

Monitoring hepatitis C treatment uptake in Australia

Issue #10 June 2019¹

Initiations of new treatment for chronic hepatitis C from 2016 to 2018

An estimated 74,600 individuals initiated direct acting antiviral (DAA) treatment for chronic hepatitis C virus (HCV) infection in Australia, including 70,260 individuals through Pharmaceutical Benefits Scheme (PBS) during 2016 to 2018, and 4,340 individuals through early DAA access avenues in 2014 and 2015. It is estimated that 33% of the people living with chronic HCV infection in Australia initiated DAA treatment.

Of individuals initiating DAA treatment during 2016 to 2018 (n=70,260), 67% were men, and 51% were 50 years old or younger. The proportion of individuals ≤50 years old initiating treatment increased from 28% in March 2016 to 67% in the last quarter of 2018.

The most commonly prescribed regimen was sofosbuvir/ledipasvir for 39%, followed by sofosbuvir+daclatasvir for 27%, and sofosbuvir/velpatasvir for 23%. Since August 2018 when both pan-genotypic regimens were available (i.e., sofosbuvir/velpatasvir and glecaprevir/pibrentasvir), 53% of individuals have been initiated on sofosbuvir/velpatasvir, 32% on glecaprevir/pibrentasvir, and 15% on other regimens.

Overall, 49% of individuals have been prescribed DAA treatment by specialists (39% by gastroenterologist, 7% by infectious diseases physicians, and 3% by other specialist), while 29% 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 41% in the last quarter of 2017, followed by a relatively constant trend in 2018. Among individuals initiating DAA treatment in 2018, 39% were initiated on treatment by GPs, and 33% by specialists.

1. The Kirby Institute. Monitoring hepatitis C treatment uptake in Australia (Issue 10). The Kirby Institute, UNSW Sydney, NSW, Australia, June 2019 (available online at: <https://kirby.unsw.edu.au/report/monitoring-hepatitis-c-treatment-uptake-australia-issue-10-june-2019>). For more information, contact Dr Behzad Hajari (bhajarizadeh@kirby.unsw.edu.au) or Professor Greg Dore (gdore@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 (PBSS):

- 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®)
- August 2018: Glecaprevir/pibrentasvir (Maviret®)
- April 2019: Sofosbuvir/velpatasvir/voxilaprevir (Vosevi®)

Issue #10 newsletter provides data on monthly uptake of DAA treatment through PBS-listing between March 2016 and December 2018 by jurisdiction, patients' gender and age, treatment regimen, and prescriber type. The data of sofosbuvir/velpatasvir/voxilaprevir have not been provided in this issue given this regimen was listed on PBS in 2019.

DAA treatment uptake

An estimated 70,260 individuals initiated DAA treatment through the PBS between March 2016 and December 2018 in Australia. In 2014 and 2015, prior to DAA regimens being listed on PBS, an estimated 4,340 individuals received DAA treatment through early DAA access avenues, including clinical trials, pharmaceutical company compassionate access programs, and generic importation.² Considering this number, an overall estimated number of 74,600 individuals received DAA treatment from 2014 to 2018.

In 2015, an estimated 227,310 individuals were living with chronic HCV infection in Australia.³ Given the overall treatment initiation in 74,600 individuals, an estimated 33% of individuals living with chronic HCV infection in Australia, initiated DAA treatment between 2014 and 2018.

At jurisdictional level, the number of individuals initiating DAA treatment through the PBS between March 2016 and December 2018 included 24,510 in New South Wales, 17,750 in Victoria, 13,830 in Queensland, 4,580 in South Australia, 5,780 in Western Australia, 1,410 in Australian Capital Territory, 1,720 in Tasmania, and 700 in Northern Territory.⁴ The estimated proportion of individuals living with chronic HCV infection initiating DAA treatment in this period varied between 19% to 39% across jurisdictions (Figure 1).

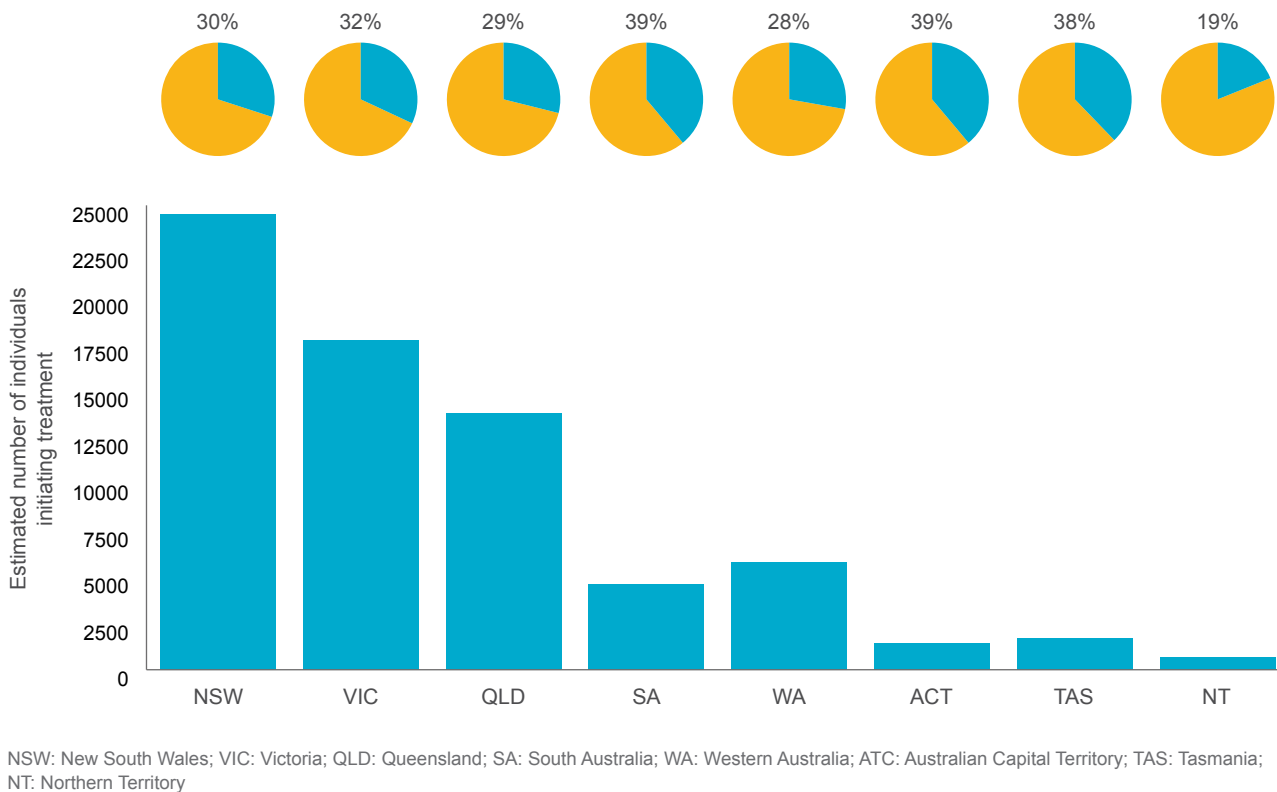
Among 70,260 individuals initiating DAA treatment through the PBS during 2016 to 2018, an estimated 2,920 individuals (4.1%) received more than one DAA treatment course. DAA retreatment could be related to response failure to the first DAA treatment (including early treatment discontinuation), or HCV reinfection after successful treatment.

2. 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* 2018; 25(6): 640-8

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

4. For a small number of individuals (n=10 to 20), more than one jurisdiction were recorded.

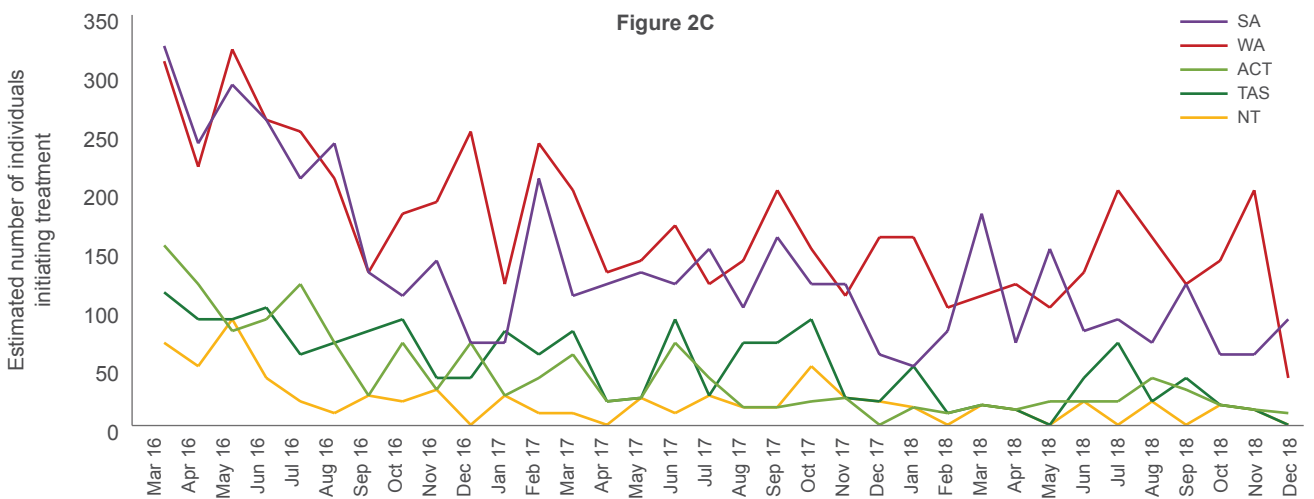
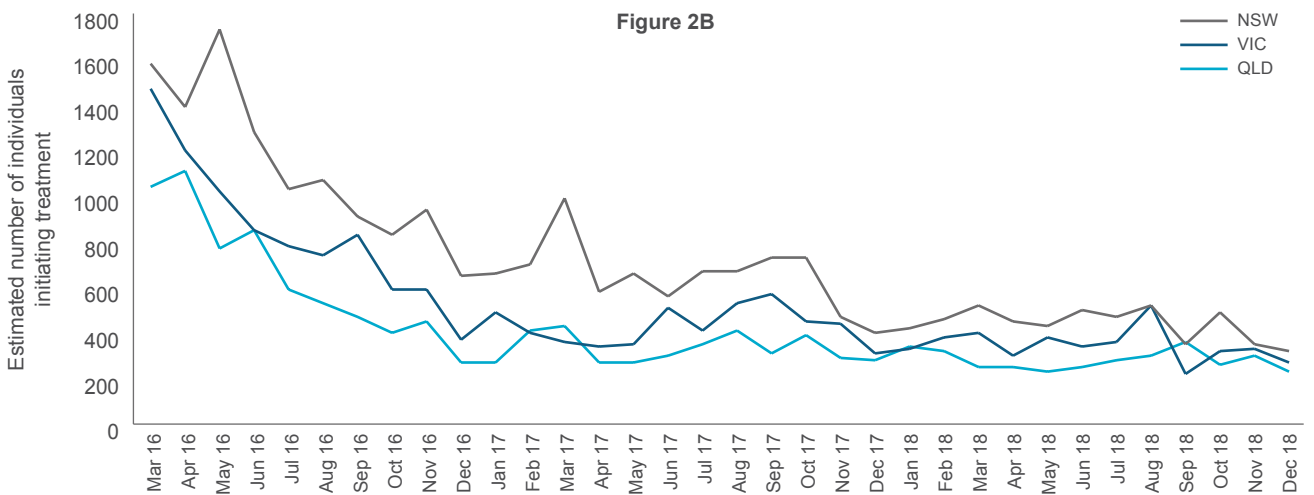
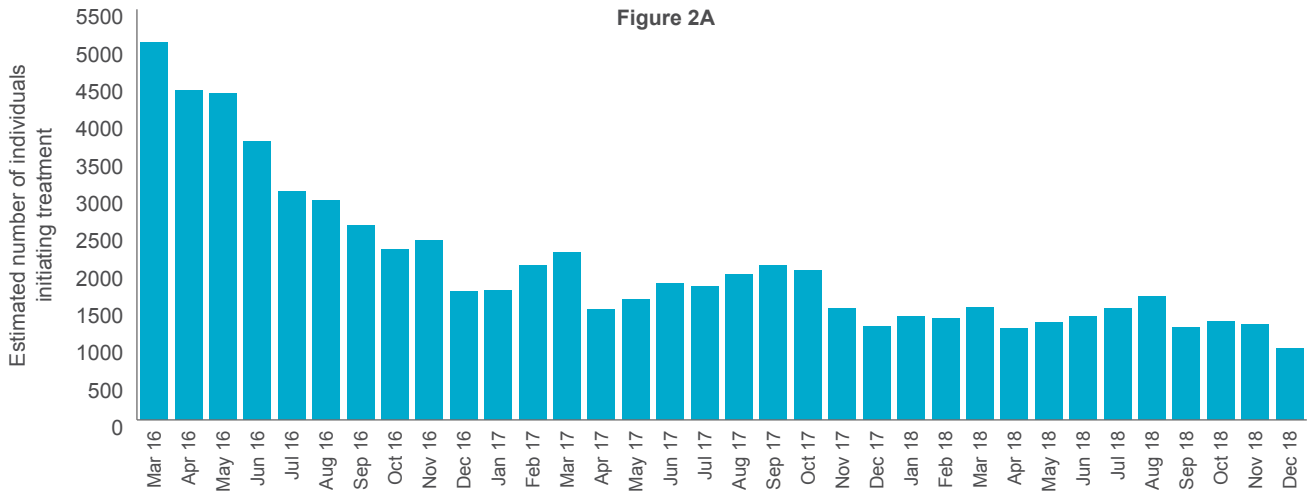
Figure 1: The estimated number of individuals initiating DAA treatment (bar charts) and the proportion of individuals living with chronic HCV infection who initiated DAA treatment (pie charts) between 2016 and 2018, by jurisdiction



The monthly trends of DAA treatment uptake in Australia and in each jurisdiction are illustrated in Figure 2. In 2016, 2017, and 2018, respectively 32,610, 21,540, and 16,110 individuals initiated DAA treatment. A modelling study indicated that 17,100 treatment initiations in 2018 and an annual 13,680 treatment initiations from 2019 onward are required to put Australia on track to achieve WHO HCV elimination targets of treating 80% of people living with HCV and 80% reduction in HCV incidence by 2030.⁵ The treatment uptake in 2018 was slightly lower than that required.

5. Kwon JA, Dore GJ, Grebely J, et al. Australia on track to achieve WHO HCV elimination targets following rapid initial DAA treatment uptake: A modelling study. *Journal of Viral Hepatitis* 2019; 26(1): 83-92.

Figure 2: Estimated number of individuals initiating DAA treatment in each month during 2016 to 2018 in Australia (A), and by Jurisdiction (B and C)



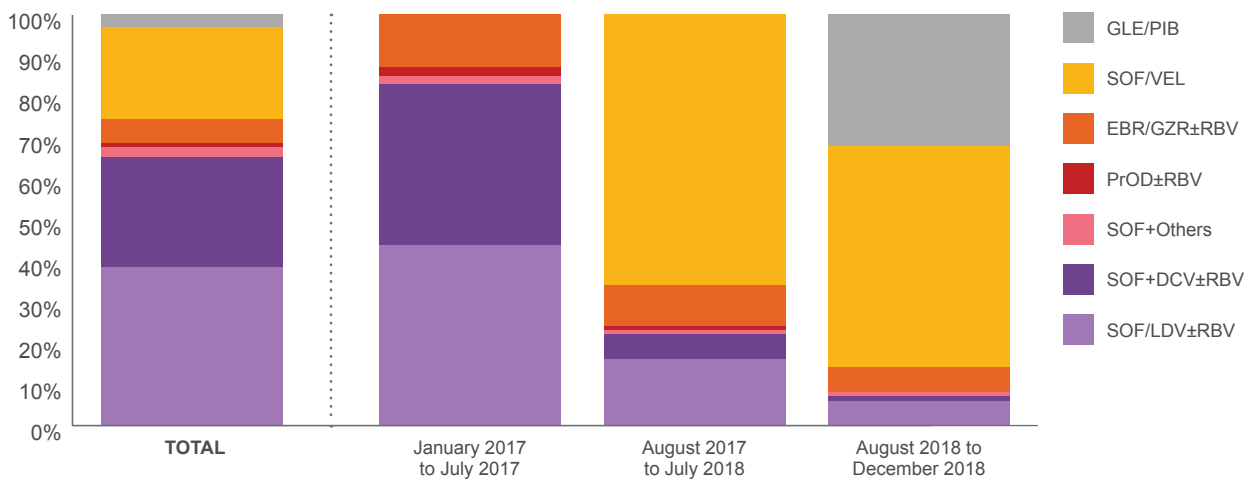
NSW: New South Wales; VIC: Victoria; QLD: Queensland; SA: South Australia; WA: Western Australia; ACT: Australian Capital Territory; TAS: Tasmania; NT: Northern Territory

Distribution of DAA regimens prescribed for individuals initiating treatment

Overall, the most commonly prescribed regimen was sofosbuvir/ledipasvir±ribavirin for 39%, followed by sofosbuvir+daclatasvir±ribavirin for 27%, and sofosbuvir/velpatasvir for 23%. Sofosbuvir/velpatasvir and glecaprevir/pibrentasvir were PBS listed on August

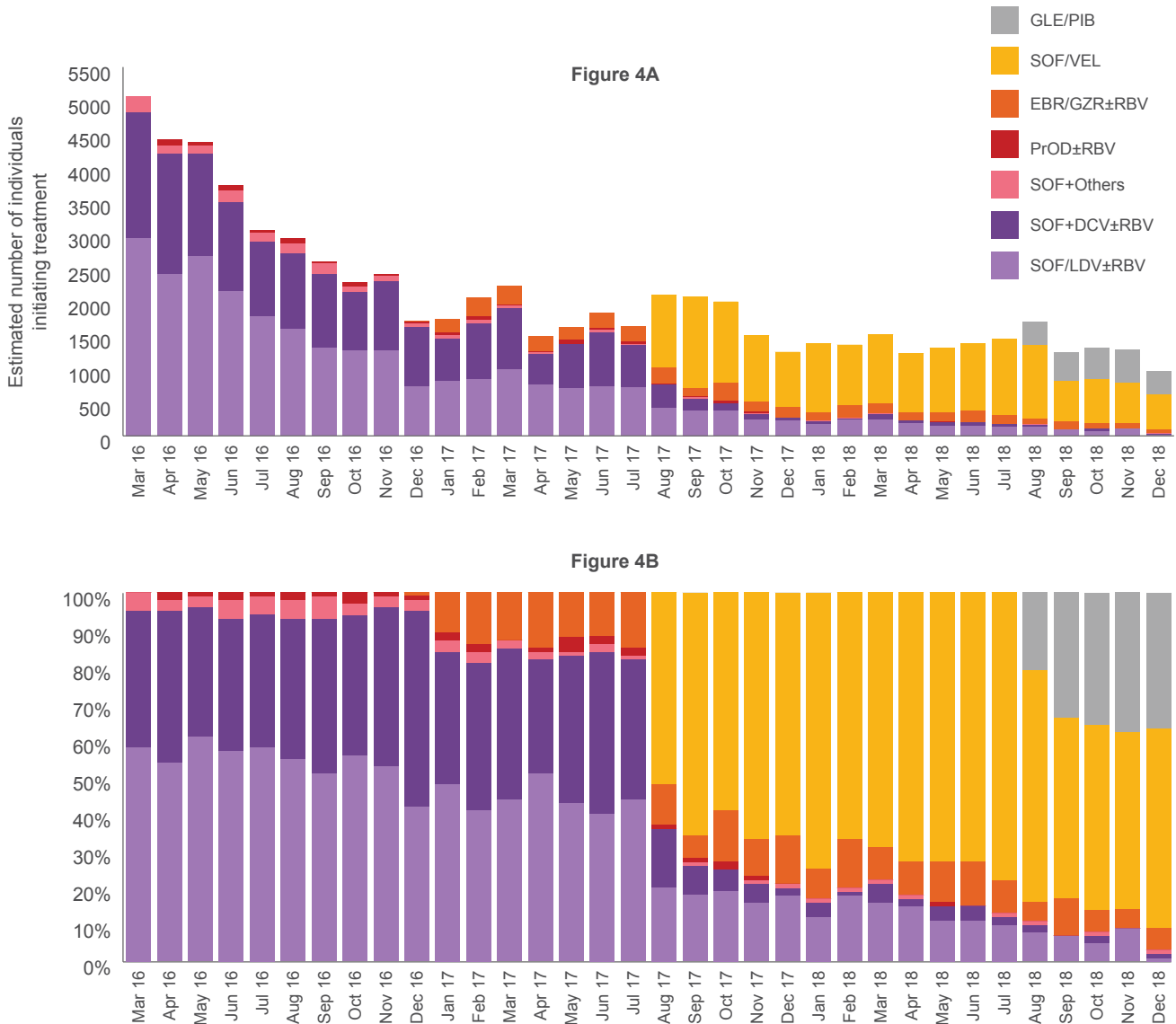
2017 and August 2018, respectively. During August 2017 to July 2018, Sofosbuvir/velpatasvir was the most commonly prescribed regimen (67%). Since August 2018, 53% of individuals initiating DAA have been prescribed sofosbuvir/velpatasvir, 32% have been prescribed glecaprevir/pibrentasvir, and 15% have been initiated on other regimens (Figures 3 and 4).

Figure 3: Distribution of DAA regimens prescribed during 2016 to 2018 (overall), January to July 2017 (seven months prior to SOF/VEL being PBS listed), August 2017 to July 2018 (before GLE/PIB being PBS listed), and August to December 2018



SOF: Sofosbuvir; LDV: Ledipasvir; DCV: Daclatasvir; EBR: Elbasvir; GZR: Grazoprevir; PrOD: Paritaprevir/ritonavir/Ombitasvir+Dasabuvir; VEL: Velpatasvir; GLE: Glecaprevir; PIB: Pibrentasvir RBV: Ribavirin

Figure 4: Absolute frequency (A) and relative frequency (B) of DAA regimens prescribed for individuals initiating DAA treatment in each month during 2016 to 2018

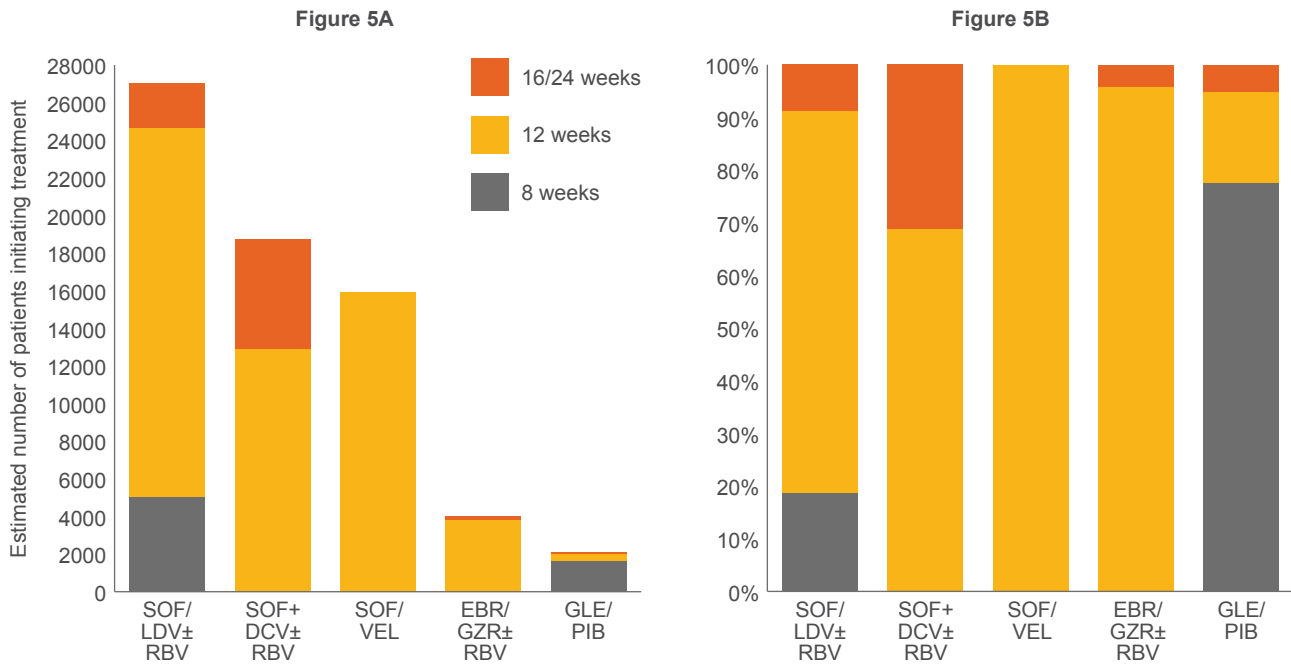


SOF: Sofosbuvir; LDV: Ledipasvir; DCV: Daclatasvir; EBR: Elbasvir; GZR: Grazoprevir; PrOD: Paritaprevir/ritonavir/Ombitasvir+Dasabuvir; VEL: Velpatasvir; GLE: Glecaprevir; PIB: Pibrentasvir RBV: Ribavirin

The breakdown of treatment initiation numbers by treatment regimen and treatment course duration is shown in Figure 5. Of individuals initiated on sofosbuvir/ledipasvir±ribavirin (n=27,050), 19% were prescribed an 8-week course, 72% a 12-week course, and 9% a 24-week course. Of individuals initiated on sofosbuvir+daclatasvir±ribavirin (n=18,720), 69% were prescribed a 12-week course, and 31% a 24-week course. Of individuals initiated on elbasvir/

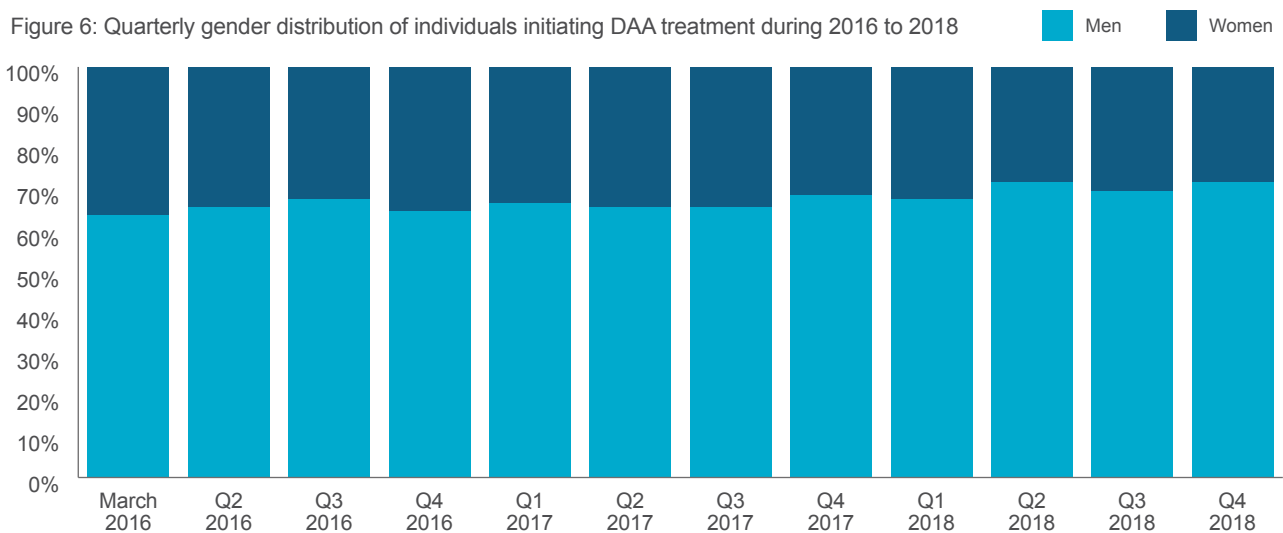
grazoprevir±ribavirin (n=3,990), 96% were prescribed a 12-week course, and 4% a 16-week course. Of individuals initiated on glecaprevir/pibrentasvir (n=2,090), 78% were prescribed an 8-week course, 17% a 12-week course, and 5% a 16-week course. Sixteen weeks glecaprevir/pibrentasvir is prescribed for individuals with a response failure to a previous DAA treatment.

Figure 5: Absolute frequency (A) and relative frequency (B) of DAA regimens prescribed during 2016 to 2018, by treatment regimen and treatment course duration



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

Figure 6: Quarterly gender distribution of individuals initiating DAA treatment during 2016 to 2018



Gender and age distribution of individuals initiating DAA treatment

Of individuals initiating DAA treatment between 2016 and 2018, 67% were men and 33% were women. The proportion of women decreased slightly over time, from 36% in March 2016 to 28% in the last quarter of 2018 (Figure 6).

Age distribution of individuals initiating DAA treatment was similar between men and women (Figure 7). The highest proportion of individuals were 51-60 years (33%), followed by 41-50 years (26%). An overall 48% were older than 50 years. Compared to the age distribution of the total population living with chronic HCV infection in Australia in 2015, a shift towards older age groups was observed among those initiating DAA treatment (Figure 7). This shift, however, is decreasing given that a trend towards younger age groups is observed over time. The proportion of individuals ≤ 50 years initiating treatment increased from 28% in March 2016 to 67% in the last quarter of 2018 (Figure 8).

Figure 7: Age distribution of individuals living with chronic HCV infection in 2015⁶ (dotted line) and those initiating DAA treatment during 2016 to 2018 (bars)

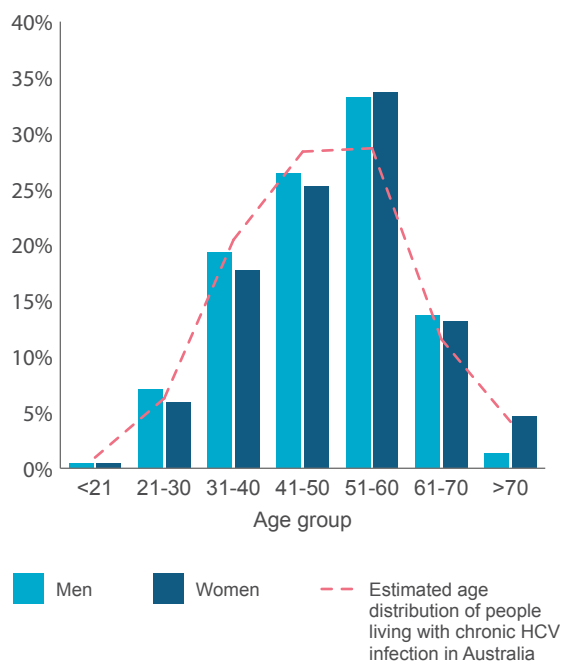
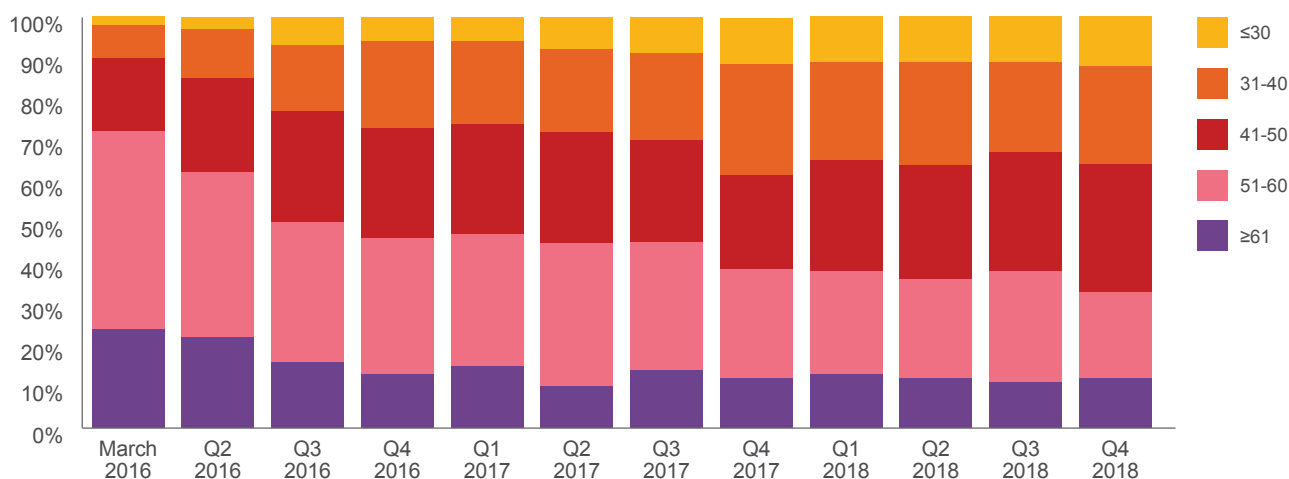


Figure 8: Quarterly age distribution of individuals initiating DAA treatment during 2016 to 2018



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

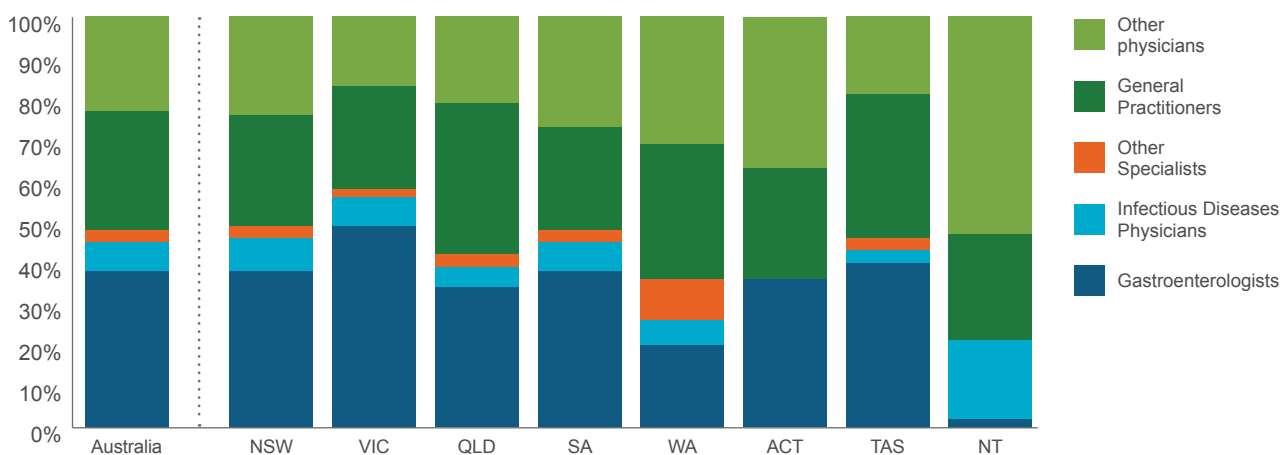
Distribution of health care providers prescribing for individuals initiating DAA treatment

Among individuals initiating DAA treatment during 2016 to 2018, the majority received their prescriptions from gastroenterologists (39%), followed by general practitioners (GPs; 29%), infectious diseases physicians (7%), and other specialists (3%). Twenty-two 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, other/unclassified non-specialist and undefined (Figure 9). Overall, 49% of individuals received their prescriptions from specialists.

Distribution of prescriber types varied across jurisdictions (Figure 9). In all jurisdictions, except for Victoria, specialists initiated DAA treatment for less than 50% of individuals. Across jurisdictions, the proportion of individuals initiated on DAA treatment by GPs was highest in Queensland (37%), Tasmania (35%), and Western Australia (34%).

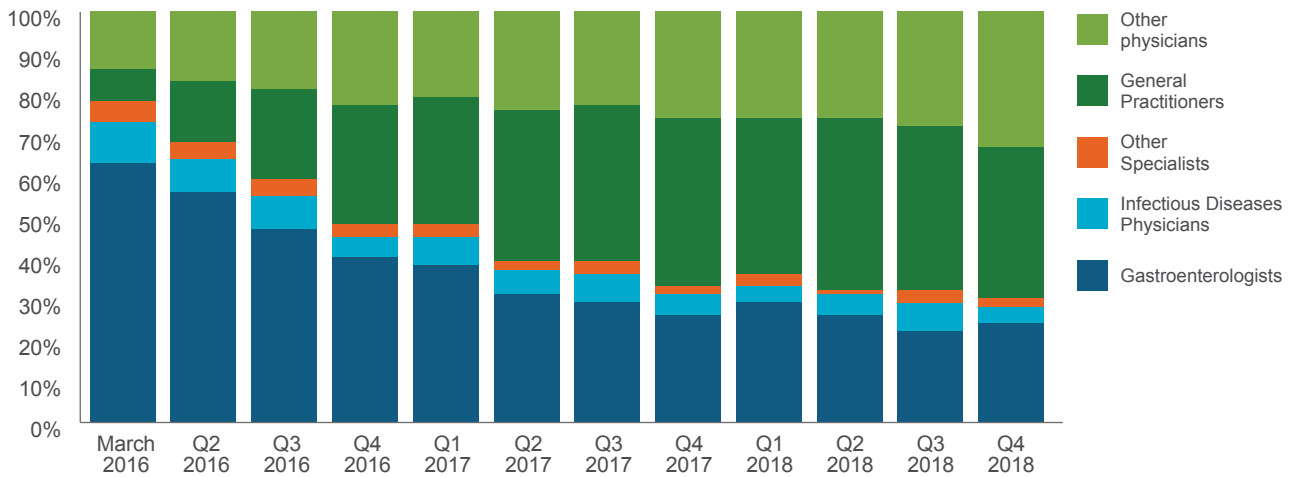
The distribution of prescriber types in each quarter is shown in Figure 10. The proportion of individuals prescribed DAA treatment by GPs increased from 8% in March 2016 to 41% in the last quarter of 2017, followed by a relatively constant trend in 2018. Among individuals initiating DAA treatment in 2018, 39% were initiated on treatment by GPs, 33% by specialists, and 28% by other physicians.

Figure 9: Distribution of prescriber types for individuals initiating DAA treatment during 2016 to 2018, 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, other/unclassified non-specialist and undefined.

Figure 10: Quarterly distribution of prescriber types for individuals initiating DAA treatment during 2016 to 2018



Other physicians included supervised medical officers (e.g., interns, resident medical officers, and registrars), public health physicians, temporary resident doctors, other/unclassified non-specialist and undefined.

Distribution of prescribed DAA regimens by prescriber type

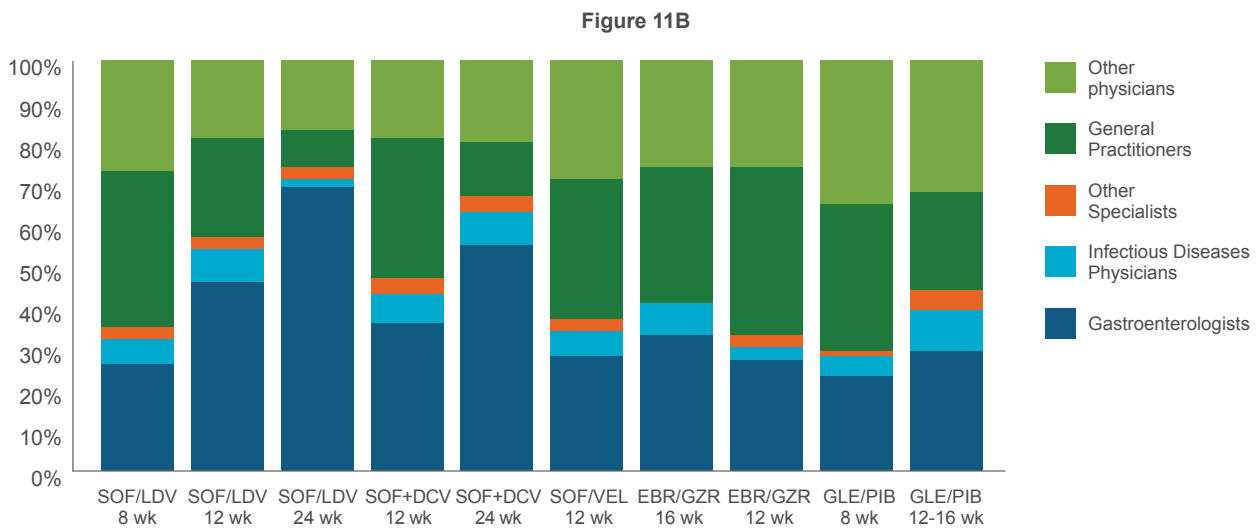
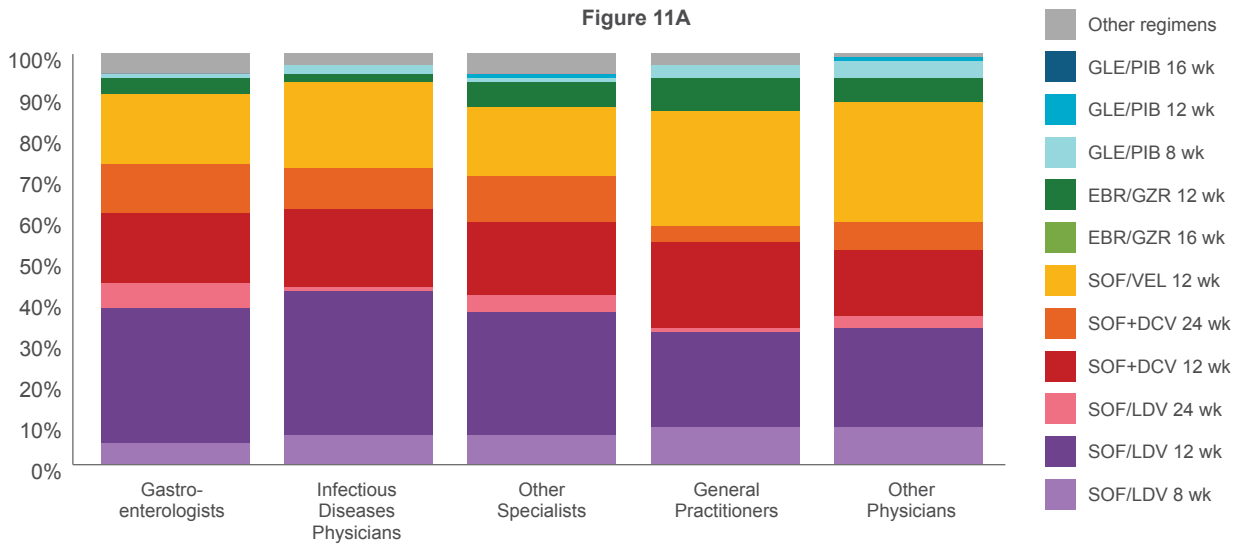
The distribution of prescribed DAA regimens by prescriber type is shown in Figure 11. Among all specialist groups, the most commonly prescribed regimen included 12 weeks sofosbuvir/ledipasvir (31-34%), while among GPs the most commonly prescribed regimen included sofosbuvir/velpatasvir (27%; Figure 11A).

Of prescriptions by specialists, 17% included an extended duration regimen (i.e., 24 weeks sofosbuvir/ledipasvir, 24 weeks sofosbuvir+daclatasvir, 16 weeks elbasvir/grazoprevir, and 12-16 weeks glecaprevir/pibrentasvir), compared to 6% of prescriptions by GPs (Figure 11A). Of the total number of prescriptions of extended duration regimens, 68% were by specialists compared to 13% by GPs (Figure 11B). These regimens are primarily prescribed for patients with cirrhosis, or those with DAA treatment failure.

Across all prescriber types, the highest proportion of 8 weeks treatment (i.e., 8 weeks sofosbuvir/ledipasvir and 8 weeks glecaprevir/pibrentasvir) was observed in prescriptions by GPs and other non-specialist physicians (12% and 13%, respectively; Figure 11A). Of the total number of prescriptions of 8 weeks treatment, 37% were by GPs and 34% by specialists (Figure 11B). This regimen is prescribed for treatment-naïve patients with no cirrhosis.

Of the total number of sofosbuvir/velpatasvir prescriptions, the proportions by specialists and GPs were comparable with 37% prescribed by specialist (28% by Gastroenterologists), and 34% by GPs (Figure 11B).

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 2016 to 2018



Other physicians included supervised medical officers (e.g., interns, resident medical officers, and registrars), public health physicians, temporary resident doctors, other/unclassified non-specialist and undefined.

SOF: Sofosbuvir; LDV: Ledipasvir; DCV: Daclatasvir; EBR: Elbasvir; GZR: Grazoprevir; VEL: Velpatasvir; GLE: Glecaprevir; PIB: Pibrentasvir



Methodology

The methods for the estimations have been described in detail elsewhere.⁷ In brief, 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 December 2018, and for all sub-group analyses of DAA treatment uptake.
- The estimated numbers of individuals living with chronic HCV infection in Australia and in each jurisdiction in 2015, and age distribution among individuals living with chronic HCV infection were extracted from a modelling study.⁸

There are some factors that should be considered in 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 early 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.

7. 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* 2018; 25(6): 640-8.

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