Maximising Adherence to Direct-Acting Antivirals Among Street-Based and Marginalised Clients: The Results of Daily Dosing

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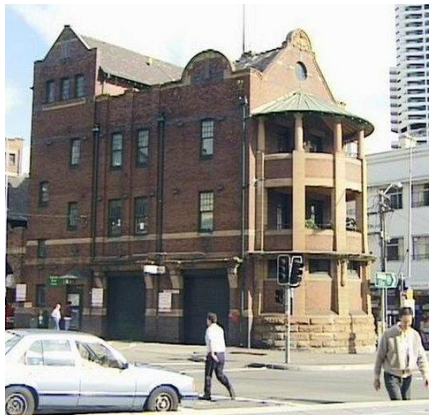
Conflict of interest

- KRC received a research grant in 2016 from Gilead Sciences to evaluate its Hep C adherence program
- PR has received speaking fees and advisory board fees from MSD, and speaking fees and associated travel from Gilead Sciences

Background: Kirketon Road Centre

- Established in Kings Cross in 1987
- An integrated primary health care service model which aims to meet the health and social welfare needs of “at risk” youth, PWID and sex workers. Also sees many clients from homeless, Aboriginal or local LGBTI communities.
- Longstanding hepatitis C service: up-scaled with DAAs and predominantly nurse-led
- Low threshold opioid substitution “access” program- methadone and suboxone
- Hep C program offers a range of support options, including dosing DAAs daily regardless of OAT enrollment



Aim

- The aim of this study was to evaluate treatment support options, and determine adherence among clients selecting supervised DAAs dosing at KRC

Methods

- All clients who commenced DAA therapy prior to March 2018 at KRC were included in this observational cohort
- A subset of clients attending daily or weekly for enhanced adherence support and dosing were analysed separately for adherence
- Demographic, behavioural, clinical measures and medication dosing was recorded and adherence calculated as the proportion of doses taken overall, and over treatment intervals
- Treatment typically extended until all pills taken, or futile to continue
- Factors associated with adherence were examined using logistic regression and generalised estimating equations.

Results: Baseline characteristics

By March 2018, 242 clients had been prescribed DAAs

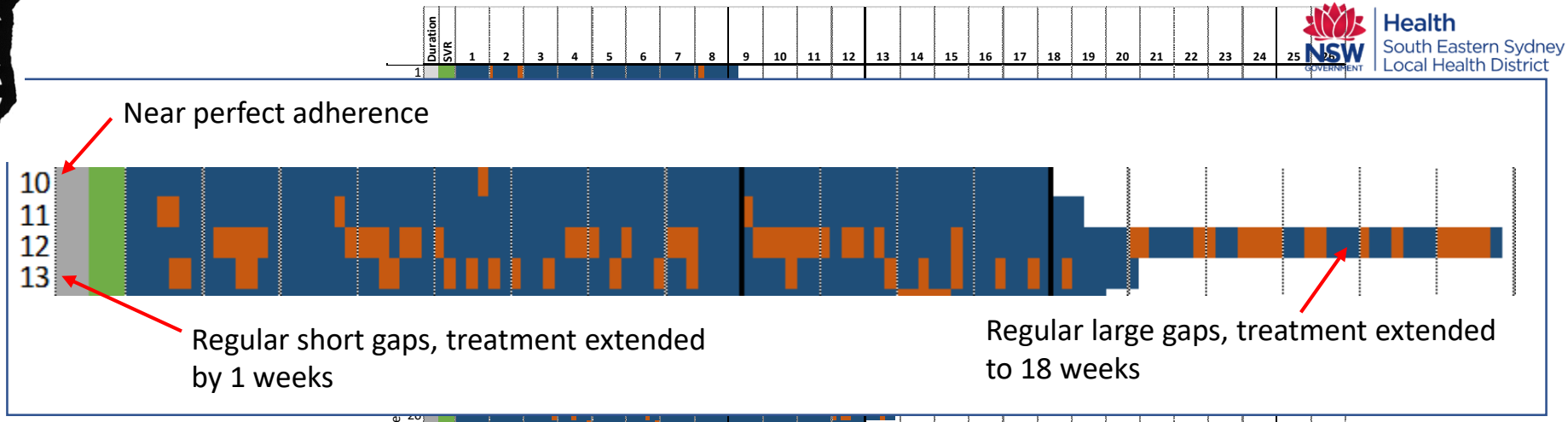
- 163 Standard care
- 79 Enhanced support
  - 43 daily with OAT
  - 6 daily without OAT
  - 30 weekly

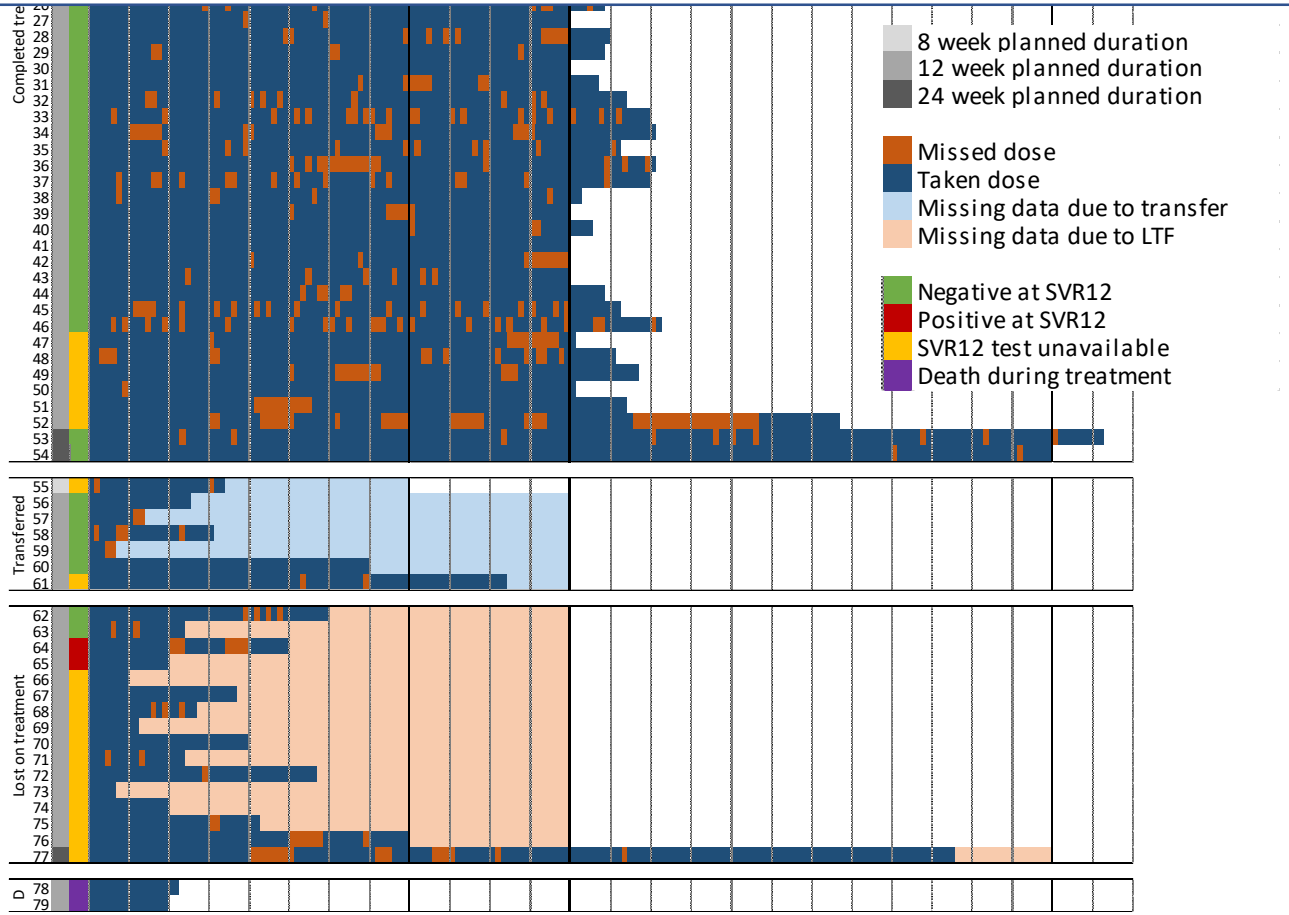
Variable	Overall (n=242)	Standard model (n=163)	Enhanced support (n=79)	p value
Age – median (IQR)	44 (37–51)	46 (39–54)	42 (33–47)	<0.001
Female sex	74 (31)	49 (30)	25 (32)	0.802
Aboriginal	63 (26)	30 (18)	33 (42)	<0.001
Homeless in last 12 months	109 (48)	56 (36)	53 (71)	<0.001
History of mental health diagnosis	106 (44)	50 (31)	56 (71)	<0.001
Injecting drug use				
Ever	235 (97)	156 (96)	79 (100)	0.062
Current, last 6 months	178 (74)	104 (65)	74 (94)	<0.001
Current OAT	90 (44)	43 (33)	47 (63)	<0.001
Age first injected – median (IQR)	18 (16–25)	19(16–26)	18 (15–22)	0.062
Frequency of injecting				
Daily or more	56 (24)	24 (16)	32 (41)	<0.001
Less than daily	107 (46)	69 (45)	38 (49)	
Did not inject in last month	68 (29)	60 (39)	8 (10)	
Receptive equipment sharing last month	52 (22)	28 (18)	24 (30)	0.104
Last drug injected				
Opioid	121 (52)	74 (48)	47 (61)	0.056
Stimulant	111 (48)	81 (52)	30 (39)	
Poly drug use, excluding cannabis	117 (58)	61 (47)	56 (78)	<0.001
HIV co-infected	16 (7)	9 (6)	7 (9)	0.346
Hepatitis B co-infected	5 (2)	2 (1)	3 (4)	0.187
Cirrhosis (F4 fibrosis)	29 (12)	22 (14)	7 (9)	0.298

Results: Adherence

- Overall adherence 85% (IQR 71-94) during planned treatment duration
- Increased to 95% (IQR 80-100%) with extension
- Median days extended was 8 (IQR 5-11)
- Extending treatment increased proportion taking every dose from 4 to 28%

Daily adherence to DAAs and treatment outcome





Results: missed dose episodes

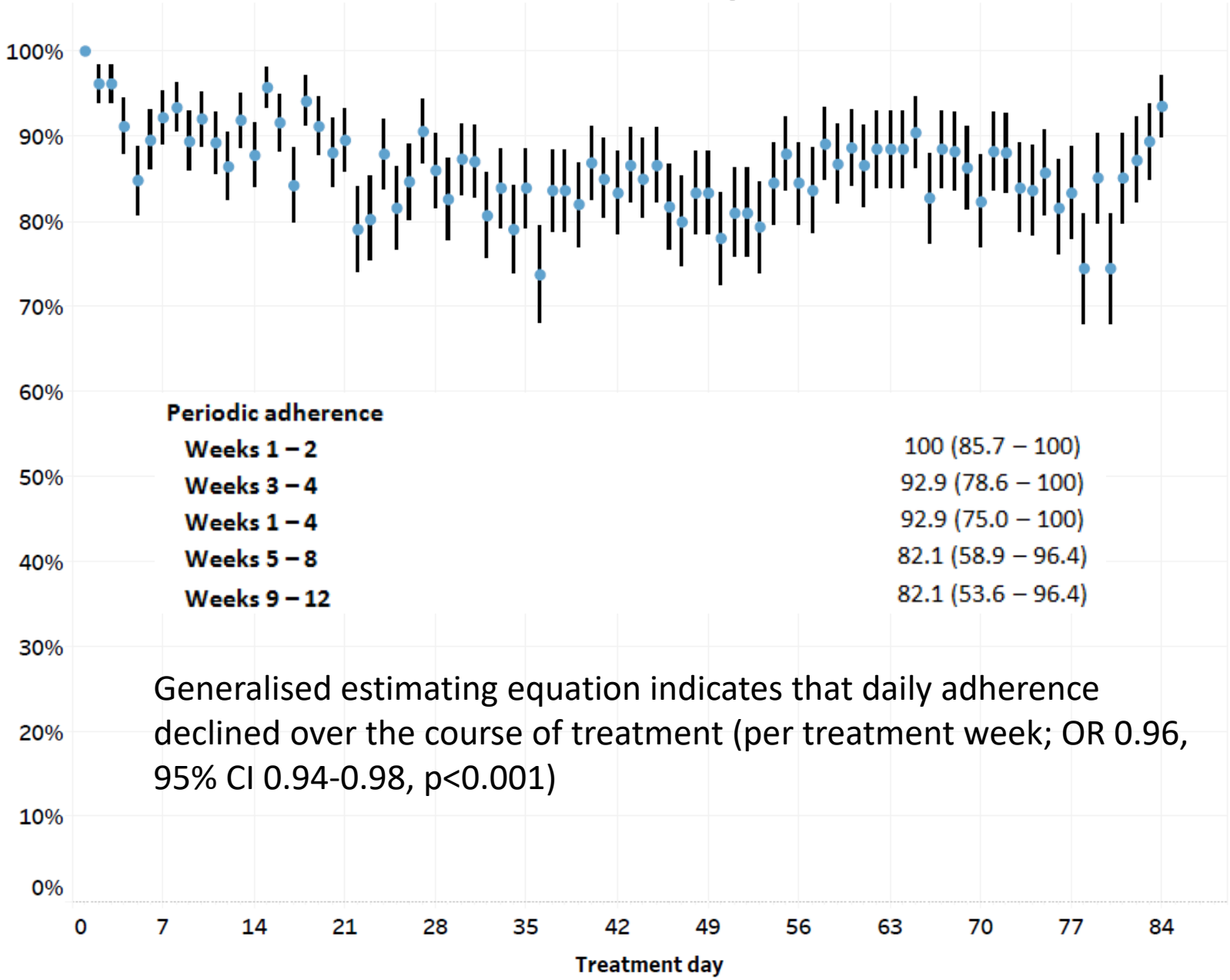
- 72/79 (91%) clients missed at least 1 dose

	N (%)	Median (IQR)
Missed any dose(s) during treatment	72 (91.1)	
First episode of missed dose(s)		
During weeks 1 – 2	39 (49.4)	
During weeks 3 – 4	17 (21.5)	
After week 4	16 (20.3)	
No missed dose(s)	7 (8.9)	
Number of missed doses		10 (4-24)
Number of missed dose episodes per client		3 (1 – 7)
Length of each missed dose episode		1 (1 – 2)

Factors associated with 90% adherence

	< 90% adherence (n=49)	≥ 90% adherence (n=30)	OR (95% CI)	p-value	aOR (95% CI)	p-value
Age – median (IQR)	40 (35-45)	42 (33-49)	1.02 (0.98-1.08)	0.332		
Gender – n (%)						
Male	35 (65)	19 (35)	1.00	-		
Female	14 (56)	11 (44)	1.45 (0.55-3.81)	0.454		
Aboriginal – n (%)	19 (58)	14 (42)	1.38 (0.55-3.46)	0.491		
Homeless in last 12 months– n (%)	36 (68)	17 (32)	0.47 (0.17-1.30)	0.148		
History of mental health diagnosis– n (%)	35 (63)	21 (38)	0.93 (0.34-2.53)	0.892		
Current injecting drug use – n (%)	47 (64)	27 (36)	0.38 (0.06-2.44)	0.309		
Current OAT – n (%)	27 (57)	20 (43)	1.85 (0.68-5.05)	0.229		
Age first injected – median (IQR)	18 (16-21)	18 (15-22)	1.01 (0.96-1.07)	0.614		
Frequency of injecting – n (%)						
Daily or more	20 (63)	12 (38)	1.00	-		
Less than daily	25 (66)	13 (34)	0.87 (0.33-2.31)	0.775		
Did not inject in last month	3 (38)	5 (63)	2.78 (0.56-13.76)	0.211		
Receptive syringe sharing last month–n(%)	15 (63)	9 (38)	0.97 (0.36-2.61)	0.954		
Last drug injected – n (%)						
Opioid	27 (57)	20 (43)	1.00	-		
Stimulant	20 (67)	10 (33)	0.68 (0.26-1.75)	0.419		
Poly drug use	34 (61)	22 (39)	1.42 (0.44-4.66)	0.559		
Month commenced DAAs – median (IQR)	13 (8-19)	9 (3-18)	0.93 (0.87-1.00)	0.053	0.92 (0.84-0.99)	0.031
First missed dose occurred in: – n (%)						
Weeks 1-2	30 (77)	9 (23)	1.00	-		
Weeks 3-4	12 (71)	5 (29)	1.39 (0.39-5.00)	0.615	1.45 (0.38-5.45)	0.585
After week 4	7 (44)	9 (56)	4.29 (1.24-14.77)	0.021	4.59 (1.25-16.93)	0.022
No missed dose(s)	0 (0)	7 (100)	NA	NA	NA	NA

Mean adherence during treatment



Periodic adherence	
Weeks 1 – 2	100 (85.7 – 100)
Weeks 3 – 4	92.9 (78.6 – 100)
Weeks 1 – 4	92.9 (75.0 – 100)
Weeks 5 – 8	82.1 (58.9 – 96.4)
Weeks 9 – 12	82.1 (53.6 – 96.4)

Generalised estimating equation indicates that daily adherence declined over the course of treatment (per treatment week; OR 0.96, 95% CI 0.94-0.98, p<0.001)

Treatment outcomes

- Overall 164/242 (68%) achieved SVR12
  - 164/166 (99%) of those tested achieved cure
  - 70 (29%) lost to follow up
  - 6 (2%) died
  - 2 who remained viraemic received 2 and 5 weeks of therapy respectively (in enhanced group)
- In enhanced support group 52/79 (66%) achieved SVR12
  - 23 LTFU and 2 died, thus 52/54 tested (96%) were cured
- No differences in LFTU or cure in both groups

Conclusion

- Real world data on adherence and outcomes in population with multiple markers of marginalisation
- Adherence support selected by the most disadvantaged, and resulted in equal outcomes
- Extension of therapy to maximise proportion of pills taken proved viable
- Adherence overall was high but variable, and most missed some doses
- Low documented failure rates demonstrate “forgiveness” of DAA regimens even in those with low adherence
- Missing doses in first 4 weeks is associated with worse overall adherence
- Loss to follow-up remains challenging

Thank you

Co-authors

Clients of KRC

Gilead Sciences

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