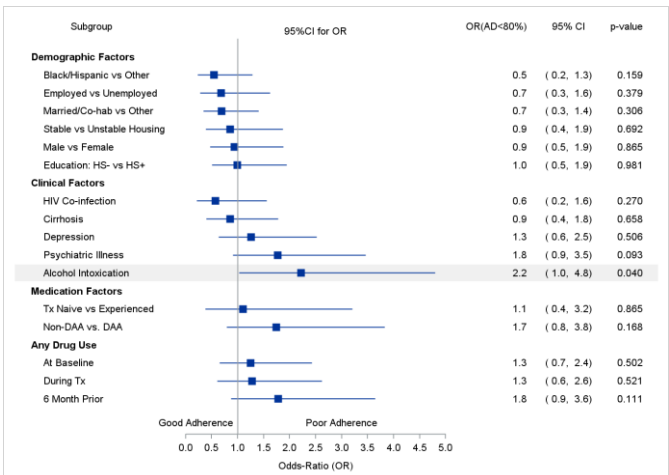
Factors associated with Poor Adherence (< 80%)



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Multivariate Analysis: Drug use not significantly associated with poor adherence (< 80%)

Predictor	OR	95% CI	P-value
Recent drug use (6 months prior)	1.6	0.7 – 3.6	0.22
Any drug use at baseline	1.2	0.6 – 2.5	0.55
Any drug use during HCV treatment	1.1	0.5 – 2.5	0.80

Separate models include age, gender, race, psychiatric illness, homeless status, alcohol intoxication, DAA regimen, and study arm.

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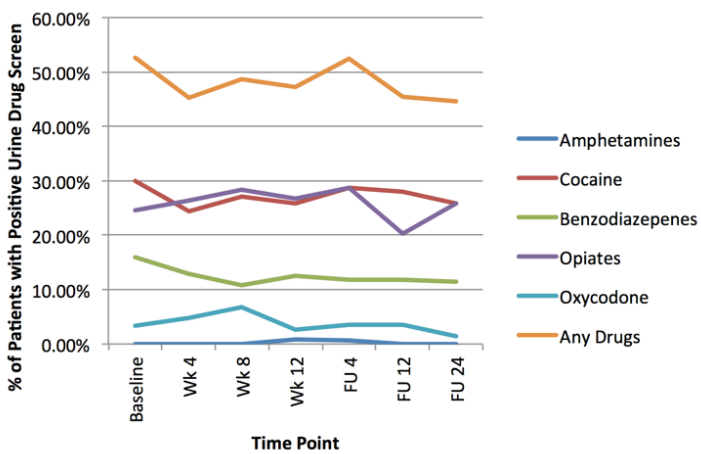
Drug use steady during study period



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Characteristics of Viral Failures (n=9)

#	ARM	Psych HIV	HCV VL	1a/1b	C	1st Tx	DAA Regimen	Drug 6 Mo pretx	Drug on tx	Adh	Viral and Clinical Outcomes
1	G	HIV	19,508,733	1b	Y	Y	**SOF/LDV 7/12 wks**	C/B	C/O	91%	TND at week 4 Deceased: cardiac
2	D	Bipolar Depression	21,382	1a	N	Y	**SOF/RBV 4/12 wks**	C/O/B	No	**79%**	**Wk 4 VL=233,110** **DOT 3x - Dced**
3	I	Depression	485,426	1b	N	Y	**SOF/RBV/P 8/12 wks**	C/O/B	No	No data	**Wk 4 VL=93,692** **Wk 8 VL=3,516** **Dced - side effects**
4	I	Bipolar Depression	188,936	1a	Y	Y	SOF/LDV 8/8 wks	No	B	**43%**	ETR, no SVR4/12
5	I	Depression	2,471,964	1a	N	Y	SOF/LDV 8/8 wks	C/O	C/O	**31%**	ETR, no SVR4/12
6	G	None	7,3000,001	1a	N	Y	SOF/LDV 12/12 wks	C/O	C/O	**38%**	No ETR TND at weeks 4/8
7	G	Depression	12,143,424	1a	N	Y	**SOF/RBV 12/24 wks**	C/O	O	**45%**	**Wk 4 VL=43** **Wk 8 VL=585,602** **Incarcerated**
8	I	Depression	621,760	1a	Y	Y	**SOF/LDV 8/12 wks**	O/B	No	86%	TND at week 8 Deceased: MVA
9	I	Depression	2,976,121	1a	Y	Y	SOF/LDV 12/12 wks	No	O	82%	ETR, no SVR12

Adherence for 9 failures = 61.9% vs. 78.2% (n=150); 53.1% if exclude 2 deceased

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Conclusions

- All three models of care effective: high proportion of completion and SVR12 in G1-infected patients on opiate agonist therapy (OAT) including those actively using drugs
- Adherence higher in DOT vs. Individual and Group
- SVR12 was higher in DOT and group arms, but differences not significant
  - Significant differences in HCV viral load over time
- Increased adherence associated with increased SVR12
- Drug use not associated with adherence or SVR12
- Data demonstrate support for treating active PWID receiving opiate agonist therapy
- We will examine cost-effectiveness and Patient Reported Outcomes in the PREVAIL study

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Research Team

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Acknowledgements

We extend our gratitude to the patients, their families, and clinical site personnel who participated in this study

- NIDA R01 DA034086
- Gilead Sciences
- New York State Department of Health
- Monogram Biosciences

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