

Monitoring hepatitis C treatment uptake in Australia

Issue #8 December 2017¹

Initiations of new treatment for chronic hepatitis C from March 2016 to June 2017

An estimated 43,360 individuals initiated direct acting antiviral (DAA) treatment for chronic hepatitis C virus (HCV) infection through Pharmaceutical Benefits Scheme (PBS) between March 2016 and June 2017, equating to 19% of the people living with chronic HCV infection in Australia. Of individuals initiating DAA treatment in this period, 66% were men, 54% were >50 years old, and 27% had cirrhosis. The most commonly prescribed regimen was sofosbuvir/ledipasvir for 53%, followed by sofosbuvir+daclatasvir for 39%. Of individuals initiated on sofosbuvir/ledipasvir, 16% were prescribed an 8-week course, 75% a 12-week course, and 10% a 24-week course. Of individuals initiated on sofosbuvir+daclatasvir, 67% were prescribed a 12-week course, and 33% a 24-week course. Overall, 57% of individuals were prescribed DAA treatment by specialists (46% by gastroenterologist, 7% by infectious diseases physicians, and 4% by other specialist), while 22% of individuals were prescribed DAA treatment by general practitioners (GPs). The proportion of individuals prescribed DAA treatment by GPs increased from 8% in March 2016 to 39% in June 2017. Of individuals initiated on 8 weeks sofosbuvir/ledipasvir, 40% were prescribed treatment by specialists while 60% were prescribed treatment by non-specialists (34% by GPs). Of individuals prescribed on 24 weeks sofosbuvir/ledipasvir or 24 weeks sofosbuvir+daclatasvir, 69% were prescribed treatment by specialists while 31% were prescribed treatment by non-specialists (10% by GPs).

1. The Kirby Institute. Monitoring hepatitis C treatment uptake in Australia (Issue 8). The Kirby Institute, UNSW Sydney, Sydney, NSW, Australia, December 2017 (available online at: <https://kirby.unsw.edu.au/report/monitoring-hepatitis-c-treatment-uptake-australia-issue-8-december-2017>). For more information, contact Professor Greg Dore (gdore@kirby.unsw.edu.au) or Dr Behzad Hajari (bhajarizadeh@kirby.unsw.edu.au).

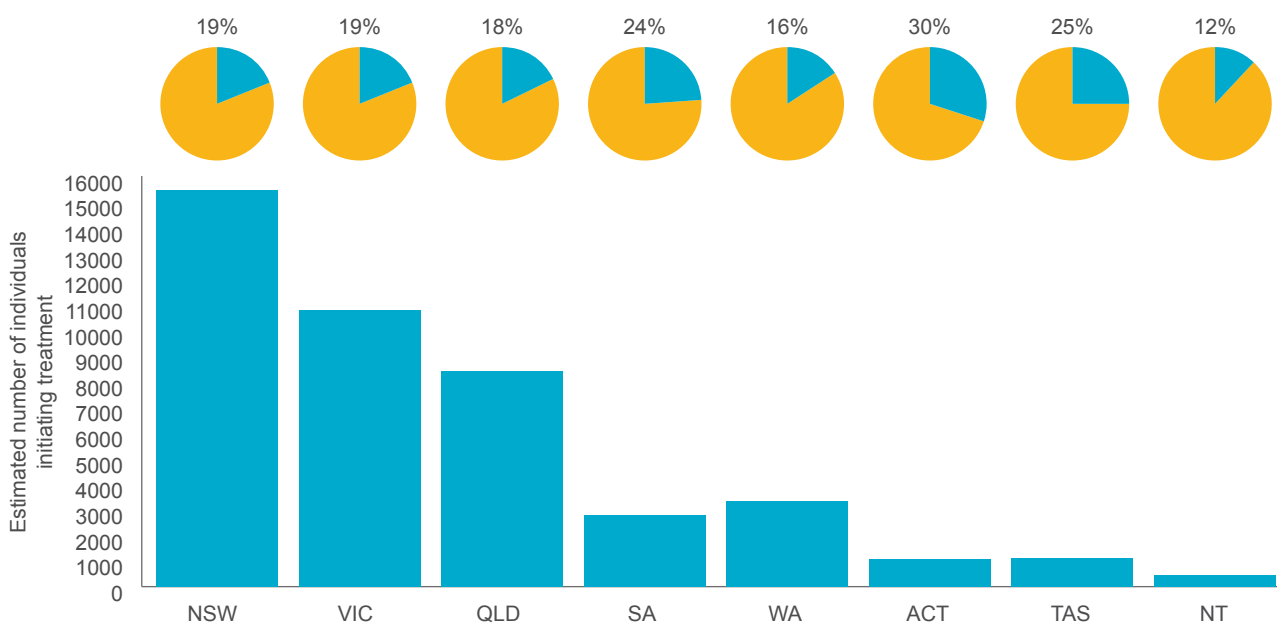
New treatments for chronic hepatitis C virus (HCV) infection, named direct acting antiviral (DAA) treatment, were listed on the Pharmaceutical Benefits Scheme (PBS):

- March 2016: Sofosbuvir/ledipasvir (Harvoni®), sofosbuvir+daclatasvir (Sovaldi®+Daklinza®), sofosbuvir+ribavirin (Sovaldi®+Ibavyr®), and sofosbuvir+pegylated interferon-alfa-2a+ribavirin (Sovaldi®+Pegasys®+ribavirin)
- May 2016: Paritaprevir/ritonavir/ombitasvir+dasabuvir (Viekira PAK®)
- January 2017: Elbasvir/grazoprevir (Zepatier®)
- August 2017: Sofosbuvir/velpatasvir (Epclusa®)²

Issue #8 newsletter provides data on:

- Uptake of DAA treatment through PBS-listing between March 2016 and June 2017 by jurisdiction, patients' gender and age, treatment regimen, and prescriber type
- Proportion of individuals living with chronic HCV infection and those with cirrhosis initiating DAA treatment between 2014 and June 2017 through PBS-listing (2016-17) and early DAA access avenues (2014-15).

Figure 1: The estimated number of individuals initiating DAA treatment (bar charts) and the proportion of individuals living with chronic HCV infection who initiated DAA treatment (pie charts) during March 2016 to June 2017, by jurisdiction.



NSW: New South Wales; VIC: Victoria; QLD: Queensland; SA: South Australia; WA: Western Australia; ATC: Australian Capital Territory; TAS: Tasmania; NT: Northern Territory

2. Data on sofosbuvir/velpatasvir were not included in this issue.

DAA treatment uptake

An estimated 43,360 individuals initiated DAA treatment through PBS-listing between March 2016 and June 2017 in Australia, including 15,470 in New South Wales, 10,770 in Victoria, 8,400 in Queensland, 2,780 in South Australia, 3,320 in Western Australia, 1,070 in Australian Capital Territory, 1,130 in Tasmania, and 430 in Northern Territory (Figure 1)³

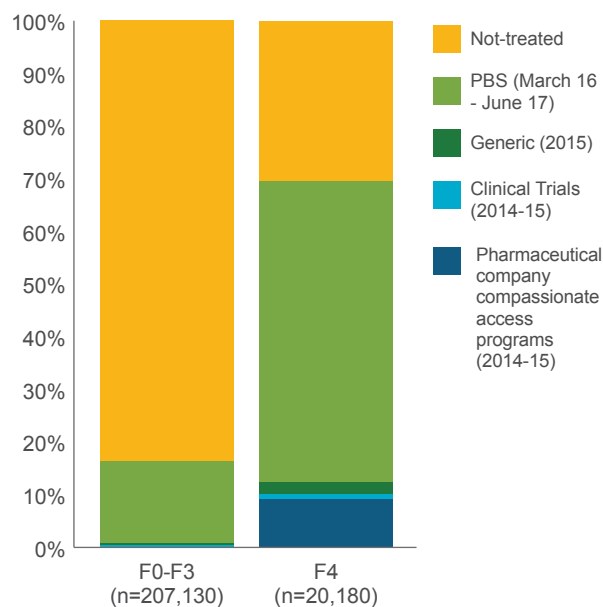
In 2015, an estimated 227,310 individuals were living with chronic HCV infection in Australia⁴, among whom 19% initiated DAA treatment through PBS-listing between March 2016 and June 2017. This proportion varied between 12% and 30% across jurisdictions (Figure 1).

Between 2014 and mid-2017, an estimated 47,700 individuals, equating to 21% of the people living with chronic HCV infection in Australia, received DAA treatment through PBS-listing, and early DAA access avenues, including clinical trials, pharmaceutical company compassionate access programs, and generic importation.

Among total population living with chronic HCV infection in Australia in 2015, an estimated 69% of those with cirrhosis (n=14,020) and 16% of those without cirrhosis (n=33,680) initiated DAA treatment up to June 2017 (Figure 2).

The monthly trends of DAA treatment uptake in Australia and in each jurisdiction are illustrated in Figure 3. After an initial decreasing trend, the monthly number of DAA initiation reached a relatively steady pattern from October 2016. The initial decline in treatment uptake was consistent with a “warehouse” effect with a large number of patients in specialist clinics awaiting DAA treatment access initiating treatment in the early months.

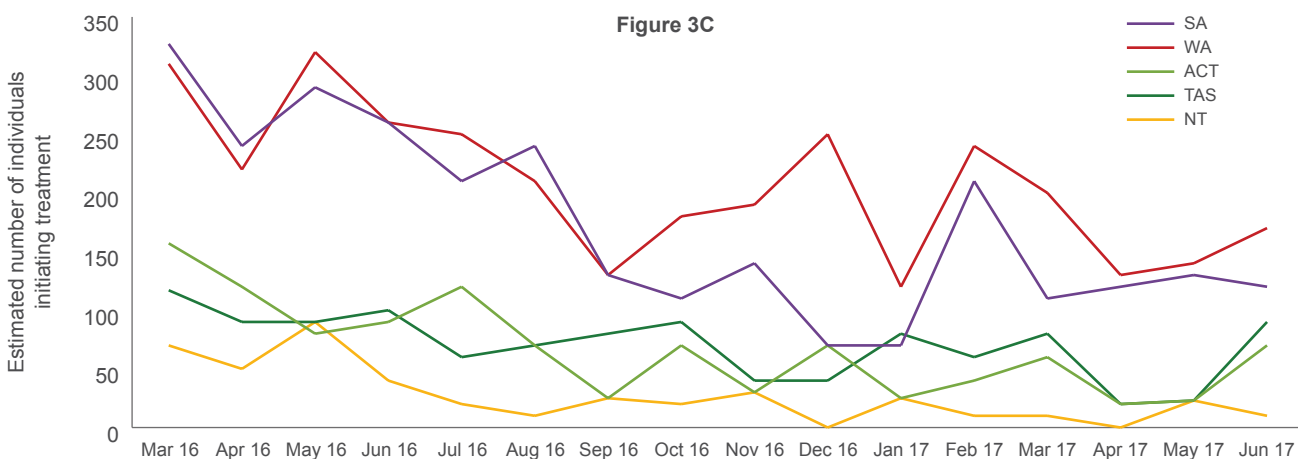
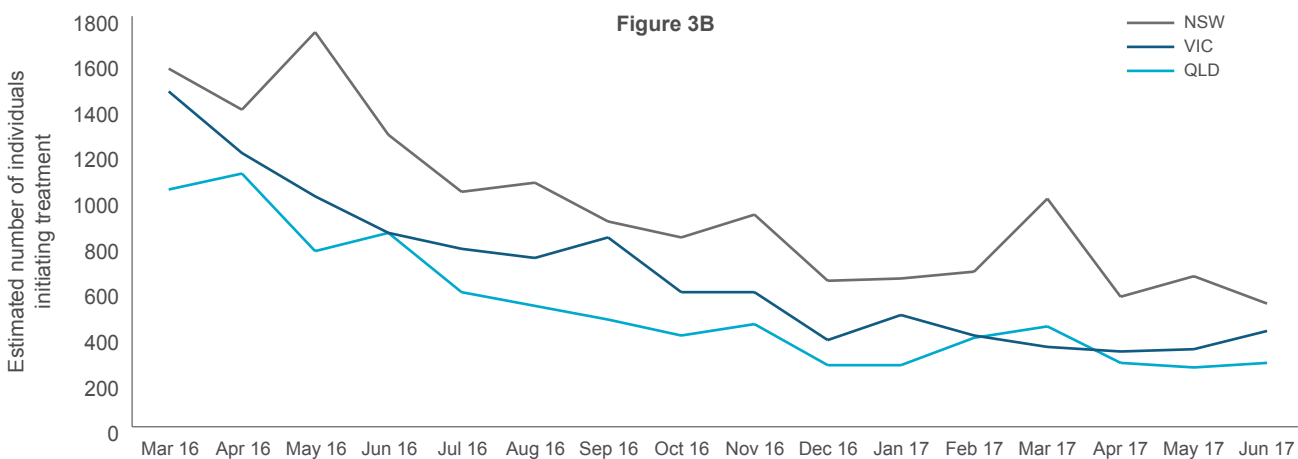
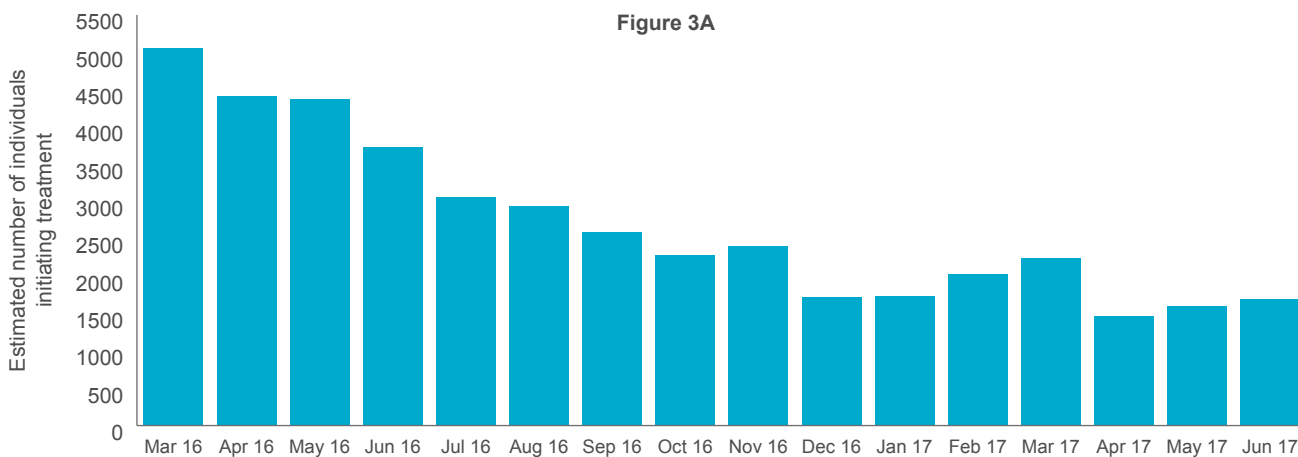
Figure 2: Estimated proportion of individuals living with chronic HCV infection in Australia who initiated DAA treatment between 2014 and mid-2017, by liver fibrosis stage



3. For an estimated 10 individuals, more than one jurisdiction was recorded.

4. The Kirby Institute. Hepatitis B and C in Australia Annual Surveillance Report Supplement 2016. The Kirby Institute, UNSW Sydney, Sydney NSW 2052

Figure 3: Estimated number of individuals initiating DAA treatment in each month during March 2016 to June 2017 in Australia (A), and by Jurisdiction (B and C)



NSW: New South Wales; VIC: Victoria; QLD: Queensland; SA: South Australia; WA: Western Australia; ACT: Australian Capital Territory; TAS: Tasmania; NT: Northern Territory

Gender and age distribution of individuals initiating DAA treatment

Of individuals initiating DAA treatment between March 2016 and June 2017, 66% were men and 34% were women.

Age distribution of individuals initiating DAA treatment was similar between men and women (Figure 4). The highest proportion of total individuals were 51-60 years old (37%), followed by 41-50 years old (25%). Compared to the age distribution of the total population

living with chronic HCV infection in Australia, a shift towards older age groups was observed among those initiating DAA treatment (Figure 4).

The age distribution of individuals initiating DAA treatment in each month showed a trend towards younger age groups from March to September 2016, while a relatively constant age distribution has been observed since then (Figure 5). An estimated 28% of individuals initiating DAA treatment in March 2016 as opposed to 55% of those initiating DAA treatment in June 2017 were ≤ 50 years old.

Figure 4: Age distribution of individuals living with chronic HCV infection in 2015 (dotted line) and those initiating DAA treatment during March 2016 to June 2017 (bars)

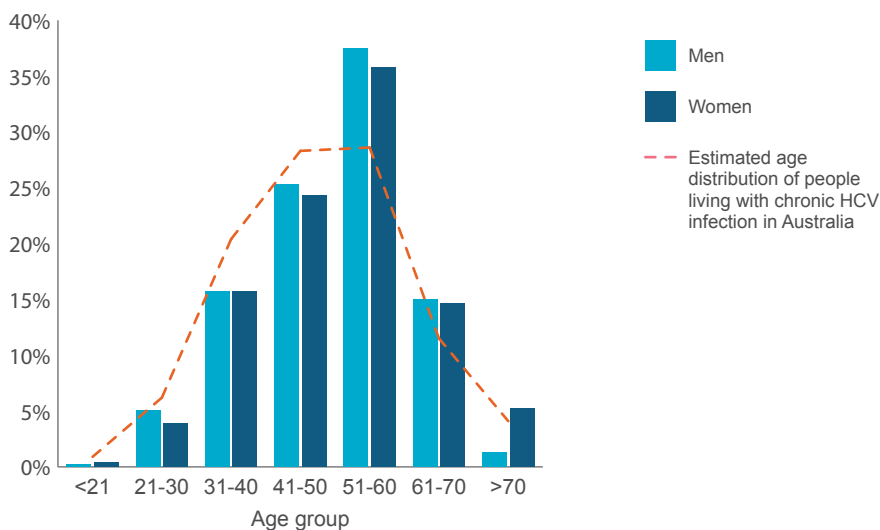
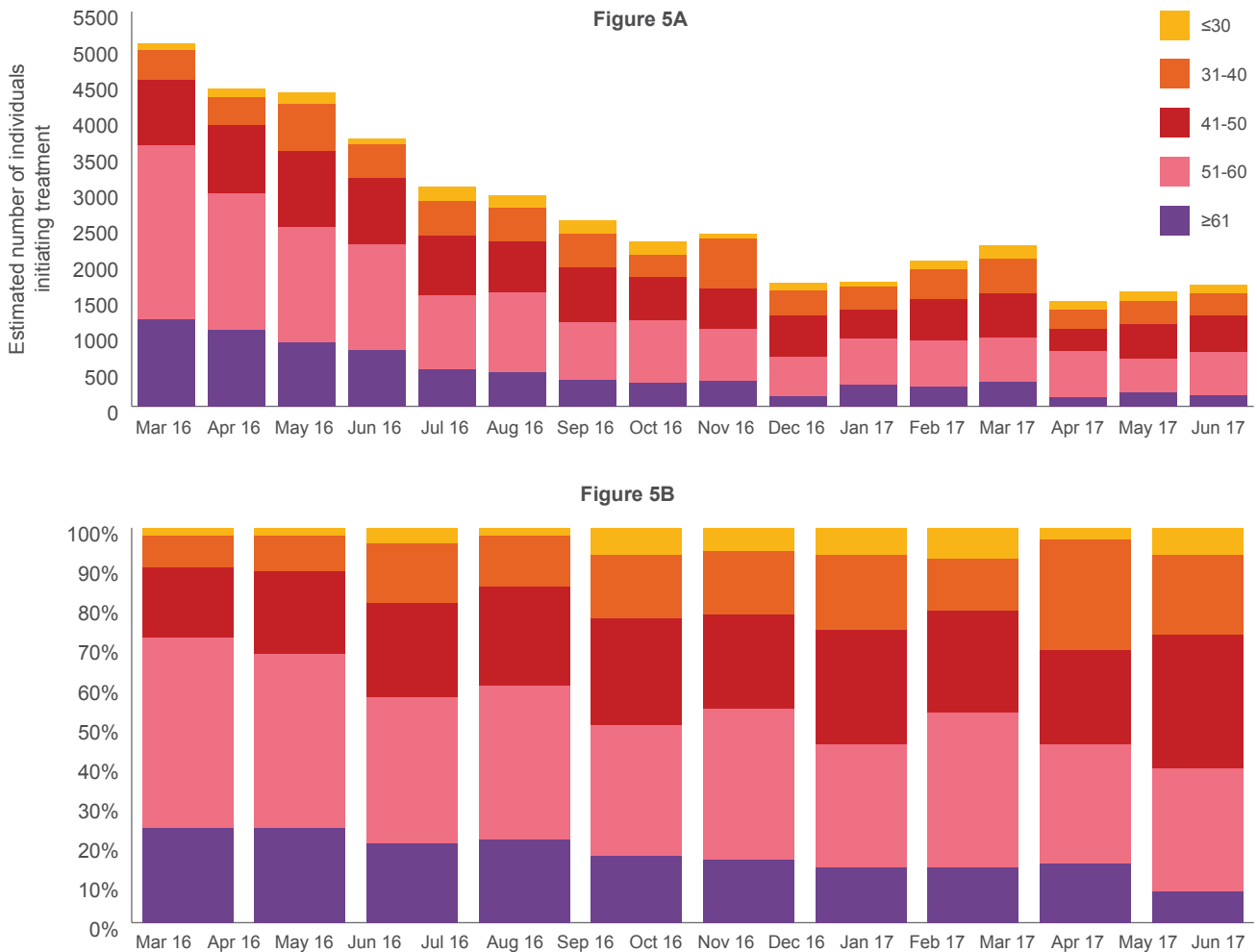


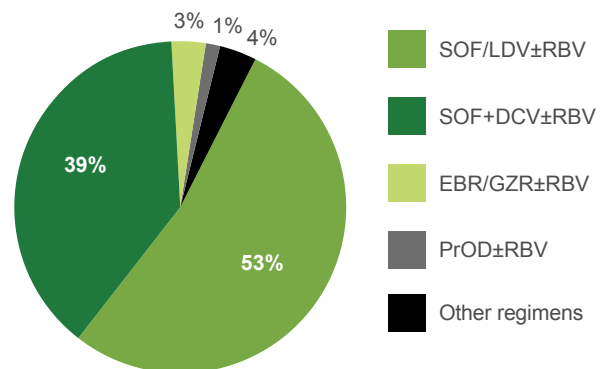
Figure 5: Absolute frequency (A) and relative frequency (B) of age groups of individuals initiating DAA treatment in each month during March 2016 to June 2017



Distribution of DAA regimens prescribed for individuals initiating DAA treatment

The most commonly prescribed regimen was sofosbuvir/ledipasvir±ribavirin for 53%, followed by sofosbuvir+daclatasvir±ribavirin for 39%, elbasvir/grazoprevir±ribavirin for 3%, and paritaprevir/ritonavir/ombitasvir+dasabuvir±ribavirin for 1%. For 4% of individuals, other DAA treatment regimens were prescribed (Figure 6).

Figure 6: Distribution of DAA regimens prescribed during March 2016 to June 2017



SOF: Sofosbuvir; LDV: Ledipasvir; DCV: Daclatasvir; EBR: Elbasvir; GZR: Grazoprevir; PrOD: Paritaprevir/ritonavir/Ombitasvir+Dasabuvir; RBV: Ribavirin

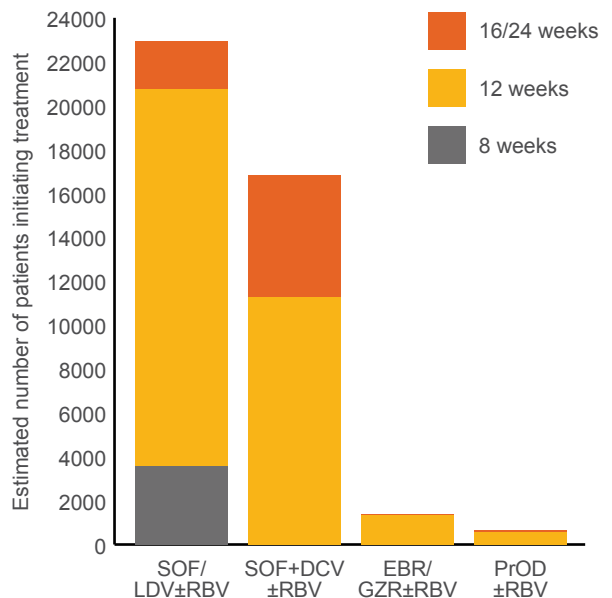
The breakdown of treatment initiation numbers by treatment regimen and treatment course duration is shown in Figure 7. Of individuals initiated on sofosbuvir/ledipasvir±ribavirin (n=22,920), 16% were prescribed an 8-week course, 75% a 12-week course, and 10% a 24-week course. Of individuals initiated on sofosbuvir+daclatasvir±ribavirin (n=16,840), 67% were prescribed a 12-week course, and 33% a 24-week course. Of individuals initiated on elbasvir/grazoprevir±ribavirin (n=1,400), 97% were prescribed a 12-week course, and 3% a 16-week course. Of individuals initiated on paritaprevir/ritonavir/ombitasvir+dasabuvir±ribavirin (n=660), 83% were prescribed a 12-week course, and 17% a 24-week course.

Sofosbuvir+daclatasvir is primarily prescribed for HCV genotype 3, with a 24-week course recommended for patients with cirrhosis and a 12-week course for those with no cirrhosis.⁵ Of total individuals initiated on sofosbuvir+daclatasvir, 67% were prescribed a 12-week course, and 33% a 24-week course.

It was estimated that 27% of total individuals initiating DAA treatment between March 2016 and June 2017 had cirrhosis.

The monthly proportion of 24-week courses to the total prescriptions of sofosbuvir+daclatasvir is shown in Figure 8. The proportion of 24-week courses of sofosbuvir+daclatasvir prescriptions decreased from 45% in March to 24% in November 2016 with a

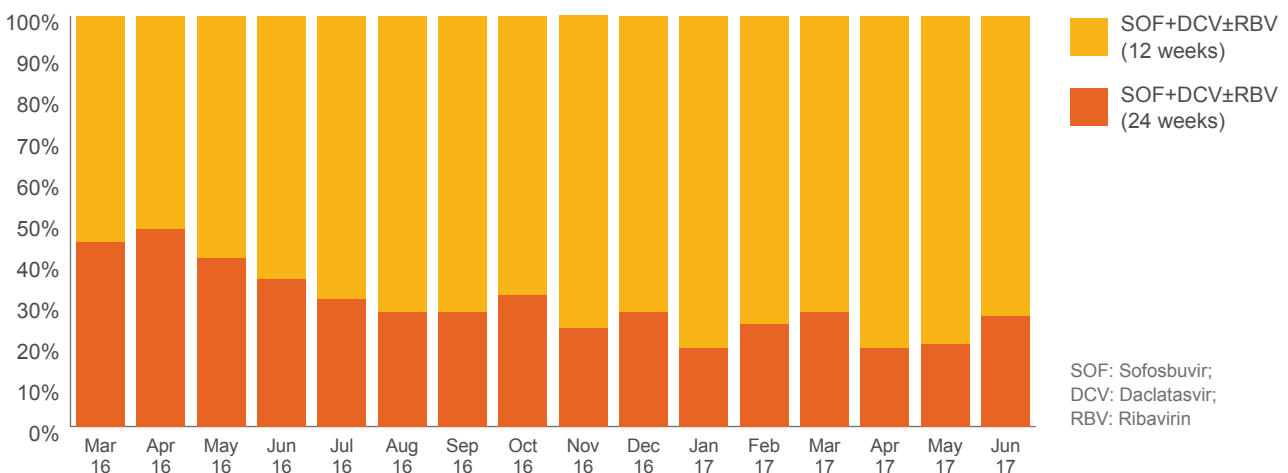
Figure 7: Distribution of DAA regimens prescribed during March 2016 to June 2017, by treatment regimen and treatment course duration (16 weeks treatment exclusively applies to EBR/GZR+RBV)



SOF: Sofosbuvir; LDV: Ledipasvir; DCV: Daclatasvir; EBR: Elbasvir; GZR: Grazoprevir; PrOD: Paritaprevir/ritonavir/Ombitasvir+Dasabuvir; RBV: Ribavirin

relatively steady pattern observed since then. In June 2017, 27% of sofosbuvir+daclatasvir prescriptions included a 24-week course treatment.

Figure 8: Proportion of individuals initiated 12 weeks versus 24 weeks sofosbuvir+daclatasvir regimen in each month during March 2016 to June 2017



SOF: Sofosbuvir; DCV: Daclatasvir; RBV: Ribavirin

5. Hepatitis C Virus Infection Consensus Statement Working Group. Australian recommendations for the management of hepatitis C virus infection: a consensus statement (August 2017). Gastroenterological Society of Australia, Melbourne, Australia, 2017.

Distribution of health care providers prescribing for individuals initiating DAA treatment

The majority of individuals initiating DAA treatment received their prescriptions from gastroenterologists (46%), followed by general practitioners (GPs; 22%), infectious diseases physicians (7%), and other specialists (4%). Twenty percent of individuals received their prescriptions from other physicians, including supervised medical officers (e.g., interns, resident medical officers, and registrars), public health physicians, temporary resident doctors, and non-vocationally registered doctors (Figure 9). Overall, 57% of individuals received their prescriptions from specialists.

Distribution of prescriber types varied across jurisdictions (Figure 9). Gastroenterologists were the prominent prescriber in most jurisdictions. In Northern

Territory, 22% of individuals were prescribed DAA treatment by infectious disease physicians, compared to 4% by gastroenterologists. In Western Australia, 26% of individuals were prescribed DAA treatment by GPs, compared to 18% by gastroenterologists. Across jurisdictions, the proportion of individuals prescribed DAA treatment by GPs was highest in Tasmania (37%), Queensland (27%), and Western Australia (26%).

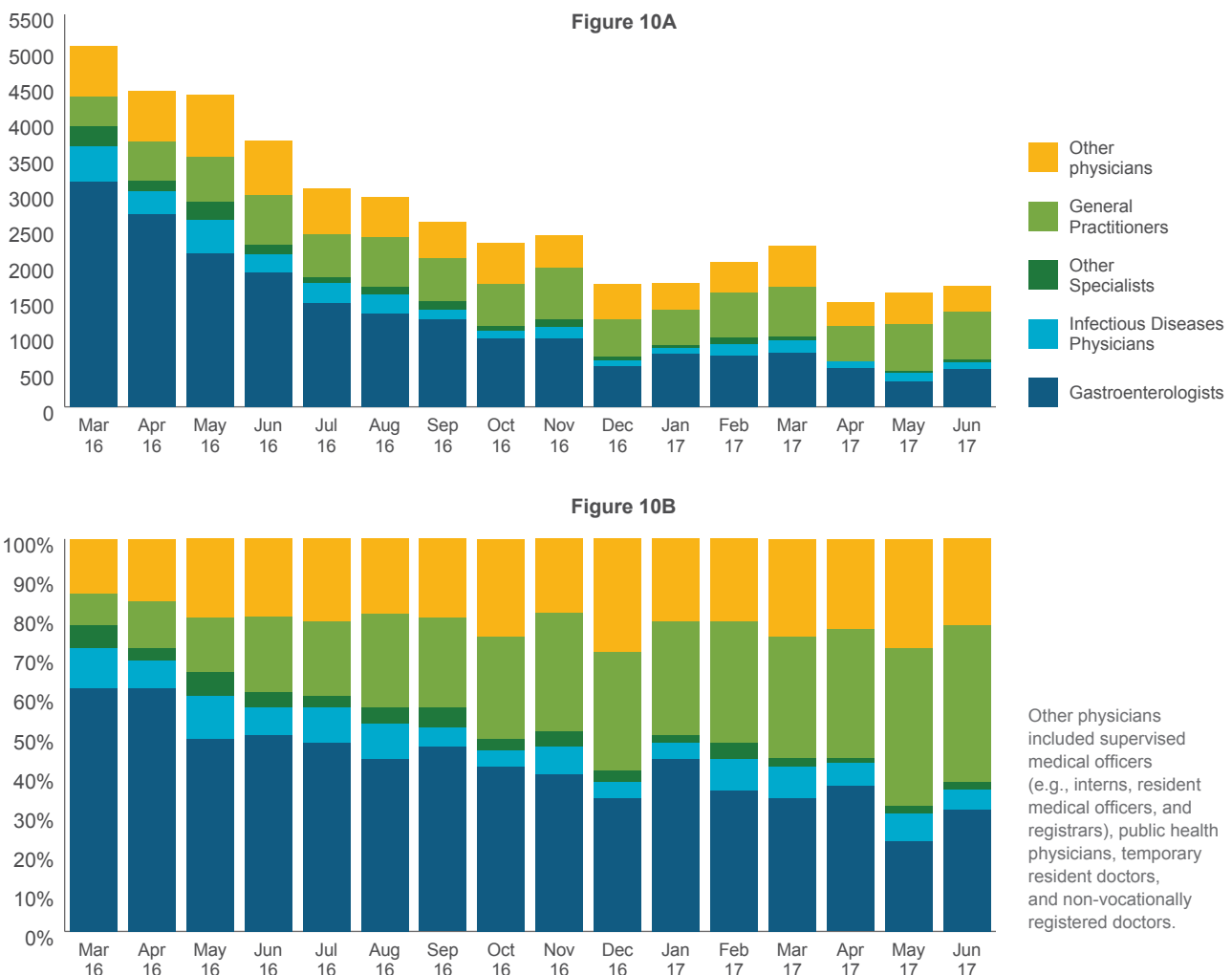
The distribution of prescriber types in each month is shown in Figure 10. The proportion of individuals prescribed DAA treatment by GPs increased from 8% in March 2016 to 39% in June 2017. Increasing contribution of GPs in DAA prescribing is also evident by increasing the absolute number of individuals initiated on DAA treatment by GPs, from 410 in March 2016 to 670 in June 2017.

Figure 9: Distribution of prescriber types for individuals initiating DAA treatment during March 2016 to June 2017, in Australia and by jurisdiction



Other physicians included supervised medical officers (e.g., interns, resident medical officers, and registrars), public health physicians, temporary resident doctors, and non-vocationally registered doctors.

Figure 10: Absolute frequency (A) and relative frequency (B) of prescriber types in each month for individuals initiating DAA treatment during March 2016 to June 2017 in Australia



Distribution of prescribed DAA regimens by prescription type

The distribution of prescribed DAA regimens by prescriber type is shown in Figure 11. Across all prescriber types, the most commonly prescribed regimens included 12 weeks sofosbuvir/ledipasvir, followed by 12 weeks sofosbuvir+daclatasvir (Figure 11A).

Of prescriptions by specialists, 7% included 24 weeks sofosbuvir/ledipasvir and 15% included 24 weeks sofosbuvir+daclatasvir. These proportions were 2% and 6%, respectively, among prescriptions by GPs (Figure 11A). Of the total number of 24

weeks sofosbuvir/ledipasvir prescriptions, 74% was by specialists compared to 8% by GPs. Similarly, of the total number of 24 weeks sofosbuvir+daclatasvir prescriptions, 67% was by specialists compared to 11% by GPs (Figure 11B). These two regimens are primarily prescribed for patients with cirrhosis.⁶

Across all prescriber types, the highest proportion of 8 weeks sofosbuvir/ledipasvir regimen was observed in prescriptions by GPs (13%, Figure 11A). Of the total number of 8 weeks sofosbuvir/ledipasvir prescriptions, the majority (34%) was by GPs. This regimen is prescribed for treatment-naïve patients with genotype 1, no cirrhosis, and pre-treatment HCV RNA <6 million IU/mL.⁶

6. Hepatitis C Virus Infection Consensus Statement Working Group. Australian recommendations for the management of hepatitis C virus infection: a consensus statement (August 2017). Gastroenterological Society of Australia, Melbourne, Australia, 2017

Figure 11: Distribution of prescribed DAA regimens by prescriber types (A) and distribution of prescriber types by prescribed DAA regimens (B) for individuals initiating DAA treatment during March 2016 to June 2017 in Australia

Figure 11A

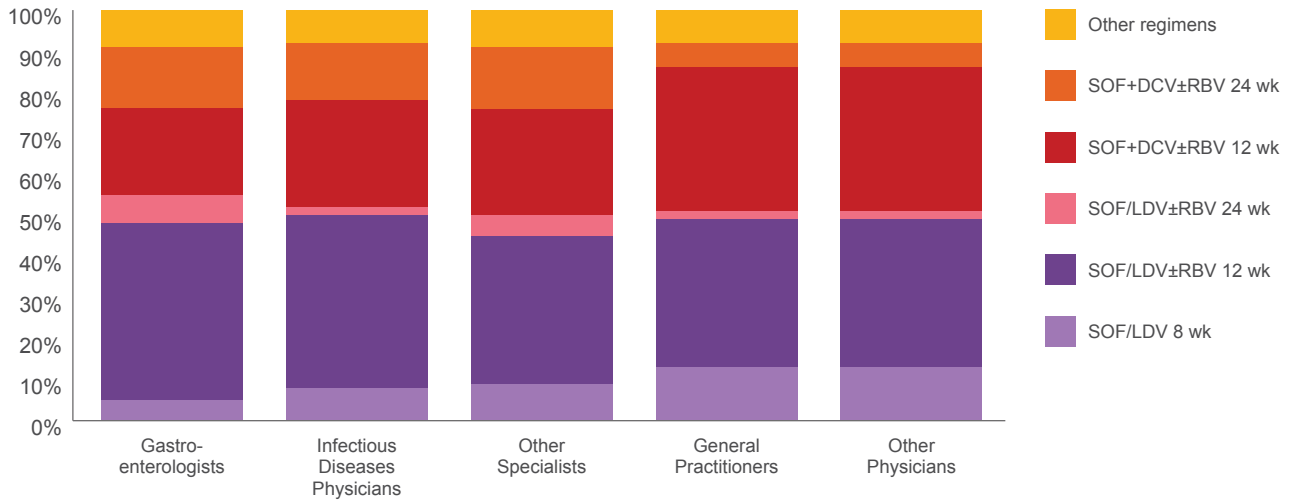
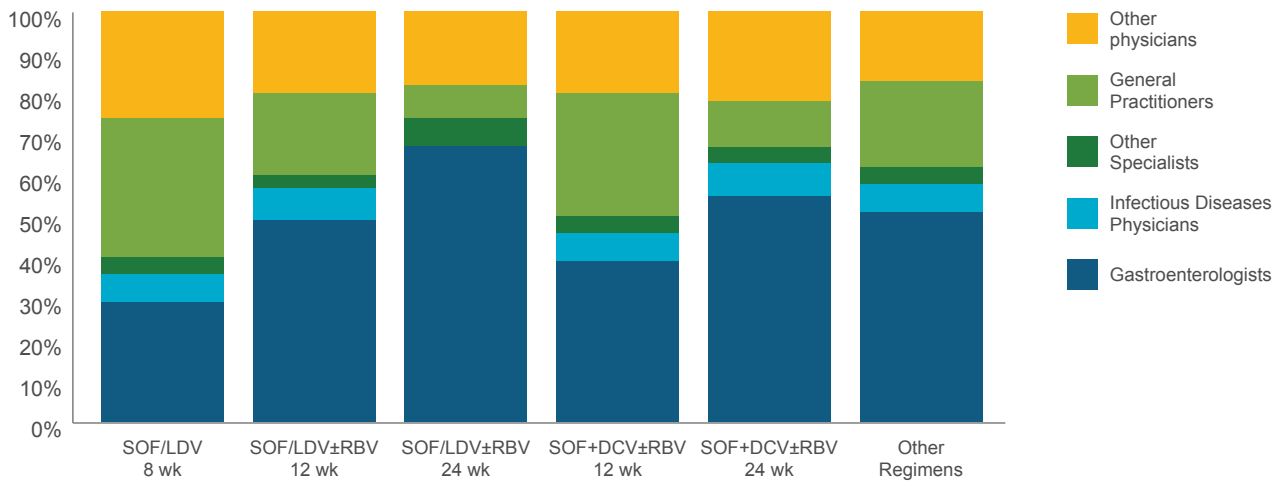


Figure 11B



Other physicians included supervised medical officers (e.g., interns, resident medical officers, and registrars), public health physicians, temporary resident doctors, and non-vocationally registered doctors.
 SOF: Sofosbuvir; LDV: Ledipasvir; DCV: Daclatasvir; RBV: Ribavirin

Methodology

The following data sources were used for analysis:

- The data of a longitudinal cohort of individuals, representing a 10% random sample of the PBS database were used to estimate the number of individuals initiating DAA between March 2016 and June 2017, and for all sub-group analyses of DAA treatment uptake.
- Real world Efficacy of Antiviral therapy in Chronic Hepatitis C (REACH-C Study) is an observational study with the data being collected from a national network of eleven diverse clinical services including specialist viral hepatitis clinics, general practice, sexual health, community and drug and alcohol centres.⁷ REACH-C Study data was used to adjust the proportion of sofosbuvir+daclatasvir regimens prescribed for patients with cirrhosis.
- The data from DAA clinical trials and compassionate access programs were collected from pharmaceutical companies.
- The estimated number of individuals receiving generic DAA was based on the data of FixHepC (<http://fixhepc.com/>), a web-based platform which facilitates generic DAA personal importation.
- The estimated numbers of individuals living with chronic HCV infection and cirrhosis in Australia in 2015 were extracted from a modelling study.⁸

The number of individuals with cirrhosis initiating DAA treatment was estimated. Among individuals initiating DAA treatment through early access avenues in 2014 and 2015, it was assumed that 25% of those in clinical trials, 95% of those in compassionate access programs, and 30% of those receiving generic DAA had cirrhosis.⁹ Sofosbuvir+daclatasvir regimen has been recommended for HCV genotype 3 (cirrhosis - 24 weeks; no cirrhosis - 12 weeks).¹⁰ Among individuals initiating DAA treatment through PBS-listing, the proportion of those initiating a 24-week course of sofosbuvir+daclatasvir to the total sofosbuvir+daclatasvir initiations was initially

adjusted, using REACH-C Study data of 24 weeks sofosbuvir+daclatasvir prescribed for those without cirrhosis (25% of prescriptions) and 12 weeks sofosbuvir+daclatasvir prescribed for those with cirrhosis (3% of prescriptions). Then, the adjusted proportion was extrapolated to the total DAA initiations during March 2016 to June 2017 to estimate the DAA treatment uptake among individuals with cirrhosis. More details of the methods for the estimations have been described elsewhere.¹¹

There are some considerations to be taken into account for interpreting the results. Given that the results are extrapolated from 10% random sample of the PBS database, the results in subgroups with small numbers might be subject to uncertainties. This analysis provided data of treatment initiations. It does not reflect the number of individuals who completed their treatment course, although treatment discontinuation is expected to be low. The jurisdiction-specific treatment initiation estimates in this report are based on data of dispensing pharmacy location, and not patient's residence location while the estimated numbers of individuals living with chronic HCV are based in part on the number of HCV notifications which are reported based on residence. Thus cross-jurisdiction dynamics should be considered in interpreting the jurisdiction-specific data. It could have more impact on the estimates from smaller jurisdictions given their smaller population as the denominator. The data of sofosbuvir+daclatasvir regimen was the basis of estimating number of individuals with cirrhosis initiating DAA treatment through PBS-listing. This regimen was primarily prescribed for genotype 3, which has been associated with more rapid liver fibrosis progression.¹² Thus, our estimation of DAA treatment uptake among those with cirrhosis could be potentially subject to an overestimation. The assumed proportion of individuals with cirrhosis among those accessed DAA treatment through clinical trials and compassionate access programs were based on expert opinion.

7. The Kirby Institute. Real world efficacy of antiviral therapy in chronic hepatitis C in Australia (Issue 1). The Kirby Institute, UNSW Sydney, Sydney, NSW, Australia, July 2017 (available online at: <https://kirby.unsw.edu.au/report/real-world-efficacy-antiviral-therapy-chronic-hepatitis-caustralia-issue-1-july-2017>)
8. The Kirby Institute. Hepatitis B and C in Australia Annual Surveillance Report Supplement 2016. The Kirby Institute, UNSW Sydney, Sydney NSW 2052
9. Freeman JA, Sallie R, Kennedy A, Jeffreys G, Savage A, Hill AM. High sustained virological response rates using legally imported, generic direct acting antiviral treatment for hepatitis C. *Hepatology* 2016; 63(1 SUPP): 444A
10. Hepatitis C Virus Infection Consensus Statement Working Group. Australian recommendations for the management of hepatitis C virus infection: a consensus statement (August 2017). Gastroenterological Society of Australia, Melbourne, Australia, 2017
11. Hajarizadeh B, Grebely J, Matthews GV, Martinello M, Dore GJ. Uptake of direct acting antiviral treatment for chronic hepatitis C in Australia. *Journal of Viral Hepatitis* 2017 [in press].
12. Hajarizadeh B, Grebely J, Dore GJ. Epidemiology and natural history of HCV infection. *Nature Review Gastroenterology Hepatology* 2013; 10(9): 553-62.