Comparing adherence to once-daily and twice-daily DAA therapy among people with recent injecting drug use or current opioid substitution therapy: the SIMPLIFY and D3FEAT studies

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Disclosures

Nothing to disclose

Background/rationale

- There is a significant burden of hepatitis C virus infection among people who inject drugs globally[1]
- In order to reach the targets set by the WHO, scale up of HCV therapy among people who inject drugs is crucial
- Treatment has been shown to be safe and effective in people who inject drugs
    - 94% SVR in SIMPLIFY, 91% if D3FEAT
- Adherence to therapy has been one of the major concerns around scale up of HCV DAA treatment among people who inject drugs

[1]Grebely et al, 2018, Addiction

Aims

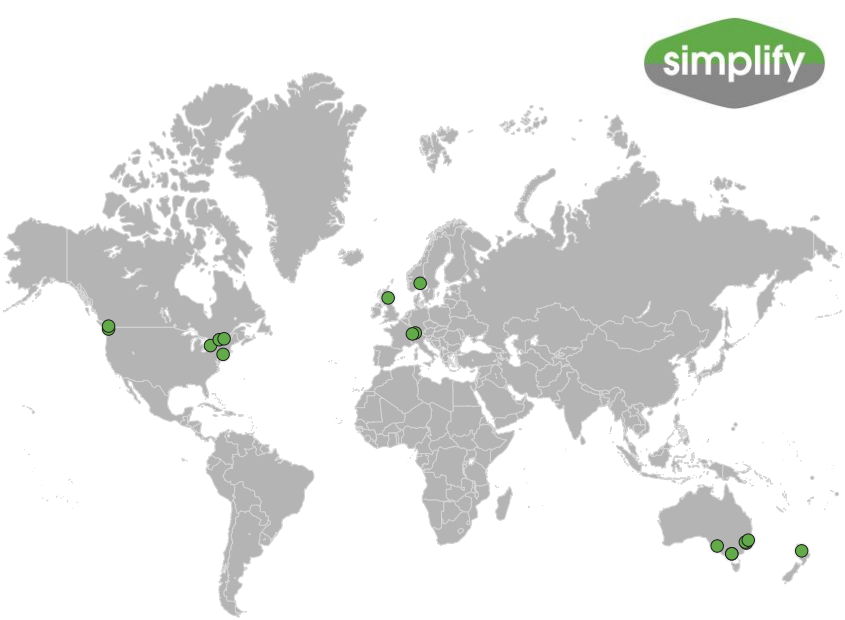
1. Investigate adherence to HCV DAA therapy and associated factors among people with recent injection drug use

2. Investigate the change in adherence over the course of treatment

3. Compare the adherence to once-daily therapy to twice-daily therapy

SIMPLIFY and D3FEAT study design

- International open-label trials of HCV DAA treatment at 25 sites in 8 countries
- Treated with sofosbuvir and velpatasvir (SIMPLIFY; n=103) or PrOD ± RBV (D3FEAT; n=87)



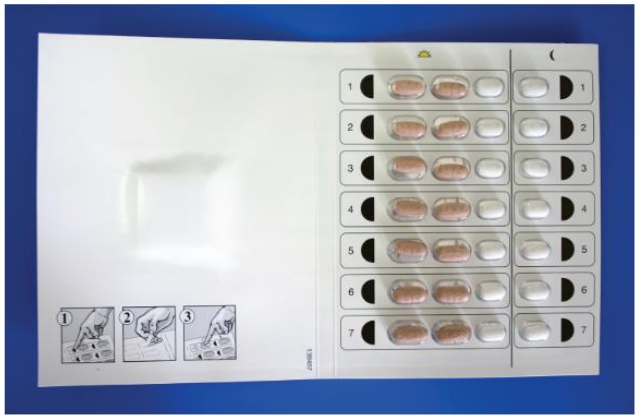
Study design and participant eligibility

- DAA treatment-naïve patients with GT1-6 chronic HCV infection (F0-4)
- People with recent injecting drug use (past six months; SIMPLIFY) or people with either recent injecting drug use or currently on OAT (D3FEAT)
- Participants with HIV and decompensated liver disease excluded

Treatment adherence

- Measured using an electronic blister-pack
  - Administered weekly
- Calculated as the number of doses removed from the blister-pack (max one/two per day) divided by the number of expected doses (84/168 doses).

A)



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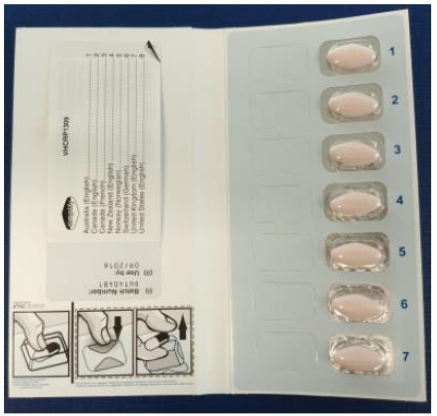


D3FEAT

simplify

Study outcomes and statistical analysis

Non-adherence

- Adherent on <90% of days to a maximum of 100% adherence per day

Ongoing daily adherence

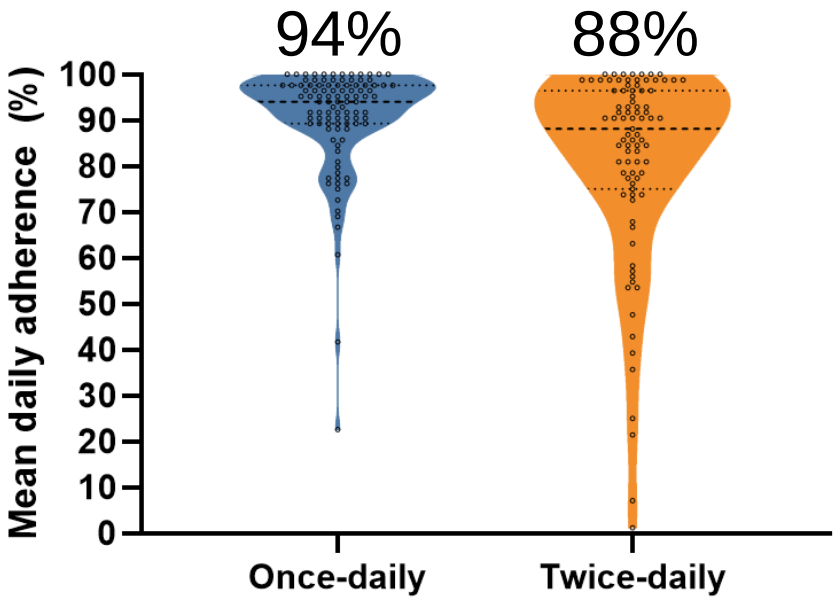
- Mean adherence for the population by treatment day

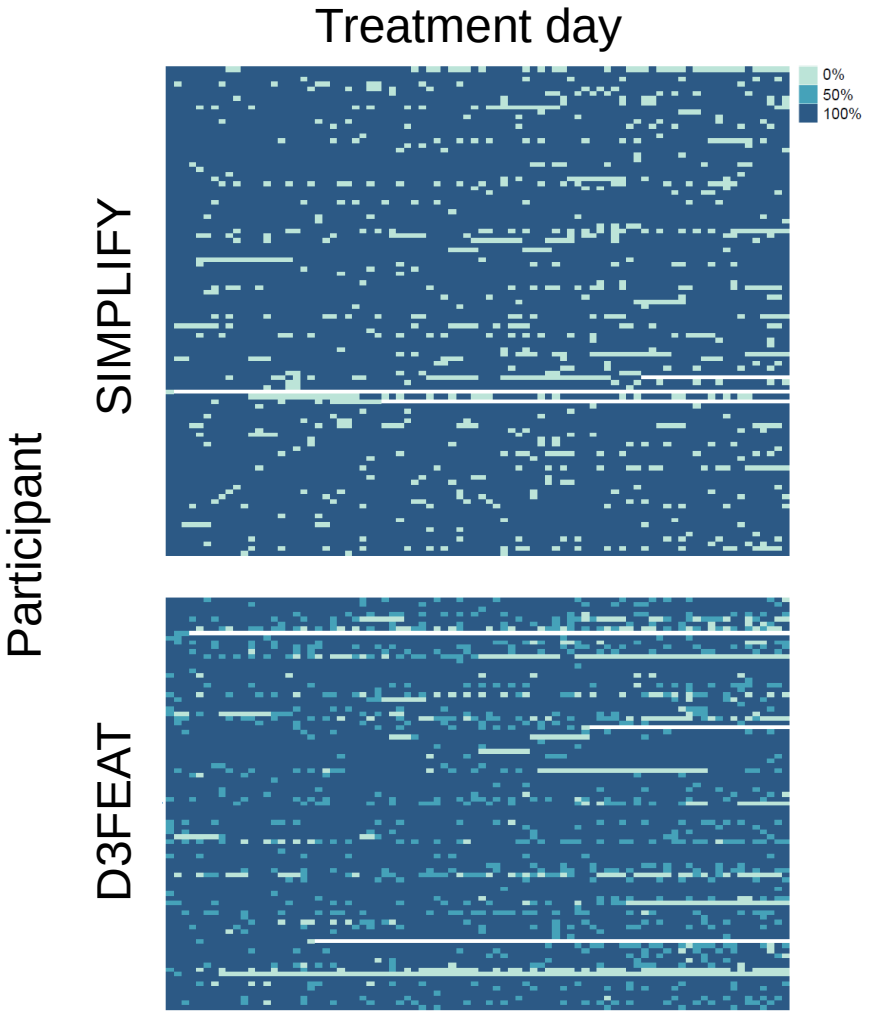
Logistic regression and generalised estimating equations (GEE) used to assess factors associated with study outcomes

Participant characteristics

	Overall (n=190)
Age, median (IQR)	48 (41-53)
Male sex	141 (74)
Unstable housing	37 (20)
Hazardous alcohol consumption	97 (51)
Any injecting drug use in the last month	115 (61)
Heroin	83 (44)
Cocaine	23 (12)
Amphetamines	46 (24)
≥daily injecting drug use	40 (21)
OAT and recent injecting (past month)	
No OAT, no recent injecting	21 (11)
No OAT, recent injecting	47 (25)
OAT, no recent injecting	52 (28)
OAT, recent injecting	68 (36)

Overall adherence of 92%





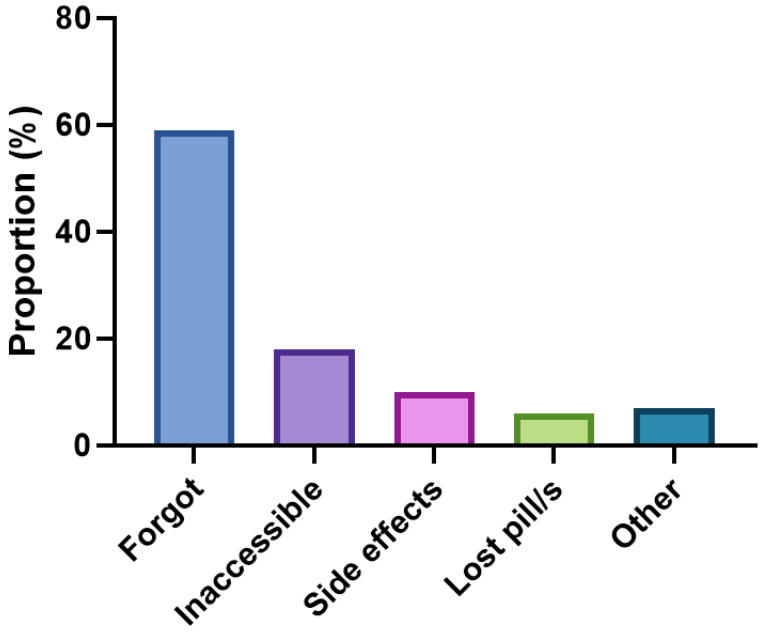
Completion and adherence

Variable	Overall (n=190) n (%)	Once-daily (n=103) n (%)	Twice-daily (n=87) n (%)
Treatment completion	184 (97)	100 (97)	84 (97)
Number of days non-adherent to therapy, n (%)			
None (100% adherent)	19 (10)	12 (12)	7 (8)
1-4 (95-<100% adherent)	56 (29)	36 (35)	20 (23)
5-8 (90-<95% adherent)	35 (18)	20 (19)	15 (17)
9-17 (80-<90% adherent)	34 (18)	17 (17)	17 (20)
≥18 (<80% adherent)	46 (24)	18 (17)	28 (32)
Longest episode of non-adherence (days)			
1	80 (42)	44 (43)	36 (41)
2	39 (21)	19 (18)	20 (23)
3	8 (4)	3 (3)	5 (6)
4	11 (6)	9 (9)	2 (2)
5	5 (3)	2 (2)	3 (3)
6	3 (2)	3 (3)	0 (0)
≥7	25 (13)	11 (11)	14 (16)

Reasons for non-adherence

Self reported reasons for missed doses

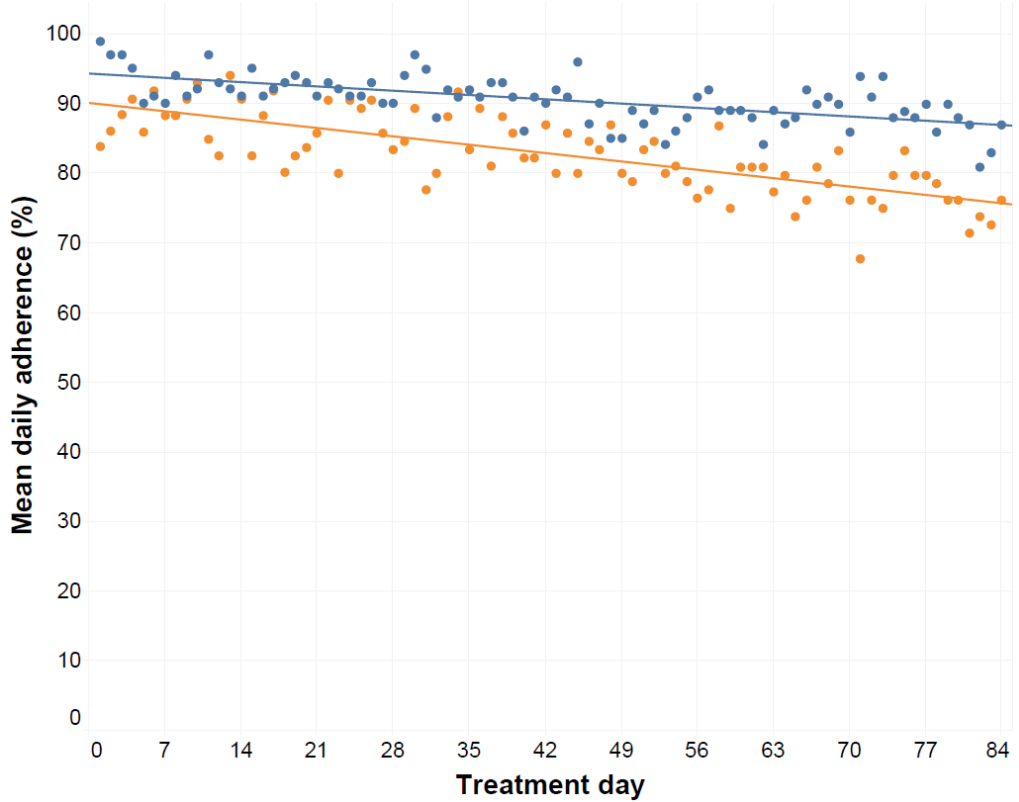
- Reported 4-weekly while on treatment



Factors associated with non-adherence

	DAA adherence of ≥90% (%; n=114)	DAA adherence of <90% (%; n=76)	Unadjusted OR	P	Adjusted OR	P
Housing						
Stable	96 (64)	53 (36)	1.00			
Unstable	17 (46)	20 (54)	2.13 (1.03-4.41)	0.042	2.18 (1.01-4.70)	0.046
Hazardous alcohol consumption						
No	95 (59)	65 (41)	1.00	-		
Yes	19 (68)	9 (32)	0.69 (0.29-1.63)	0.398		
Current OAT						
No	44 (65)	24 (35)	1.00	-		
Yes	69 (58)	51 (43)	1.36 (0.73-2.51)	0.333		
Injecting (last month)						
No	51 (70)	22 (30)	1.00	-		
Yes	63 (55)	52 (45)	1.91 (1.03-3.56)	0.040		
Frequency of injecting (last month)						
Never	51 (70)	22 (30)	1.00	-		
Less than daily	40 (53)	35 (47)	2.03 (1.03-3.98)	0.040		
Daily or greater	23 (58)	17 (43)	1.71 (0.77-3.82)	0.188		
Cocaine/amphetamine injecting (last month)						
No	82 (66)	42 (34)	1.00	-		
Yes	31 (48)	33 (52)	2.08 (1.12-3.85)	0.020	2.48 (1.28-4.82)	0.007
Dosing pattern						
Once-daily	71 (69)	32 (31)	1.00	-		
Twice-daily	43 (49)	44 (51)	2.27 (1.26-4.11)	0.007	2.81 (1.47-5.36)	0.002

Decline in adherence over treatment course



Per treatment week:
aOR=1.08 (95% CI 1.06-1.09)

Impact on SVR

- Overall SVR was 93%
- Three virologic failures (all in D3FEAT)
  - Adherence of 99%, 98% and 86%

- No difference in SVR between those who did/did not miss doses
  - 92% vs 95%, P=0.711
- No difference in SVR between those who did/did not miss 7 consecutive doses
  - 92% vs 93%, P=0.897
- 11 cases of adherence <50%
  - 6 achieved SVR, 5 were lost to follow-up; no virologic failures

Discussion

- Overall high adherence and treatment completion
- Adherence was lower among those receiving twice-daily therapy
- Unstable housing, stimulant injecting, and twice-daily therapy were predictors of lower adherence
- Adherence decreased while on therapy
- Did not impact SVR
  - Research needed to investigate the impact of adherence on shortened duration therapy/simplified monitoring

Acknowledgements

SIMPLIFY and D3FEAT study participants

Study coordination staff: Sophie, Amanda, Pip, Ecaterina, Mahshid

SIMPLIFY study group

D3FEAT study group

Protocol Steering Committee – Gregory Dore (Chair, UNSW Sydney, Sydney, Australia), Philip Bruggmann (Arud Centres for Addiction Medicine, Zurich, Switzerland), Jason Grebely (UNSW Sydney, Sydney, Australia), Philippa Marks (UNSW Sydney, Sydney, Australia), Julie Bruneau (Centre Hospitalier de l'Université de Montréal, Canada), Tracy Swan (Médecins Sans Frontières, New York, United States), Olav Dalgard (Akershus University Hospital, Oslo, Norway), Jude Byrne (Australian Injecting & Illicit Drug Users League), Melanie Lacalamita (Poliklinik für Infektiologie, Inselspital, Bern, Switzerland) and Adrian Dunlop (Newcastle Pharmacotherapy Service, Newcastle, Australia).

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