Real world efficacy of antiviral therapy in chronic hepatitis C in Australia

Issue #2 July 2018[1]

Uptake and outcomes of new treatment for chronic hepatitis C during 2016-2017 in the REACH-C network

The REACH-C project comprises a national network of diverse clinical services. Within the network, 4223 individuals initiated direct acting antiviral (DAA) treatment for chronic hepatitis C virus (HCV) infection between March 2016 and December 2017. Of these individuals, 69% were men, 57% were ≥50 years old and 22% had cirrhosis. The majority of individuals (79%) had not received prior HCV therapy. The most commonly prescribed regimen was sofosbuvir/ledipasvir (48%), followed by sofosbuvir/daclatasvir (37%) and sofosbuvir/velpatasvir (7%). Of individuals expected to reach 12 weeks post-treatment (SVR12) by 31 March 2018, treatment outcomes were unknown in 16%. In 3805 individuals with known treatment outcomes, 96% achieved SVR12. SVR12 rates were high across all treatment settings and baseline characteristics, with a slight reduction in those with cirrhosis vs no cirrhosis (92% vs 97%) and in treatment-experienced individuals vs treatment-naïve (92% vs 97%). People who injected drugs and received opioid substitution therapy were more likely to have a missing SVR12 outcome (26%) than individuals who did neither (11%). Forty individuals treated between March 2016 and December 2017 were subsequently retreated, most commonly with sofosbuvir/velpatasvir (38%) and sofosbuvir/daclatasvir (23%).

1. The Kirby Institute. Real world efficacy of antiviral therapy in chronic hepatitis C in Australia (Issue 2). The Kirby Institute, UNSW Sydney, Sydney, NSW, Australia, July 2018 (available online at: https://kirby.unsw.edu.au). For more information, contact Associate Professor Gail Matthews (gmatthews@kirby.unsw.edu.au) or Dr Jasmine Yee (jyee@kirby.unsw.edu.au).

Since March 2016, new treatments for chronic hepatitis C virus (HCV) have been listed on the Pharmaceutical Benefits Scheme (PBS). These direct acting antiviral (DAA) therapies included:

- March 2016
  - » sofosbuvir/ledipasvir (Harvoni®)
  - » sofosbuvir+daclatasvir (Sovaldi®+Daklinza®)
  - » sofosbuvir+ribavirin (Sovaldi®+Ibavyr®)
  - » sofosbuvir+pegylated interferon-alfa-2a+ribavirin (Sovaldi®+Pegysus®+ribavirin)
- May 2016
  - » ombitasvir/paritaprevir/ritonavir/dasabuvir (Viekira PAK®)
- January 2017
  - » grazoprevir/elbasvir (Zepatier®)
- August 2017
  - » sofosbuvir/velpatasvir (Epclusa®)

The REACH-C project comprises an observational cohort from a national network of 17 diverse clinical services, including specialist liver clinics, drug and alcohol services, sexual health clinics, general practice, community health clinics and prisons. Details of participating clinics are given in Table 1.

Newsletter Issue #2 provides data on the following from within the REACH-C network:

- characteristics of individuals initiating treatment between March 2016 and December 2017
- treatment outcomes of individuals expected to reach 12 weeks post-treatment (SVR12) by 31 March 2018
- characteristics of individuals who failed treatment and were subsequently retreated

Table 1. Details of REACH-C clinics

Clinic	Patients	Location	Type of service/s
Asquith Medical Centre*	24	Sydney, NSW	General practice
Dubbo Community Health Centre*	157	Dubbo, NSW	Community health clinic
East Sydney Doctors*	61	Sydney, NSW	General practice
Kirketon Road Centre	214	Sydney, NSW	Community health clinic
Langton Centre	61	Sydney, NSW	Drug and alcohol
Matthew Talbot Hostel	28	Sydney, NSW	Community health clinic
Prince St Medical Centre	136	Orange, NSW	General practice
Shoalhaven Hospital*	217	Shoalhaven, NSW	Specialist liver clinic, drug and alcohol service, sexual health clinic, general practice
St Vincent's Hospital	690	Sydney , NSW	Specialist liver clinic, drug and alcohol service
The Albion Centre*	102	Sydney, NSW	Sexual health clinic
The Byrne Surgery	36	Sydney, NSW	Drug and alcohol service
Toormina Medical Centre	60	Coffs Harbour, NSW	General practice
Cairns and Hinterland HHS	895	Cairns, QLD	Specialist liver clinic, drug and alcohol service, sexual health clinic, general practice, community health clinic, prison
Royal Adelaide Hospital	237	Adelaide, SA	Specialist liver clinic, community health clinic
The Queen Elizabeth Hospital*	651	Adelaide, SA	Specialist liver clinic, drug and alcohol service, general practice, community health clinic, prison
Scope Gastroenterology	390	Melbourne, VIC	Specialist liver clinic
University Hospital Geelong*	264	Geelong, VIC	Specialist liver clinic

*not previously reported in Newsletter Issue #1

Hepatitis C DAA treatment uptake

Across Australia, an estimated 58,480 individuals initiated treatment for chronic hepatitis C from March 2016 to December 2017[2].

Within the REACH-C network, 4223 individuals initiated chronic HCV therapy between March 2016 and December 2017. Fifty seven percent were aged 50 years or older and 69% were male (Table 2). HCV genotype was reported as 1 and 3 in 53% and 36% of individuals, respectively. These characteristics are similar to the overall Australian population that initiated DAA treatment in 2016-2017.

In the REACH-C cohort, 6% were coinfected with HIV, 16% were engaged in opioid substitution therapy (OST) and 15% had injected drugs in the past 6 months. The majority of individuals (79%) had not received any prior HCV therapy.

The most commonly prescribed regimen was sofosbuvir/ledipasvir (48%), followed by sofosbuvir/daclatasvir (37%) and sofosbuvir/velpatasvir (7%). Of the individuals who were treated with sofosbuvir/ledipasvir, 21% received 8 weeks of treatment and 8% received 24 weeks.

Based on treatment guidelines[3], it was expected that the majority of individuals prescribed sofosbuvir/daclatasvir for 24 weeks would be genotype 3-infected individuals with cirrhosis. However, 17% of those who received sofosbuvir/daclatasvir for 24 weeks were genotype 3 without cirrhosis.

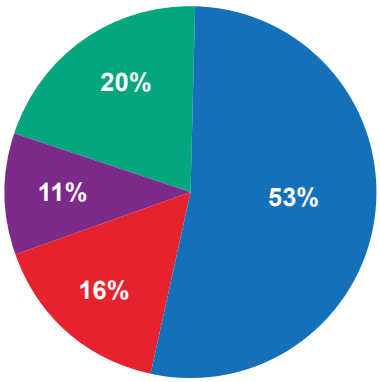


Figure 1. Distribution of liver disease in all patients who commenced treatment in 2016-2017 (n=4223)

F0-1: No or mild fibrosis

F2: Moderate fibrosis

F3: Advanced fibrosis

F4: Cirrhosis

Unknown: n=1322

Hepatitis C DAA treatment regimens for genotype 1

Of the 2242 individuals with genotype 1, 76% (n=1706) had details of all clinical characteristics, including HCV RNA level, relevant to treatment prescription.

Sofosbuvir/ledipasvir prescribed for treatment-naïve individuals without cirrhosis and with pre-treatment HCV RNA <6 million IU/mL, may be delivered as an 8-week treatment course[3]. Of the 806 individuals eligible for 8 weeks of treatment, 42% received an 8-week course, 57% a 12-week course and 1% a 24-week course (Figure 2A).

The majority (96%) of treatment-naïve individuals without cirrhosis who were prescribed sofosbuvir/daclatasvir received it for 12 weeks, in accordance with treatment guidelines[3].

One hundred and three treatment-experienced individuals with cirrhosis commenced treatment, most commonly with sofosbuvir/ledipasvir (86%) or sofosbuvir/daclatasvir (10%; Figure 2B). The majority received a 24-week treatment course (91%), the recommended duration for both regimens in this subgroup[3].

2. Dore and Hajarizadeh (2018) Elimination of Hepatitis C Virus in Australia: Laying the Foundation. Infect Dis Clin N Am 32(2) 269-279.
3. Pharmaceutical Benefits Scheme. General statement for drugs for the treatment of hepatitis C. Canberra: PBS, 1 August 2017. Available at http://www.pbs.gov.au/info/healthpro/explanatory-notes/general-statement-hep-c [Accessed 1 July 2018]

Table 2. Baseline characteristics for all patients who commenced treatment between March 2016 and December 2017 (n=4223) by common regimens

Characteristic	All patients (n=4223)	SOF/LDV 8 weeks (n=421)	SOF/LDV 12 weeks (n=1367)	SOF/LDV 24 weeks (n=176)	SOF+DCV 12 weeks (n=1085)	SOF+DCV 24 weeks (n=427)	GRZ/ELB 12 weeks (n=104)	SOF/VEL 12 weeks (n=240)
Age, n (%)								
≥50 years	2425 (57.4)	190 (45.1)	926 (67.7)	145 (82.4)	461 (42.5)	303 (71.0)	50 (48.1)	118 (49.2)
<50 years	1780 (42.2)	230 (54.6)	432 (31.6)	31 (17.6)	620 (57.1)	123 (28.8)	54 (51.9)	121 (50.4)
Unknown	18 (0.4)	1 (0.2)	9 (0.7)	0 (0)	4 (0.4)	1 (0.2)	0 (0)	1 (0.4)
Gender, n (%)								
Male	2907 (68.8)	256 (60.8)	953 (69.6)	133 (75.6)	734 (67.7)	317 (74.2)	79 (76.0)	164 (68.3)
Female	1304 (30.9)	165 (39.1)	410 (30.0)	43 (24.4)	347 (32.0)	110 (25.8)	25 (24.0)	72 (30.0)
Transgender	7 (0.2)	0 (0)	2 (0.2)	0 (0)	4 (0.4)	0 (0)	0 (0)	1 (0.4)
Unknown	2 (0.1)	0 (0)	2 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1.3)
HIV status n (%)								
Positive	264 (6.3)	4 (1.0)	117 (8.6)	12 (6.8)	84 (7.7)	22 (5.2)	4 (3.9)	16 (6.7)
Negative	3882 (91.9)	412 (97.9)	1217 (89.0)	161 (91.5)	991 (91.3)	399 (93.4)	99 (95.2)	216 (90.0)
Unknown	77 (1.8)	5 (1.2)	33 (2.4)	3 (1.7)	10 (0.9)	6 (1.4)	1 (1.0)	8 (3.3)
Cirrhosis[Δ], n (%)								
Yes	928 (22.0)	5 (1.2)	241 (17.6)	136 (77.3)	50 (4.6)	349 (81.2)	14 (13.5)	57 (23.7)
No	3288 (77.9)	416 (98.8)	1124 (82.2)	39 (22.2)	1032 (95.1)	78 (18.3)	90 (86.5)	182 (75.8)
Unknown	7 (0.2)	0 (0)	2 (0.2)	1 (0.6)	3 (0.3)	0 (0)	0 (0)	1 (0.4)
FibroScan-based staging, n(%)								
No or mild fibrosis (F0-F1)	1546 (36.6)	257 (61.1)	547 (40.0)	8 (4.6)	541 (49.9)	15 (3.5)	40 (38.5)	88 (36.7)
Moderate fibrosis (F2)	468 (11.1)	50 (11.9)	188 (13.8)	9 (5.1)	147 (13.6)	15 (3.5)	13 (12.5)	21 (8.8)
Severe fibrosis (F3)	302 (7.15)	11 (2.6)	112 (8.2)	15 (8.5)	75 (6.9)	43 (10.1)	7 (6.7)	20 (8.3)
Cirrhosis (F4)	585 (13.9)	3 (0.7)	163 (11.9)	97 (55.1)	35 (3.2)	211 (49.4)	7 (6.7)	43 (17.9)
Unknown	1322 (31.1)	100 (3.8)	357 (26.1)	47 (26.7)	287 (26.5)	143 (33.5)	37 (35.6)	68 (28.3)
HCV genotype, n (%)								
1								
1a	1758 (41.6)	327 (77.7)	1006 (73.6)	127 (72.2)	46 (4.2)	12 (2.8)	76 (73.1)	44 (18.3)
1b	357 (8.5)	61 (14.5)	193 (14.1)	22 (12.5)	8 (0.7)	0 (0)	7 (6.7)	15 (6.3)
1, not specified	127 (3.0)	21 (5.0)	80 (5.9)	12 (6.8)	3 (0.3)	4 (0.9)	3 (2.9)	2 (0.8)
2	173 (4.1)	0 (0)	1 (0.1)	0 (0)	49 (4.5)	7 (1.6)	0 (0)	24 (10.0)
3	1538 (36.4)	3 (0.7)	5 (0.4)	6 (3.4)	929 (85.6)	377 (88.3)	0 (0)	115 (47.9)
4	45 (1.1)	0 (0)	12 (0.9)	3 (1.7	3 (0.3)	1 (0.2)	16 (15.4)	6 (2.5)
5	2 (0.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.8)
6	49 (1.2)	0 (0)	10 (0.7)	2 (1.1)	0 (0)	0 (0)	0 (0)	12 (5.0)
Mixed/Other	25 (0.6)	0 (0)	1 (0.1)	0 (0)	13 (1.2)	3 (0.7)	2 (1.9)	1 (1.7)
Unknown	149 (3.5)	9 (2.1)	59 (4.3)	4 (2.3)	34 (3.1)	23 (5.4)	0 (0)	16 (6.7)
HCV RNA, n (%)								
<6 million IU/mL	2345 (55.5)	356 (84.6)	733 (53.6)	95 (54.0)	626 (57.7)	241 (56.4)	58 (55.8)	141 (58.8)
>6 million IU/mL	556 (13.2)	12 (2.9)	244 (17.9)	25 (14.2)	134 (12.4)	63 (14.8)	14 (13.5)	46 (19.2)
Unknown	1322 (31.3)	53 (12.6)	390 (28.5)	56 (31.8)	325 (30.0)	123 (28.8)	32 (30.1)	52 (22.1)
Previous HCV therapy, n (%)								
No	3318 (78.6)	406 (96.4)	1180 (86.3)	56 (31.8)	954 (87.9)	316 (74.0)	91 (87.5)	191 (79.6)
Yes, interferon-containing	479 (11.3)	4 (1.0)	149 (10.9)	97 (55.1)	97 (8.9)	92 (21.6)	6 (5.8)	19 (7.9)
Yes, interferon-free	63 (1.5)	1 (0.2)	5 (0.4)	10 (5.7)	9 (0.8)	11 (2.6)	4 (3.9)	9 (3.8)
Yes, not specified	21 (0.5)	0 (0)	3 (0.2)	10 (5.7)	2 (0.2)	4 (0.9)	0 (0)	2 (0.8)
Unknown	342 (8.1)	10 (2.4)	30 (2.2)	3 (1.7)	23 (2.1)	4 (0.9)	3 (2.9)	19 (7.9)
IDU past 6 months, n (%)								
Yes	640 (15.2)	93 (22.1)	143 (10.5)	10 (5.7)	199 (18.3)	52 (12.2)	24 (23.1)	62 (25.8)
No	2991 (70.8)	270 (64.1)	1024 (74.9)	147 (83.5)	688 (63.4)	317 (74.2)	67 (64.4)	148 (61.7)
Unknown	592 (14.0)	58 (13.8)	200 (14.6)	19 (10.8)	198 (18.3)	58 (13.6)	13 (12.5)	30 (12.5)
Current OST, n (%)								
Yes	694 (16.4)	92 (21.9)	207 (15.14)	15 (8.5)	224 (20.7)	82 (19.2)	11 (10.6)	50 (20.8)
No	2505 (59.3)	278 (66.0)	866 (63.4)	118 (67.1)	626 (57.7)	261 (61.1)	68 (65.4)	176 (73.3)
Unknown	1024 (24.3)	51 (12.1)	294 (21.5)	43 (24.4)	235 (21.7)	84 (19.7)	25 (24.0)	14 (5.8)

[Δ]determined by FibroScan, APRI or other methods;
SOF: sofosbuvir; LDV: ledipasvir; DCV: daclatasvir; GRZ: grazoprevir; ELB: elbasvir; VEL: velpatasvir; IDU: injecting drug use; OST: opioid substitution therapy

Figure 2. Prescribed treatment durations for all Genotype 1 patients without cirrhosis (A) and with cirrhosis (B) who initiated treatment from March 2016 to December 2017 (n=1706)

Figure 2A

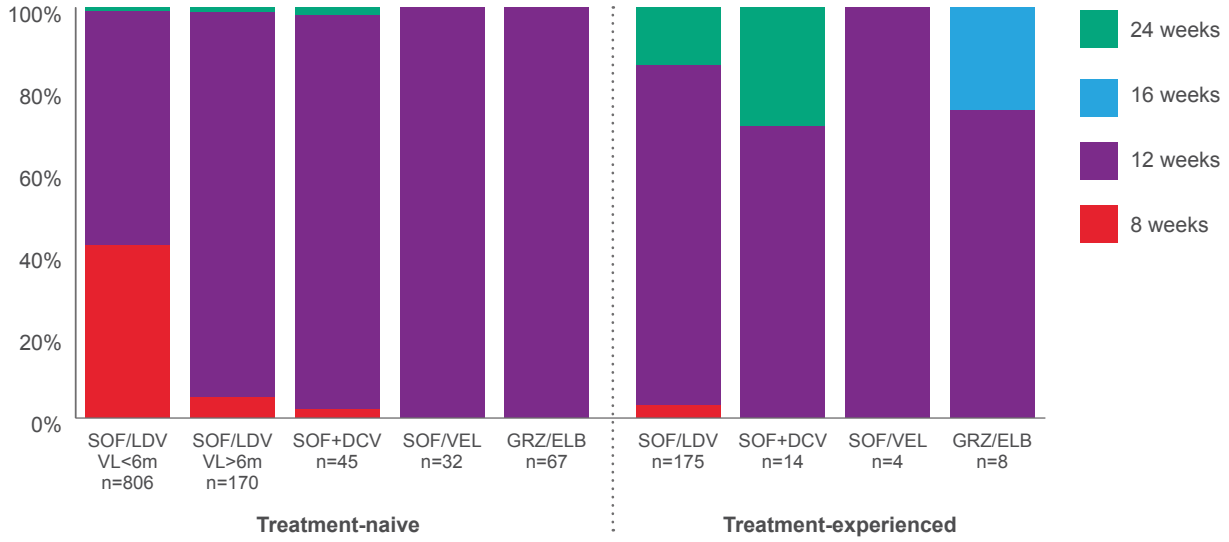
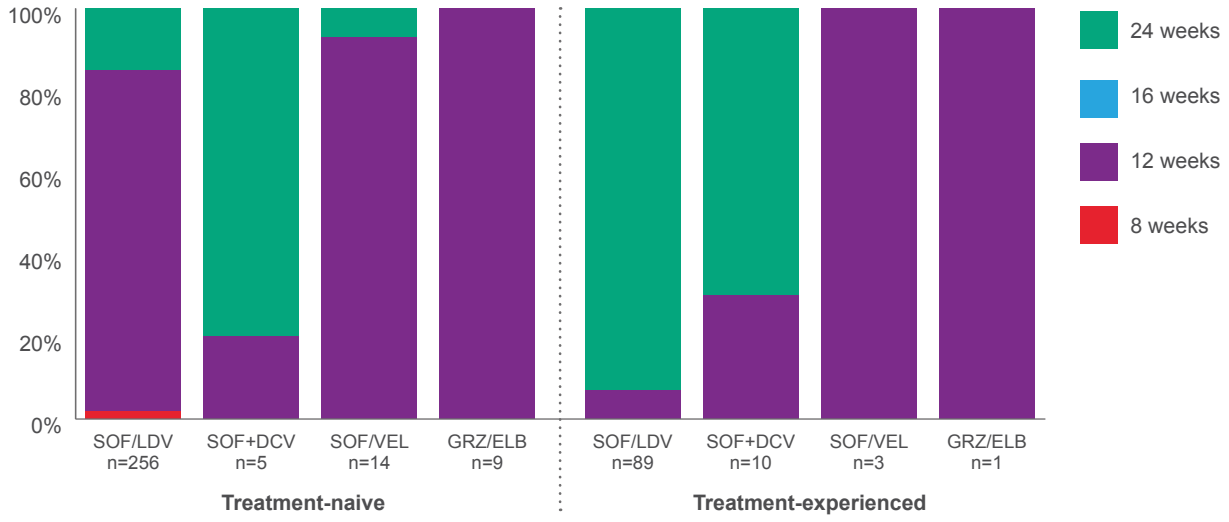


Figure 2B



SOF: Sofosbuvir; LDV: Ledipasvir; DCV: Daclatasvir; GRZ: grazoprevir; ELB: elbasvir; VEL: velpatasvir; VL<6m: HCV RNA viral load <6million IU/mL; VL>6m: HCV RNA viral load <6million IU/mL

Hepatitis C DAA treatment uptake throughout 2016 and 2017

Individuals initiating DAA treatment was highest in March 2016 (14%), followed by April 2016 (11%) and May 2016 (9%; Figure 3A). The initial decreasing trend, which reached a relative plateau around November 2016, is consistent with Australia-wide PBS data[4]. This results from a "warehouse" effect, where large numbers of patients awaiting access to DAAs were treated in the initial months of PBS listing.

The distribution of prescribed regimens in each month from March 2016 to December 2017 is shown in Figure 3B. The proportion of individuals receiving sofosbuvir/ledipasvir decreased from 59% in March 2016 to 26% in December 2017. The most commonly prescribed regimen in December 2017 was sofosbuvir/velpatasvir (69%).

Figure 3. Absolute frequency (A) and relative frequency (B) of treatment regimen and duration of individuals initiating treatment in each month between March 2016 and December 2017 (n=4223)

Figure 3A

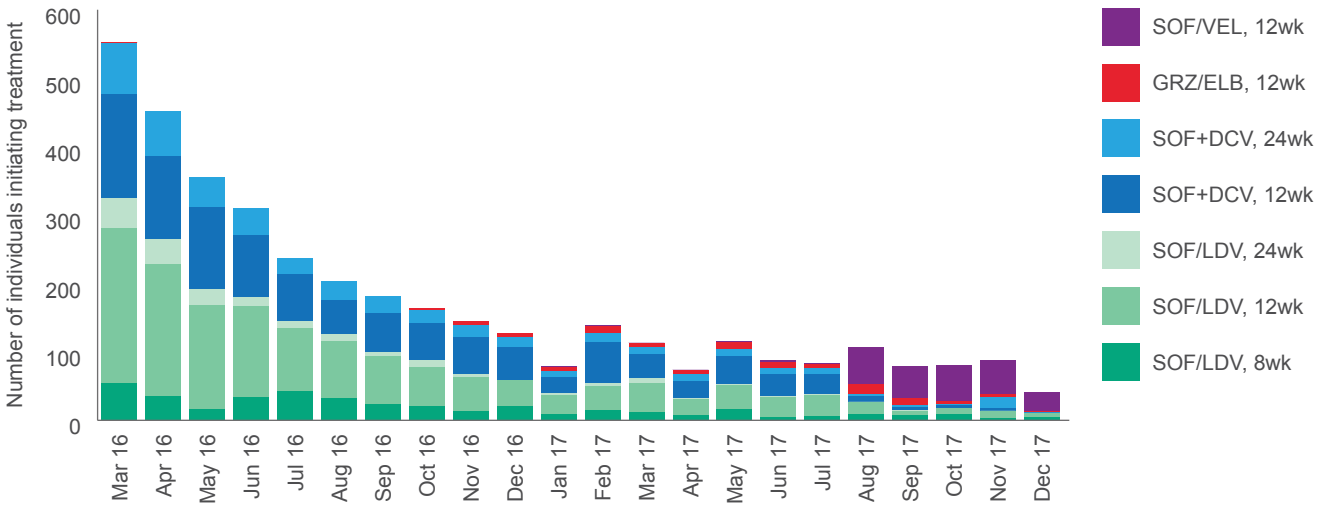
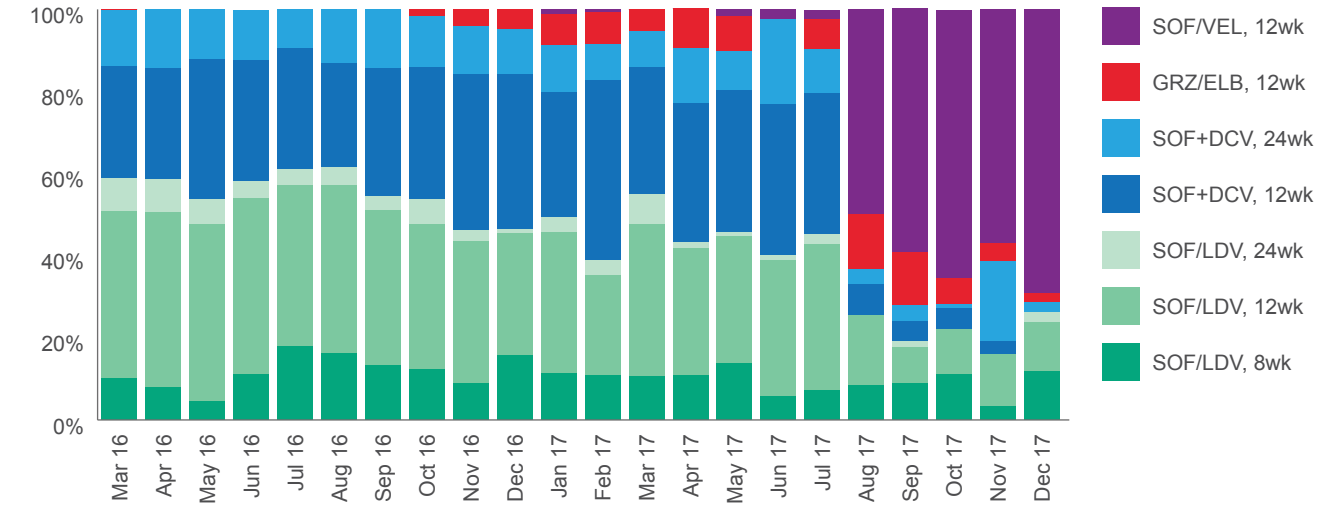


Figure 3B



SOF: sofosbuvir; LDV: ledipasvir; DCV: daclatasvir; GRZ: grazoprevir; ELB: elbasvir; VEL: velpatasvir

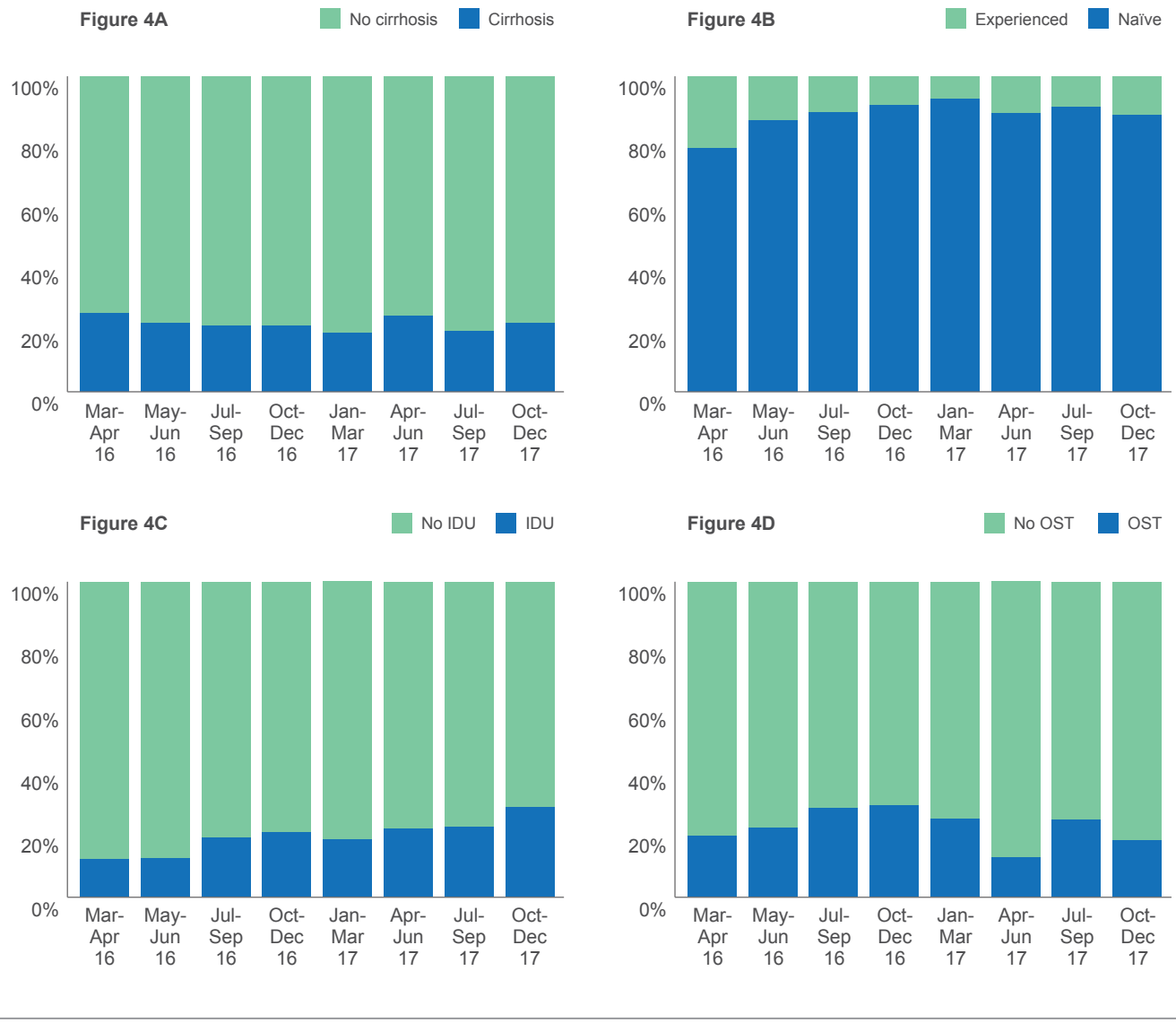
4. Dore and Hajarizadeh (2018) Elimination of Hepatitis C Virus in Australia: Laying the Foundation. Infect Dis Clin N Am 32(2) 269-279.

Hepatitis C DAA treatment uptake throughout 2016 and 2017 by clinical characteristics

The proportion of individuals initiating treatment in 2-3 monthly intervals between March 2016 and December 2017, by clinical characteristics, is presented in Figure 4.

There was a steady increase in the proportion of treatment initiations in people with recent injecting drug use (past 6 months), from 14% in March-April 2016 to 21% in October-December 2017.

Figure 4. Distribution of individuals initiating treatment in each month during March 2016 to December 2017, by cirrhosis status (A), HCV treatment history (B), injecting drug use in the past 6 months (C) and OST (D).



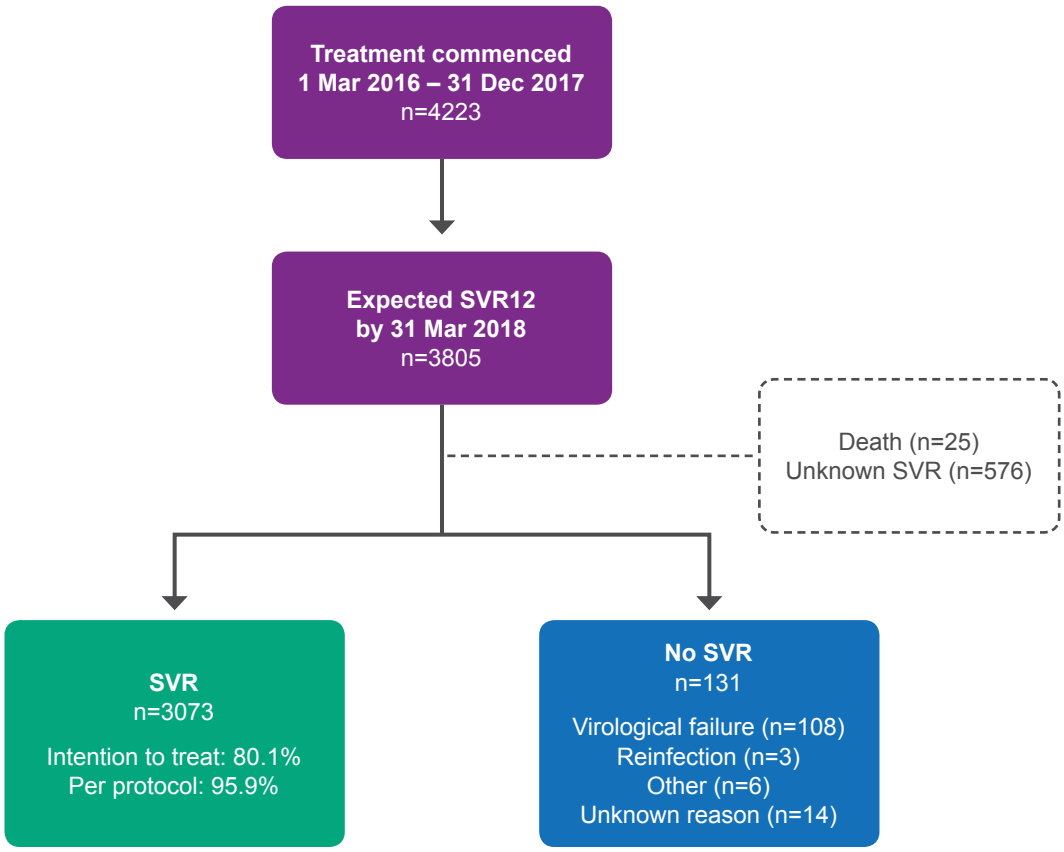
Overall hepatitis C DAA treatment outcomes

Of the 4223 individuals who commenced treatment between March 2016 and December 2017, 3805 individuals were expected to reach 12 weeks post-treatment (SVR12) by 31 March 2018 (Figure 5).

Overall, 3073 of 4223 individuals (80.1%) achieved SVR12 in the intention to treat (ITT) population. In the per protocol (PP) analysis, 3073 of 3204 individuals (95.9%) achieved SVR12.

At 12 weeks post-treatment, 108 cases of virological failure have been reported (2.6%) and three cases of reinfection (<0.1%).

Figure 5. Patient disposition. ITT population n=3805, PP population n=3204.



SVR12: sustained virological response 12 weeks after treatment; ITT: intention to treat; PP: per protocol

Hepatitis C DAA treatment outcomes (per protocol analysis)

In individuals who received sofosbuvir/ledipasvir, the SVR12 rate was 98% for a 12-week course and 94% for a 24-week course. In those who received 8 weeks of sofosbuvir/ledipasvir, there were seven individuals who did not achieve SVR12, resulting in an SVR12 rate of 98%.

SVR12 rates were high across all baseline characteristics (Table 3). There was a slight reduction in SVR12 in those with cirrhosis vs no cirrhosis (92% vs 97%) and in treatment-experienced individuals vs naïve (92% vs 97%; Figure 6A). SVR12 rates were similar in those with and without HIV (98% vs 96%), on OST (97% vs 96%) and with a history of injecting in the last 6 months (97% vs 95%).

Among individuals with genotype 1a and 1b, SVR12 rates in the PP population were 97% and 99%, respectively (Figure 6B). The SVR12 rate was 94% for genotype 3.

SVR12 rates were high across all treatment settings, including less traditional hepatitis C services such as general practice (95%), drug and alcohol services (98%) and community health clinics (99%; Figure 6C).

Table 3. SVR12 rates in the per protocol population

Characteristic	SVR12, % (n=3204)
Overall	95.9 (3073/3204)
Age, n (%)	
≥50 years	95.5 (1875/1963)
<50 years	96.5 (1187/1230)
Unknown	100 (11/11)
Gender, n (%)	
Male	94.9 (2104/2216)
Female	98.1 (962/981)
Transgender	100 (5/5
Unknown	100 (2/2)
HIV status n (%)	
Positive	98.2 (216/220)
Negative	95.8 (2810/2934)
Unknown	94.0 (47/50)
Cirrhosis[A], n (%)	
Yes	92.3 (679/736)
No	97.0 (2390/2464)
Unknown	100 (4/4)
HCV genotype, n (%)	
1	
1a	97.3 (1316/1352)
1b	99.0 (284/287)
1, not specified	96.4 (108/112)
2	94.1 (127/135)
3	94.1 (1068/1135)
4	90.6 (29/32)
5	83.3 (15/18)
6	100 (17/17)
Mixed/Other	94.0 (109/116)
Unknown	149 (3.5)
HCV RNA, n (%)	
<6 million IU/mL	95.9 (1831/1909)
>6 million IU/mL	95.8 (430/449)
Unknown	96.0 (812/846)
Previous HCV therapy, n (%)	
No	96.8 (2585/2670)
Yes, interferon-containing	93.8 (407/434)
Yes, interferon-free	80.4 (37/46)
Yes, not specified	82.4 (14/17)
Unknown	342 (8.1)
IDU past 6 months, n (%)	
Yes	96.6 (367/380)
No	95.4 (2254/2362)
Unknown	97.8 (452/462)
Current OST, n (%)	
Yes	96.6 (488/505)
No	95.6 (1869/1956)
Unknown	96.4 (716/743)

Figure 6. SVR12 rates by clinical characteristics (A), genotype (B) and treatment setting (C) in the PP population

Figure 6A

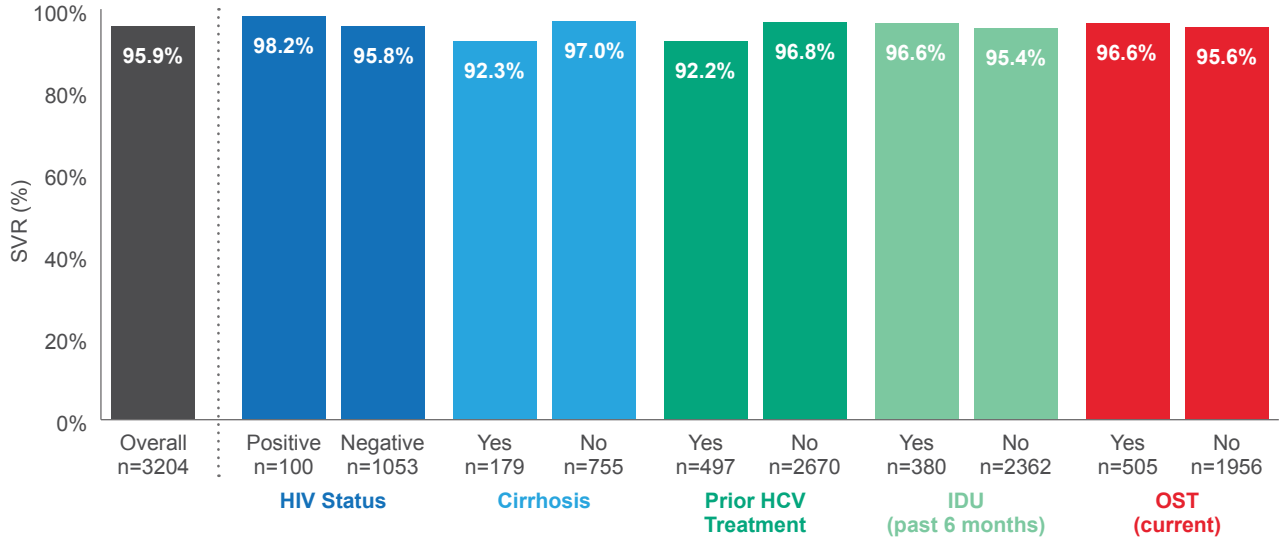


Figure 6B

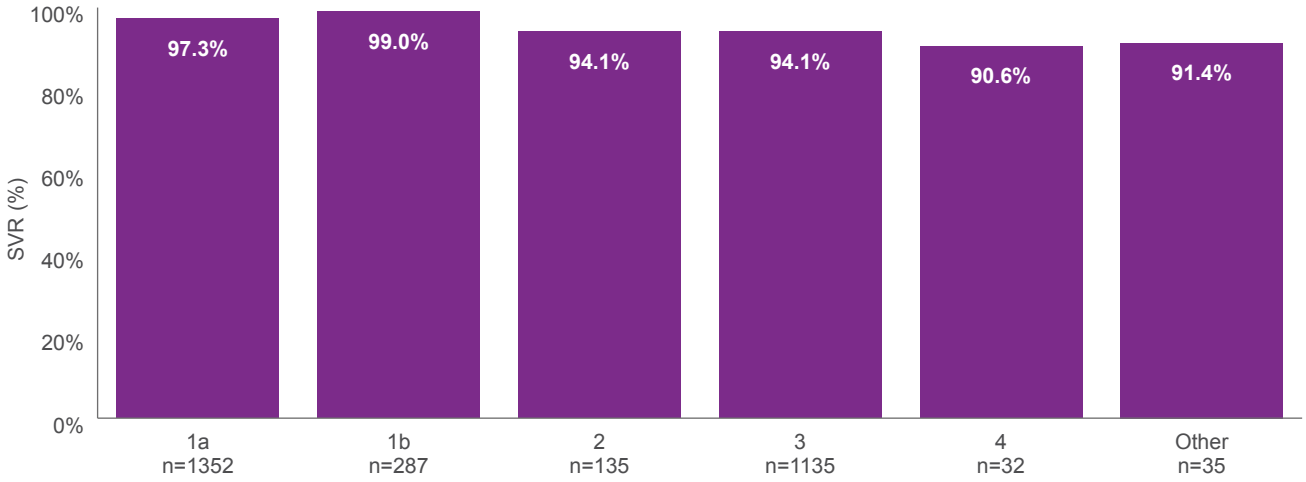
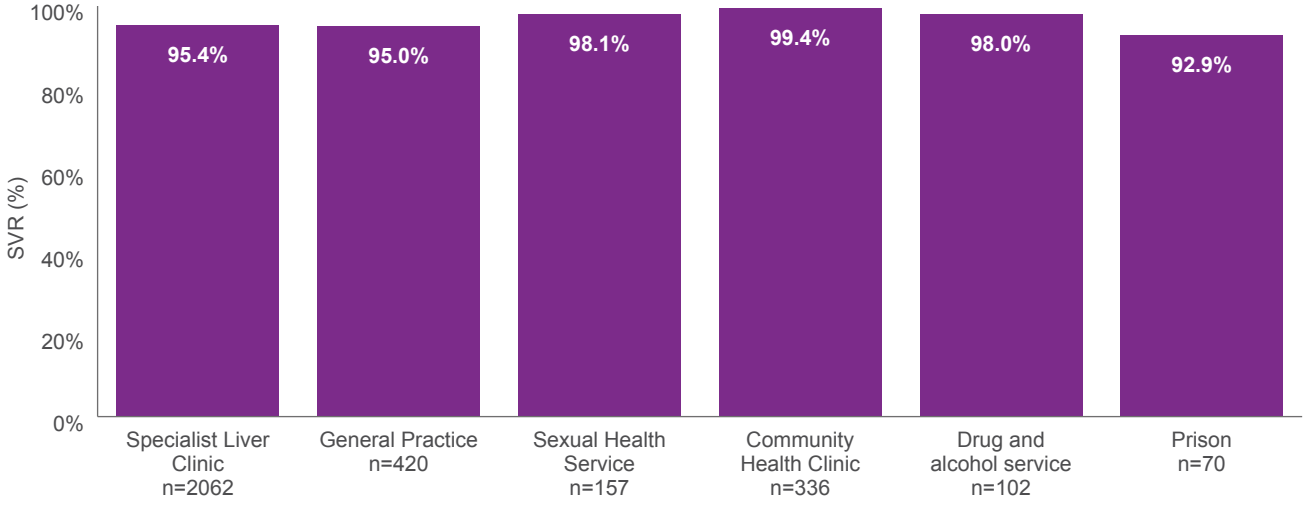


Figure 6C



IDU: injecting drug use; OST: opioid substitution therapy

Hepatitis C DAA treatment outcome (intention to treat analysis)

The overall SVR12 rate by ITT analysis was considerably lower than by per protocol analysis, driven by a proportion of individuals in whom SVR12 follow-up data could not be obtained.

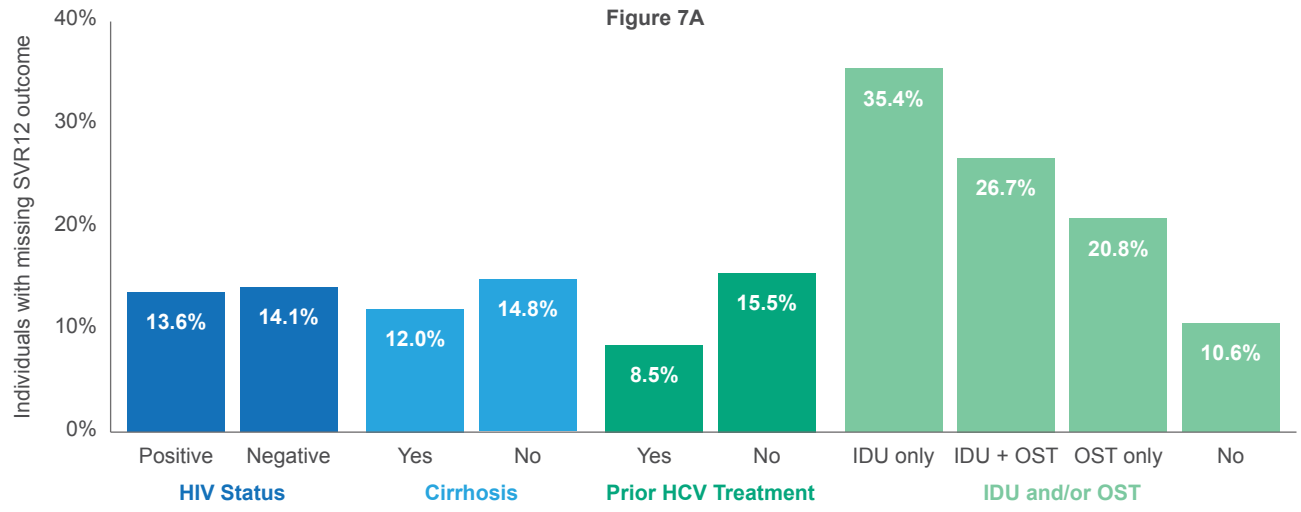
Of the 3805 individuals with expected SVR12 by March 2017, 16% did not have treatment outcomes available (Figure 5). Given the ongoing nature of REACH-C data collection, it is anticipated that treatment outcomes will be obtainable for many individuals currently missing this information.

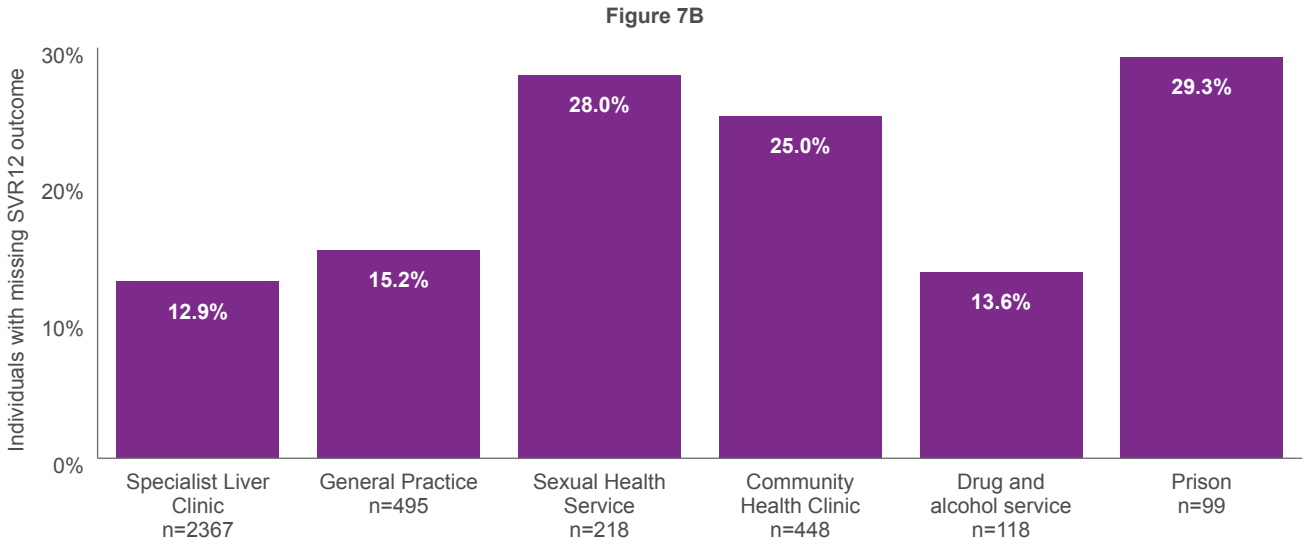
People who injected drugs in the 6 months prior to treatment initiation were more likely to have a missing SVR12 outcome if they were not engaged in OST (35%) compared to those receiving OST (27%; Figure 7A). Treatment outcomes were unknown in 11% of individuals with no recent injecting drug use or OST.

No major differences were seen in missing data by cirrhosis or HIV status. A trend to less missing data was observed in those with treatment experience, likely reflecting higher engagement in care.

The proportion of individuals missing SVR12 varied across treatment settings (Figure 7B). Lost to follow-up was lowest in specialist liver clinics (13%), drug and alcohol services (14%) and general practice (15%).

Figure 7. Distribution of individuals with missing SVR12 outcome by baseline characteristics (A) and treatment setting (B)





IDU: injecting drug use (past 6 months); OST: opioid substitution therapy (current)

Hepatitis C DAA retreatments

Forty individuals treated between March 2016 and December 2017 were subsequently retreated (Table 4). Reasons for retreatment included virological failure (65%), reinfection (13%), unknown (18%) and other (5%).

A variety of regimens were adopted for retreatment, most commonly sofosbuvir/velpatasvir (38%) and sofosbuvir/daclatasvir (23%).

Table 4. Cirrhosis status and genotype for all retreated patients by retreatment regimen (n=40)

Characteristic	All retreatments (n=40)	SOF/LDV (n=4)	SOF+DCV (n=9)	GRZ/ELB (n=6)	GRZ/ELB +SOF (n=4)	SOF/VEL (n=15)	PrOD (n=1)	Unknown (n=1)
Cirrhosis, n (%)								
Yes	11 (27.5)	0 (0)	2 (22.2)	1 (16.7)	4 (100)	3 (20.0)	0 (0)	1 (100)
No	28 (70.0)	3 (75.0)	7 (77.8)	5 (83.3)	0 (0)	12 (80.0)	1 (100)	0 (0)
Unknown	1 (2.5)	1 (25.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
HCV genotype, n (%)								
1								
1a	15 (37.5)	3 (75.0)	2 (22.2)	4 (66.7)	1 (25.)	5 (33.3)	0 (0)	0 (0)
1b	1 (2.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)
1, not specified	1 (2.5)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.7)	0 (0)	0 (0)
2	2 (5.0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (13.3)	0 (0)	0 (0)
3	14 (35.0)	0 (0)	6 (66.7)	1 (16.7)	3 (75.0)	3 (20.0)	0 (0)	1 (100)
4	1 (2.5)	0 (0)	0 (0)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
5	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
6	2 (5.0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (13.3)	0 (0)	0 (0)
Other	1 (2.5)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.7)	0 (0)	0 (0)
Unknown	3 (7.5)	1 (25.0)	1 (11.1)	0 (0)	0 (0)	1 (6.7)	0 (0)	0 (0)

SOF: sofosbuvir; LDV: ledipasvir; DCV: daclatasvir; GRZ: grazoprevir; ELB: elbasvir; VEL: velpatasvir; PrOD: paritaprevir/ritonavir/ombitasvir+dasabuvir

Methodology

REACH-C is a national prospective multi-centre observational cohort. The choice of regimen and duration of treatment was at the discretion of the treating clinician as individuals were treated in routine practice.

Consecutive individuals commencing treatment for HCV with DAAs were identified at each clinic. Baseline characteristics such as gender, HCV genotype, cirrhosis status and HCV treatment history were collected through review of medical records. Information about planned treatment regimen, duration and date of prescription was also recorded. All individuals who initiated treatment between March 2016 and December 2017 were included in analysis of baseline characteristics.

Efficacy of treatment was determined by the proportion of individuals who achieved a sustained virological response, defined as undetectable HCV RNA 12 weeks post-treatment (SVR12).

Treatment outcomes were examined in individuals who were expected to reach SVR12 by 31 March 2018. Clinics reported whether individuals achieved SVR12, and were asked to provide a reason if SVR12 was not achieved (virological failure, reinfection, lost to follow-up, death, other).

Analysis of treatment outcomes was performed using two approaches;

i) Intention to treat (ITT): all individuals with expected SVR12 by 31 March 2018, including those who were lost to follow-up, died, or with an unknown SVR12 (counted as treatment failures).

ii) Per protocol (PP): individuals with a known SVR12 virological outcome by 31 March 2018.

It should be noted that data collection from clinics is ongoing and the information presented herein may not include every individual in the network who initiated treatment during 2016-2017. Additionally, a portion of reported missing data may be retrievable from clinics in the future.