

Monitoring hepatitis C treatment uptake in Australia

Issue #7 July 2017¹

Initiations of new treatment for chronic hepatitis C in 2016

An estimated 32,400 individuals initiated direct acting antiviral (DAA) treatment for chronic hepatitis C virus (HCV) infection in 2016 (March-December), equating to 14% of the people living with chronic HCV infection in Australia. Of individuals initiating DAA treatment in 2016, 66% were men, 57% were >50 years old, and 36% had cirrhosis. The most commonly prescribed regimen was sofosbuvir/ledipasvir for 56%, followed by sofosbuvir+daclatasvir for 39%. Of individuals initiated on sofosbuvir/ledipasvir, 14% were prescribed an 8-week course, 75% a 12-week course, and 11% a 24-week course. Of individuals initiated on sofosbuvir+daclatasvir, 64% were prescribed a 12-week course, and 36% a 24-week course. Overall, 62% of individuals were prescribed DAA treatment by specialists (50% by gastroenterologist, 8% by infectious diseases physicians, and 4% by other specialist), while 19% of individuals were prescribed DAA treatment by general practitioners (GPs). The proportion of individuals prescribed DAA treatment by GPs increased from 8% in March to 31% in December.

1. The Kirby Institute. Monitoring hepatitis C treatment uptake in Australia (Issue 7). The Kirby Institute, UNSW Sydney, Sydney, NSW, Australia, July 2017 (available online at: <https://kirby.unsw.edu.au/report/monitoring-hepatitis-c-treatment-uptake-australia-issue-7-july-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®)²

Issue #7 newsletter provides data on:

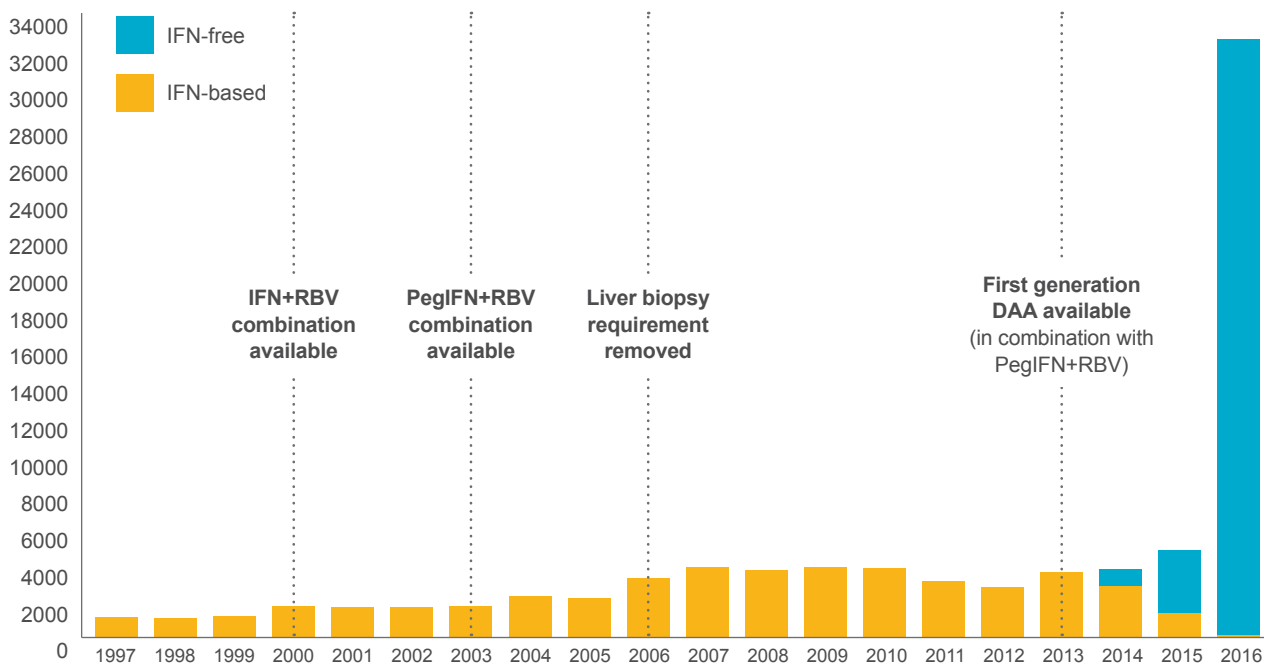
- Annual uptake of HCV treatment, including interferon-based and interferon-free treatment from 1997 to 2016
- Number of individuals with cirrhosis initiating DAA treatment between 2014 and 2016.
- Uptake of DAA treatment in 2016, by jurisdiction, patients' gender and age, treatment regimen, and prescriber type

Annual HCV treatment uptake, 1997-2016

Between 1997 and 2016, an estimated 83,050 individuals initiated HCV treatment, including 46,310 with interferon-based and 36,740 with interferon-free DAA treatment. Among those initiating DAA treatment, 32,400 individuals received treatment through PBS in 2016 and 4,340 received treatment through clinical trials, pharmaceutical company compassionate access programs, and generic importation in 2014, and 2015. HCV treatment uptake increased markedly following unrestricted access to DAA treatment, from 4,740 in 2015 (1,310 interferon-based, and 3,430 interferon-free) to 32,560 in 2016 (160 interferon-based, and 32,400 interferon-free; Figure 1).

It is estimated that 14,190 individuals with cirrhosis initiated DAA treatment between 2014 and 2016 of whom 11,670 individuals received treatment through PBS, and 2,520 through early DAA access avenues, including clinical trials, generic importation, and pharmaceutical company compassionate access programs.

Figure 1: Estimated annual number of individuals with chronic HCV infection initiating HCV treatment from 1997 to 2016 in Australia.



IFN: interferon; PegIFN: pegylated interferon; RBV: ribavirin; DAA: Direct acting antiviral

2. Data on elbasvir/grazoprevir were not included in this analysis.

In 2015, an estimated 227,310 individuals were living with chronic HCV infection in Australia, including 20,180 individuals with HCV-related cirrhosis.³ An estimated 70% of the total population living with HCV-related cirrhosis in Australia initiated DAA treatment between 2014 and 2016 (Figure 2).

DAA treatment uptake, 2016

An estimated 32,400 individuals initiated DAA treatment in 2016 (March-December) in Australia, including 11,310 in New South Wales, 8,400 in Victoria, 6,430 in Queensland, 2,000 in South Australia, 2,270 in Western Australia, 830 in Australian Capital Territory, 770 in Tasmania, and 360 in Northern Territory (Figure 2). For 30 individuals, the jurisdiction data was not available.

It is estimated that 14% of total people living with chronic HCV infection in Australia initiated DAA treatment in 2016. This proportion varied between 10% and 23% across jurisdictions (Figure 2).

Figure 2: The estimated proportion of individuals living with chronic HCV infection in Australia who initiated DAA treatment between 2014 and 2016, by liver fibrosis stage

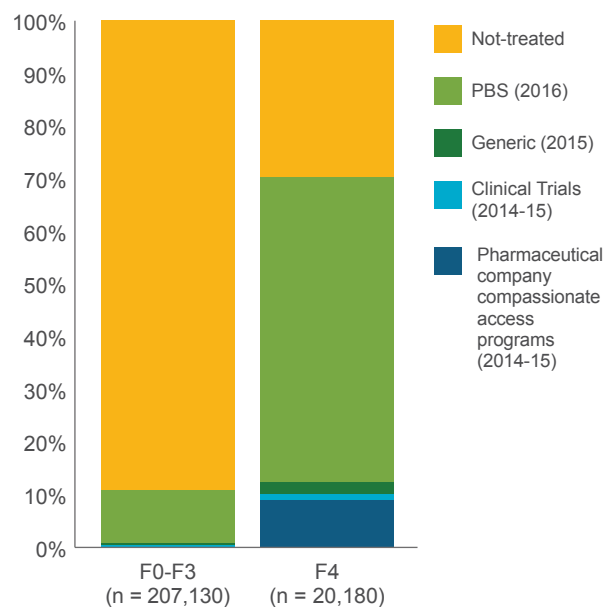
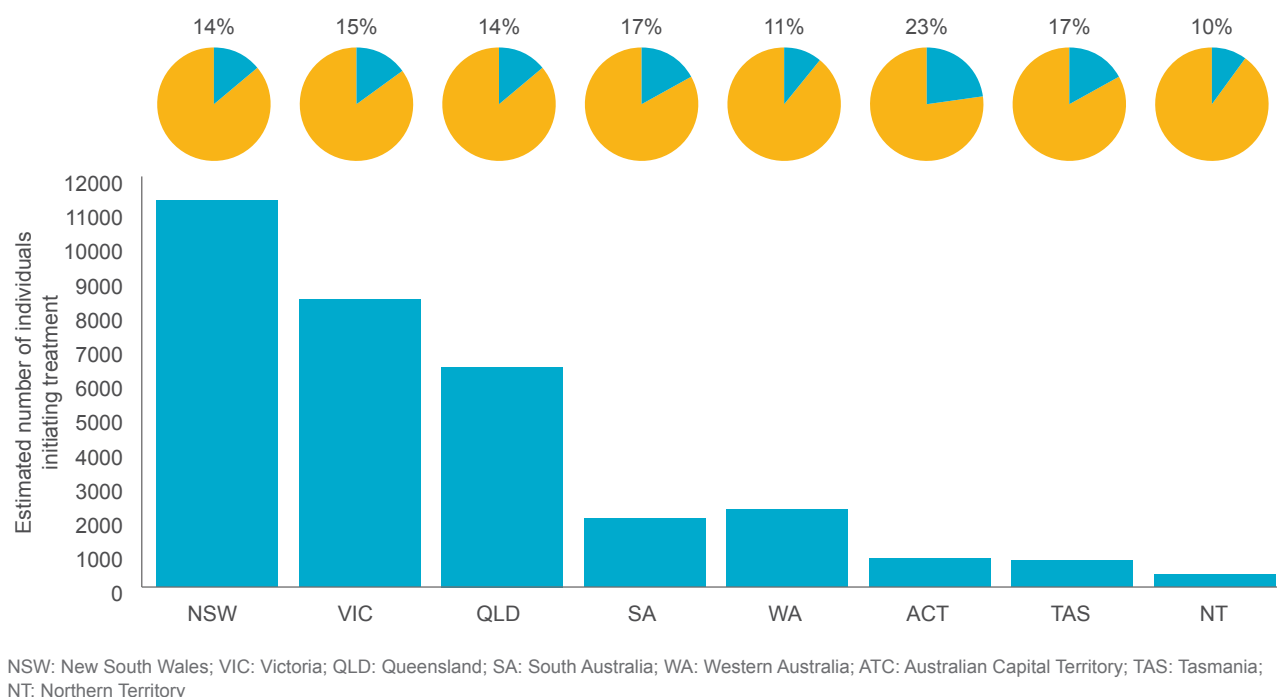


Figure 3: The estimated number of individuals initiating DAA treatment (bar charts) and the proportion of individuals living with chronic HCV infection who initiated DAA treatment (pie charts) in 2016, by jurisdiction



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

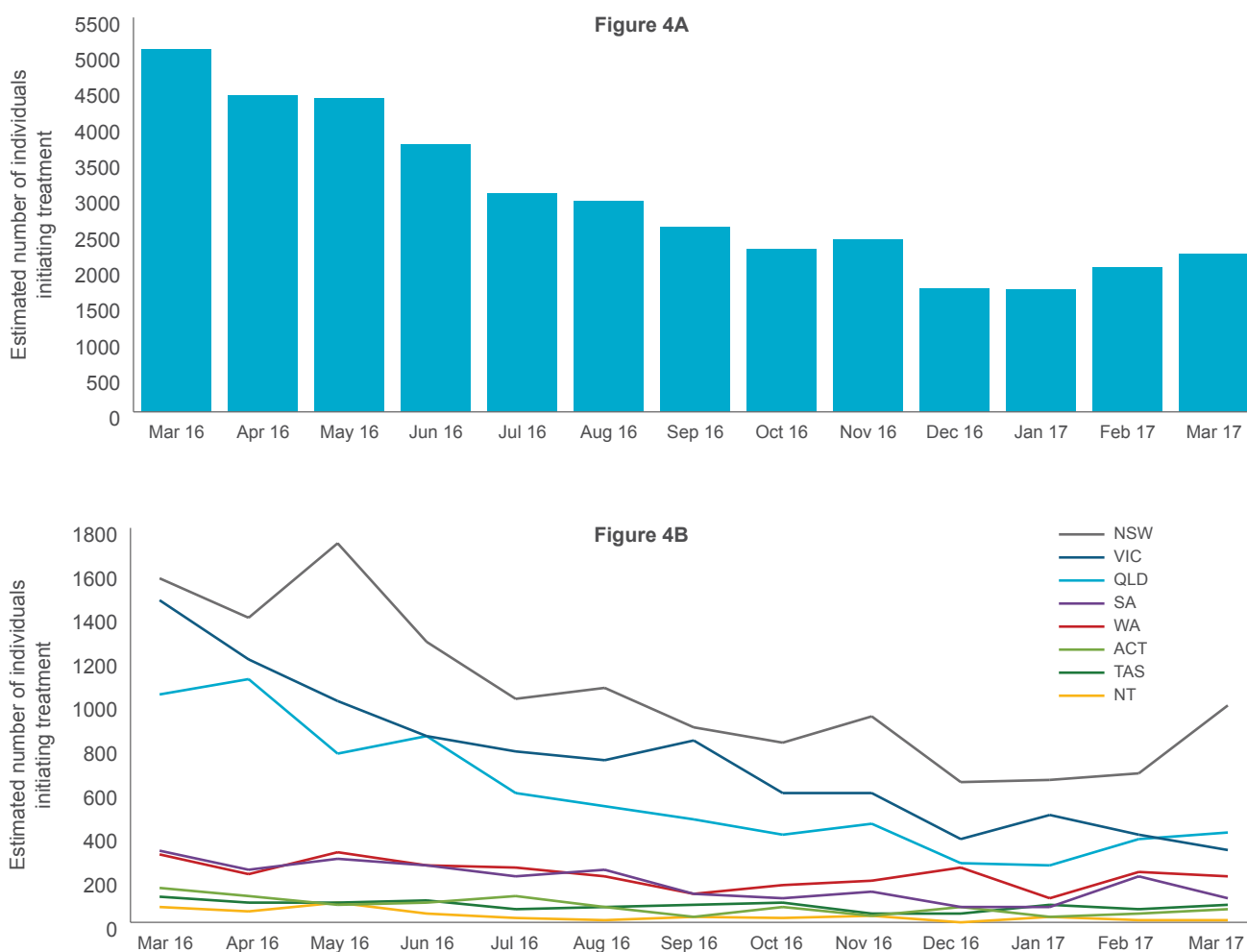
DAA treatment uptake, 2016 and 2017 (January-March)

Data on monthly DAA treatment uptake were available up to March 2017. After an initial decreasing trend, the monthly number of DAA initiation has reached a relatively steady pattern since October 2016 (Figure 4A). 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. The monthly trend of DAA treatment

uptake in each jurisdiction is illustrated in Figure 4B. A total of 38,470 individuals initiated DAA treatment between March 2016 and March 2017.

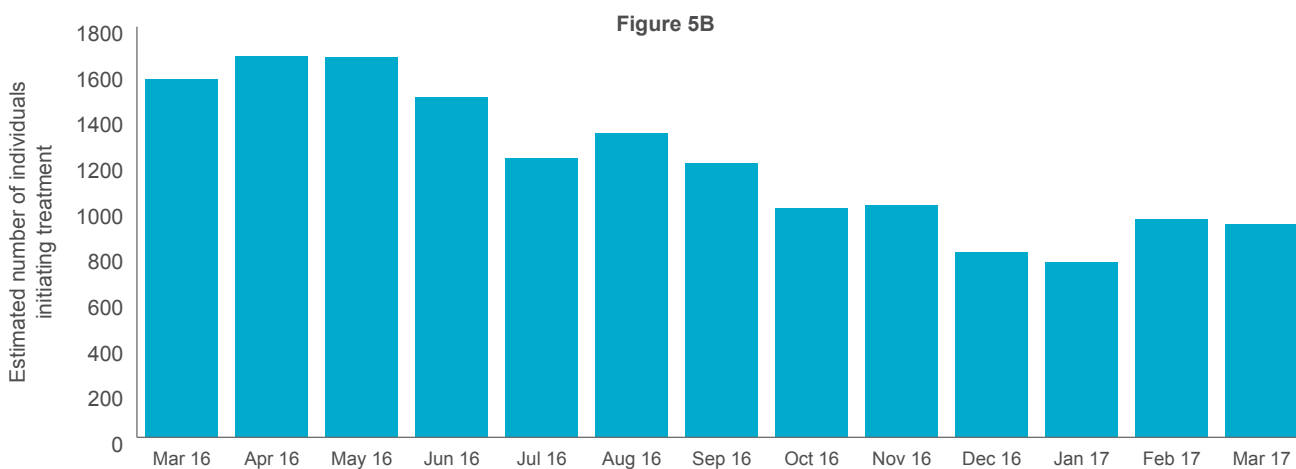
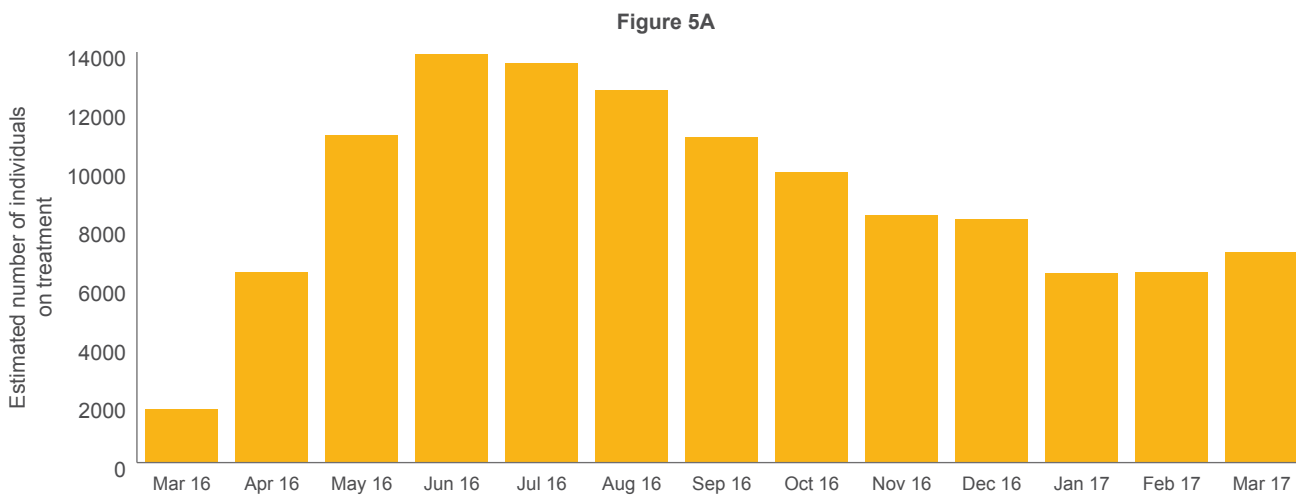
A similar overall pattern in DAA treatment uptake was observed using other data sources (Figure 5). Figure 5A shows the number of individuals receiving DAA treatment in each month which is a combination of those initiating and continuing treatment. Figure 5B shows the monthly number of individuals initiating DAA treatment, using data collected from a panel of over 3,500 community pharmacies.

Figure 4: The estimated number of individuals initiating DAA treatment in each month during March 2016 to March 2017 in Australia (A), and by Jurisdiction (B)



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

Figure 5: Number of individuals receiving DAA treatment (initiation plus continuation) in each month during March 2016 to March 2017, based on the Pharmaceutical Benefits Schedule Item Reports⁴ (A), and number of individuals initiating DAA treatment in each month during March 2016 to March 2017, based on the data collected from a panel of >3500 community pharmacies (B)⁵



4. Data Source: Pharmaceutical Benefits Schedule Item Reports (available at: http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp)
 5. Data Source: QuintilesIMS™ and NostraData

Gender and age distribution of individuals initiating DAA treatment

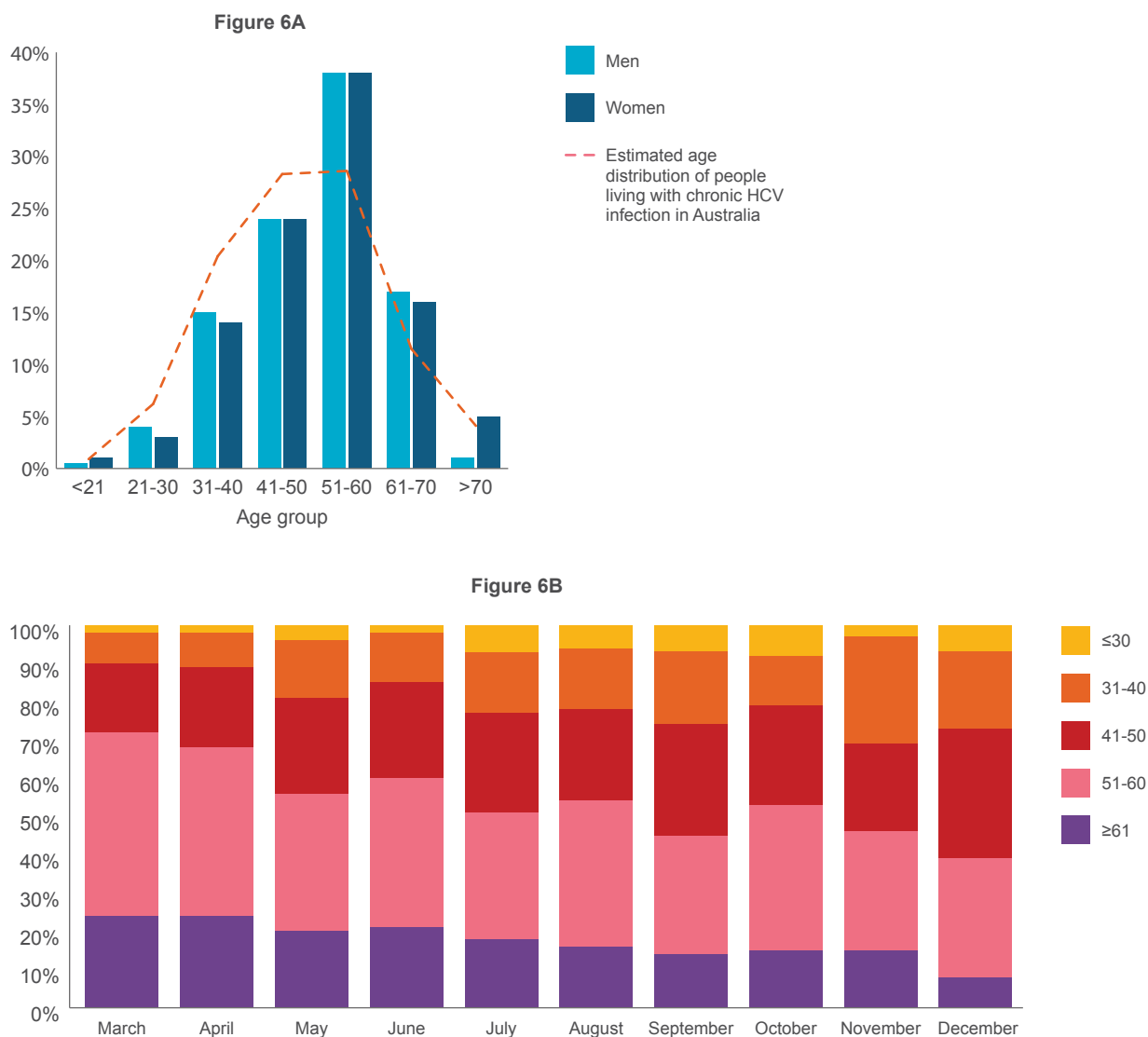
Of individuals initiating DAA treatment in 2016, 66% were men and 34% were women.

Age distribution of individuals initiating treatment was similar between men and women (Figure 6A). The highest proportion of total individuals were 51-60 years old (38%), followed by 41-50 years old (24%). 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 6A).

The age distribution of individuals initiating DAA treatment in each month showed a trend towards younger age groups (Figure 6B). While 43% of individuals initiating DAA treatment in 2016 were ≤50 years old, the proportion increased from 31% in March to 61% in December.

Figure 6: Age distribution of individuals initiating DAA treatment in 2016, by gender (A) and month of treatment initiation (B).



Distribution of DAA regimens prescribed for individuals initiating DAA treatment

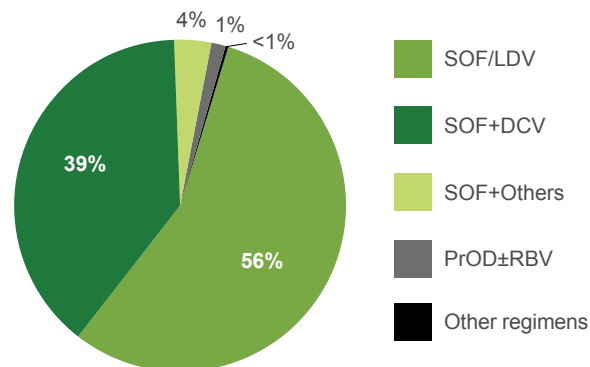
The most commonly prescribed regimen was sofosbuvir/ledipasvir±ribavirin for 56%, followed by sofosbuvir+daclatasvir±ribavirin for 39%, sofosbuvir+other agents for 4% and paritaprevir/ritonavir/ombitasvir+dasabuvir±ribavirin for 1% (Figure 7). Other antiviral agents used in combination with sofosbuvir included ribavirin, or pegylated interferon+ribavirin.

The breakdown of treatment initiation numbers by treatment regimen and treatment course duration is shown in Figure 8. Of individuals initiated on sofosbuvir/ledipasvir±ribavirin (n=18,020), 14% were prescribed an 8-week course, 75% a 12-week course, and 11% a 24-week course. Of individuals initiated on sofosbuvir+daclatasvir±ribavirin (n=12,600), 64% were prescribed a 12-week course, and 36% a 24-week course. Of individuals initiated on paritaprevir/ritonavir/ombitasvir+dasabuvir±ribavirin (n=460), 85% (n=390) were prescribed a 12-week course, and 15% (n=70) a 24-week course.

Distribution of health care providers prescribing for individuals initiating DAA treatment

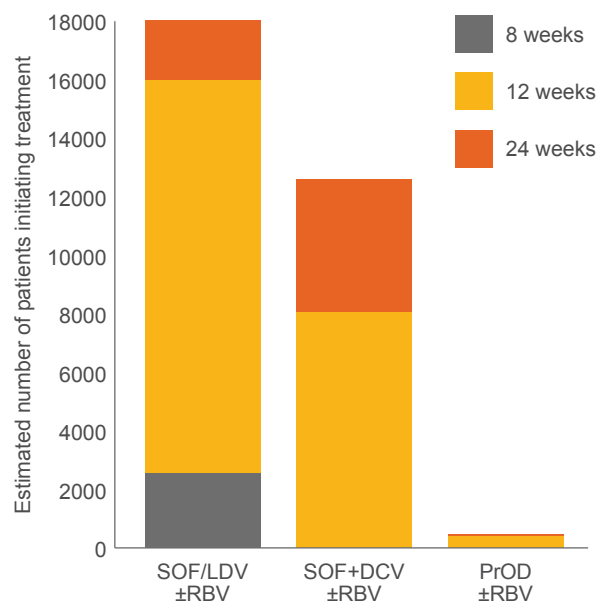
The majority of individuals initiating DAA treatment received their prescriptions from gastroenterologists (50%), followed by general practitioners (GPs; 19%), infectious diseases physicians (8%), and other specialists (4%). Twenty percent of individuals received their prescriptions from other physicians, 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, 62% of individuals received their prescriptions from specialists.

Figure 7: Distribution of DAA regimens prescribed in 2016



SOF: Sofosbuvir; LDV: Ledipasvir; DCV: Daclatasvir; PrOD: Parataprevir/ritonavir/Ombitasvir/Dasabuvir; RBV: Ribavirin

Figure 8: Distribution of DAA regimens prescribed in 2016, by treatment regimen and treatment course duration



SOF: Sofosbuvir; LDV: Ledipasvir; DCV: Daclatasvir; PrOD: Parataprevir/ritonavir/Ombitasvir/Dasabuvir; RBV: Ribavirin

Distribution of prescriber types varied across jurisdictions (Figure 9). Gastroenterologists were the prominent prescriber in most jurisdictions. In Northern Territory, 27% of individuals were prescribed DAA treatment by infectious disease physicians, compared to 10% by gastroenterologist. Across jurisdictions, the proportion of individuals prescribed DAA treatment by GPs was highest in Tasmania (29%) and Queensland (25%). In Western Australia, the proportion of individuals prescribed

DAA treatment by gastroenterologists and GPs were comparable with 21% and 19% of individuals receiving their prescriptions from gastroenterologists and GPs, respectively.

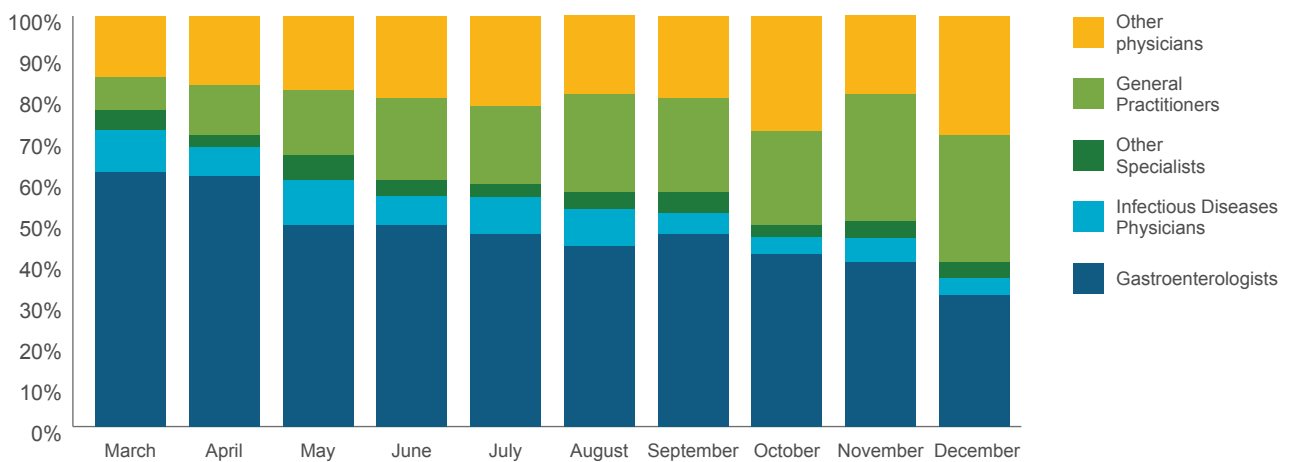
The distribution of prescriber types in each month is shown in Figure 10. The proportion of individuals prescribed DAA by GPs increased from 8% in March to 31% in December.

Figure 9: Distribution of prescriber types for individuals initiating DAA treatment in 2016, 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: Distribution of prescriber types in each month for individuals initiating DAA treatment in 2016 in Australia



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.

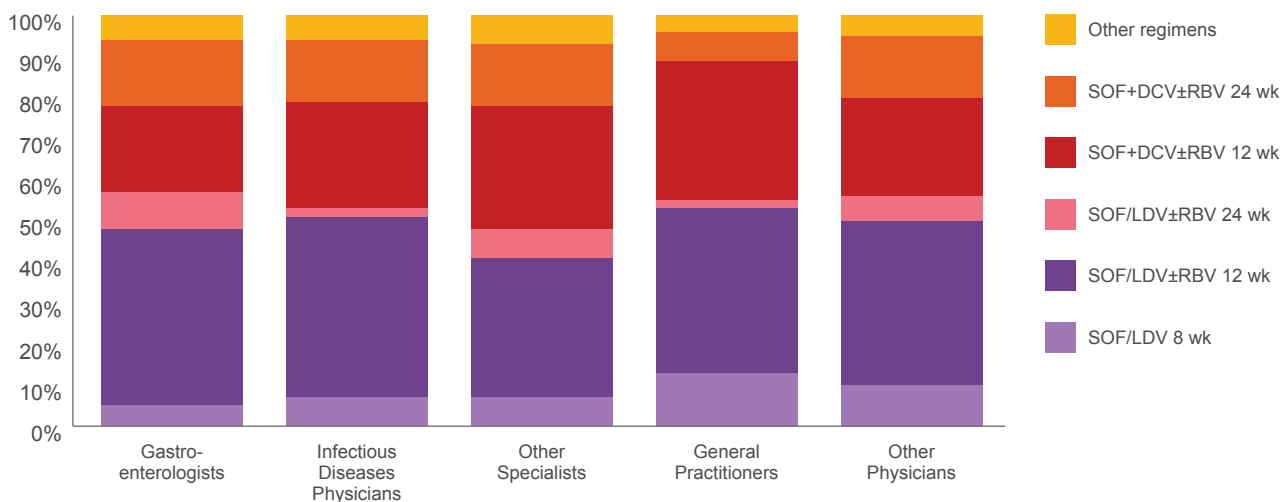
Distribution of prescribed DAA regimens by prescription type

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±ribavirin, followed by 12 weeks sofosbuvir+daclatasvir±ribavirin. Of prescriptions by specialists, 8% included 24 weeks sofosbuvir/ledipasvir±ribavirin and 16% included 24 weeks sofosbuvir+daclatasvir±ribavirin. These proportions were 2% and 7%, respectively, among prescriptions by GPs. These two regimens are primarily prescribed

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

The proportion of 24-week courses to the total prescriptions of sofosbuvir+daclatasvir by GPs was 5%. Extrapolating this proportion to the total DAA initiations by GPs, an estimated 320 individuals with cirrhosis were prescribed DAA treatment by GPs, equating to only 3% of the total number of individuals with cirrhosis initiating DAA treatment in 2016.

Figure 11: Distribution of prescribed DAA regimens by prescriber types for individuals initiating DAA treatment in 2016



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.

Methodology

The following data sources were used for analysis:

- The PBS receives the administrative records of dispensed prescriptions from pharmacies across Australia and has reported the aggregated data since 1992. These data were used to estimate the number of individuals initiating HCV treatments from 1997 to 2012. The details of the methods for the estimations were previously described.⁶
- 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 interferon-based treatments from 2013 to 2016, and those initiating interferon-free DAA treatments in 2016. These data were also used for all sub-group analyses of DAA treatment uptake in 2016.
- 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.⁷

The number of individuals with cirrhosis initiating DAA treatment was estimated. Among individuals initiating DAA treatment 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.⁸ Among individuals initiating DAA treatment in 2016 through PBS-listing, sofosbuvir+daclatasvir was primarily prescribed for HCV genotype 3 (cirrhosis – 24 weeks; no cirrhosis - 12 weeks). The proportion of those

initiating a 24-week sofosbuvir+daclatasvir to the total sofosbuvir+daclatasvir initiations was extrapolated to the total DAA initiations to estimate the DAA treatment uptake among individuals with cirrhosis in 2016.

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. For estimating the number of individuals with cirrhosis initiating DAA treatment through PBS, it was assumed that a 24-week sofosbuvir+daclatasvir regimen was prescribed for individuals with genotype 3 and cirrhosis. This regimen might have been used for some individuals with pre-cirrhosis, particularly those with severe fibrosis (F3), potentially leading to an overestimation of the number of individuals with cirrhosis treated with DAA treatment. The assumed proportion of individuals with cirrhosis among those accessed DAA treatment through clinical trials and compassionate access programs were based on expert opinion.

6. Hajarizadeh B, Grebely J, McManus H, et al. Chronic hepatitis C burden and care cascade in Australia in the era of interferon-based treatment. *Journal of Gastroenterology and Hepatology* 2017; 32(1): 229-36.

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

8. 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