Monitoring hepatitis C treatment uptake in Australia

Issue #13 July 2023[1]

Executive summary

A total of 105,024 individuals have initiated direct acting antiviral (DAA) treatment for chronic hepatitis C virus (HCV) infection in Australia, including 100,684 individuals through Pharmaceutical Benefits Scheme (PBS) during 2016 to 2022, and an estimated 4,340 individuals through early DAA access avenues in 2014-15. In 2022, 5,205 individuals initiated treatment (first course), increasing from 1,141 in the first quarter to 1,432 in the last quarter of 2022. The recent increase in treatment uptake could be explained by enhanced HCV testing programs implemented in the community and prisons in several jurisdictions.

Among individuals initiating DAA treatment during 2016 to 2022 (n=100,684), 68% were men, and median age was 47 years (quartiles 1-3: 38-57). 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, 41% on glecaprevir/pibrentasvir, and 6% on other regimens.

Most individuals initiating DAA treatment, received their prescriptions from general practitioners (GPs; 46%), followed by gastroenterologists (35%). Overall, 52% of individuals were initiated on treatment by specialists, and 48% by non-specialists (i.e., GPs and nurse practitioners). A total of 2,048 individuals were initiated on treatment by nurse practitioners, increasing from 92 in 2017 to 535 in 2022.

Among individuals initiating DAA treatment during 2016 to 2022, 8.6% discontinued treatment, including 4.0% early discontinuation (i.e., dispensed 28 days of treatment) and 4.6% late discontinuation (i.e., dispensed at least 56 days of treatment, but not all recommended duration). The proportion of early discontinuation increased from less than 3% in 2016 to 8-9% in 2021, followed by a relatively stable trend during 2022. Among individuals who discontinued treatment, 26% received re-treatment.

Among individuals initiating DAA treatment during 2016 to 2022, 8.5% received at least one course of re-treatment. Among re-treatment initiations, an estimated 57% were for HCV re-infection and 43% for treatment failure. The number of re-treatment initiations for treatment failure increased during the second quarter of 2019, corresponding to sofosbuvir/velpatasvir/voxilaprevir availability through PBS (April 2019), and has decreased since. The number of re-treatment initiations for HCV re-infection increased until mid-2020, stabilised during 2020-21, and increased again in 2022. This latest increase could be the result of enhanced HCV testing programs implemented in several jurisdictions through which many individuals with HCV re-infection were diagnosed and linked to clinical care.

1. Hajarizadeh B, Carson JM, Dore GJ. Monitoring hepatitis C treatment uptake in Australia (Issue 13). The Kirby Institute, UNSW, Sydney NSW, Australia, July 2023, DOI: 10.26190/81wp-fr56 (available online at: https://www.kirby.unsw.edu.au/research/reports/monitoring-hepatitis-c-treatment-uptake-australia-issue-13-july-2023). For more information, contact Dr Behzad Hajarizadeh (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®)
- August 2018: Glecaprevir/pibrentasvir (Maviret®)
- April 2019: Sofosbuvir/velpatasvir/voxilaprevir (Vosevi®)

Issue #13 newsletter provides data on uptake of DAA treatment through PBS-listing between March 2016 and December 2022 by jurisdiction, patients' gender and age, treatment regimen, and prescriber type. This report also includes a detailed analysis of treatment discontinuation, and uptake of re-treatment.

Methodology

Initial treatment uptake

The PBS data of DAA dispensation for all individuals who initiated treatment between March 2016 and December 2022 in Australia were used in the analysis. The data used for estimating the initial treatment uptake included the first DAA treatment course prescribed for each individual. The data of the second or further courses of treatment (for treatment failure or HCV reinfection) were only included for estimating re-treatment uptake. In instances where the first regimen prescribed was discontinued and the second regimen was initiated after less than four weeks, the second regimen was considered as the initiating treatment. Prescriber speciality was based on the prescriber derived major speciality codes recorded by PBS. In this coding system, medical trainees (i.e., registrars) are considered as specialists. Jurisdictions are based on the patient residence at the time of treatment prescription. More details of methodology were described previously.[2] Longitudinal data of DAA treatment uptake were provided for between 2019 and 2021 to enable a better evaluation of the recent trends in treatment uptake, given implementation of HCV testing programs in several jurisdictions in late-2021 and 2022.

Treatment discontinuation

DAA treatment is typically dispensed in 28-day packages (four weeks supply at a time). To identify individuals who discontinued DAA treatment before completion, first, the anticipated end of treatment for each prescription was estimated based on the date of the first prescription dispensation and duration of the DAA regimen prescribed. Then, treatment discontinuation was defined as one or more repeat authorized prescription courses (28-day supply) not dispensed. Early discontinuation was defined as discontinuing after the first 28 days of the treatment course had been dispensed (a maximum of 28 days of treatment course were dispensed). Late discontinuation was defined as discontinuing after 56 days or more had been dispensed. Individuals who discontinued initial treatment and restarted a different regimen ≤28 days before the estimated end of treatment were considered treatment switches and were not considered treatment discontinuations. Individuals who initiated treatment during the last quarter of 2022 (October-December 2022) were excluded from this analysis to enable sufficient time for completion of treatment. Individuals who were dispensed the whole treatment course at a single time were also excluded from this analysis. More details of methodology were described previously.[3]

Re-treatment uptake

Re-treatment (different regimen) was defined as commencement of a different DAA regimen any time after estimated end of initial treatment date. Re-treatment (same regimen) was defined as commencement of the same DAA regimen ≥28 days after the last dispensation of the initial treatment, to exclude cases where prescribers had probably extended duration of therapy due to non-adherence. Re-treatment could be due to the initial treatment failure or re-infection following initial treatment. The PBS does not collect the reason for re-treatment. We developed a machine learning model to classify retreatments as reinfection or treatment failure.

2. Stafford F, Dore GJ, Clackett S, Martinello M, Matthews GV, Grebely J, Balcomb AC, Hajarizadeh B. Prescribing of direct-acting antiviral therapy by general practitioners for people with hepatitis C in an unrestricted treatment program. Medical Journal of Australia 2021; 215(7): 332-3.
3. Carson J, Barbieri S, Matthews GV, Dore GJ, Hajarizadeh B. Increasing national trend of direct-acting antiviral discontinuation among people treated for HCV 2016–2021. Hepatology Communications 2023; 7(4): e0125.

The Real-world Effectiveness of Antiviral therapy in Chronic hepatitis C (REACH-C)[4] study is a national observational cohort study including 10,843 individuals with HCV initiating DAA therapy through the PBS between March 2016 to June 2019, including 300 individuals who received re-treatment with available reason for retreatment (n=213 treatment failure; n=87 re-infection).[5,6]

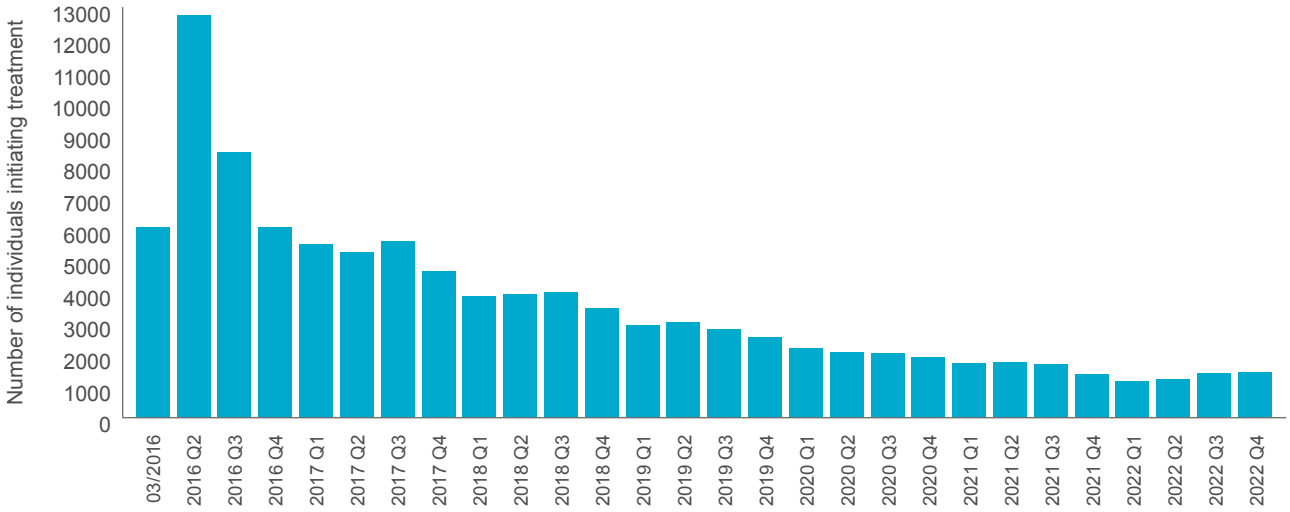
The machine learning models were developed and trained to predict the reason for re-treatment using variables in REACH-C that were also available in PBS data. Variables included age, sex, HIV coinfection, prescriber type, DAA class (i.e., genotype-specific, pan-genotypic, salvage), regimen, and duration at (re)treatment, addition of ribavirin at (re)treatment, year of (re)treatment, time between end of initial treatment and commencing re-treatment, and missed dispensations. The REACH-C data were divided into randomized training and validation datasets using 3 × 10-fold nested cross validation. Several models were developed, and the best performing model was re-fitted to the whole REACH-C data and applied to the PBS data to classify retreatments as either reinfection or treatment failure. More details of the machine learning algorithms, model training procedure, and the model performance metrics were described previously.[7]

DAA treatment uptake

A total of 100,684 individuals initiated DAA treatment (first course) through the PBS between March 2016 and December 2022 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.[8] Considering this number, an overall number of 105,024 individuals received DAA treatment from 2014 to 2022.

At jurisdictional level, the number of individuals initiating DAA treatment through the PBS between March 2016 and December 2022 included 34,186 in New South Wales, 24,125 in Victoria, 22,181 in Queensland, 9,500 in Western Australia, 5,899 in South Australia, 2,429 in Tasmania, 1,446 in Australian Capital Territory, and 902 in Northern Territory.[9]

Figure 1: Number of individuals initiating DAA treatment in each quarter during 2016 to 2022 in Australia



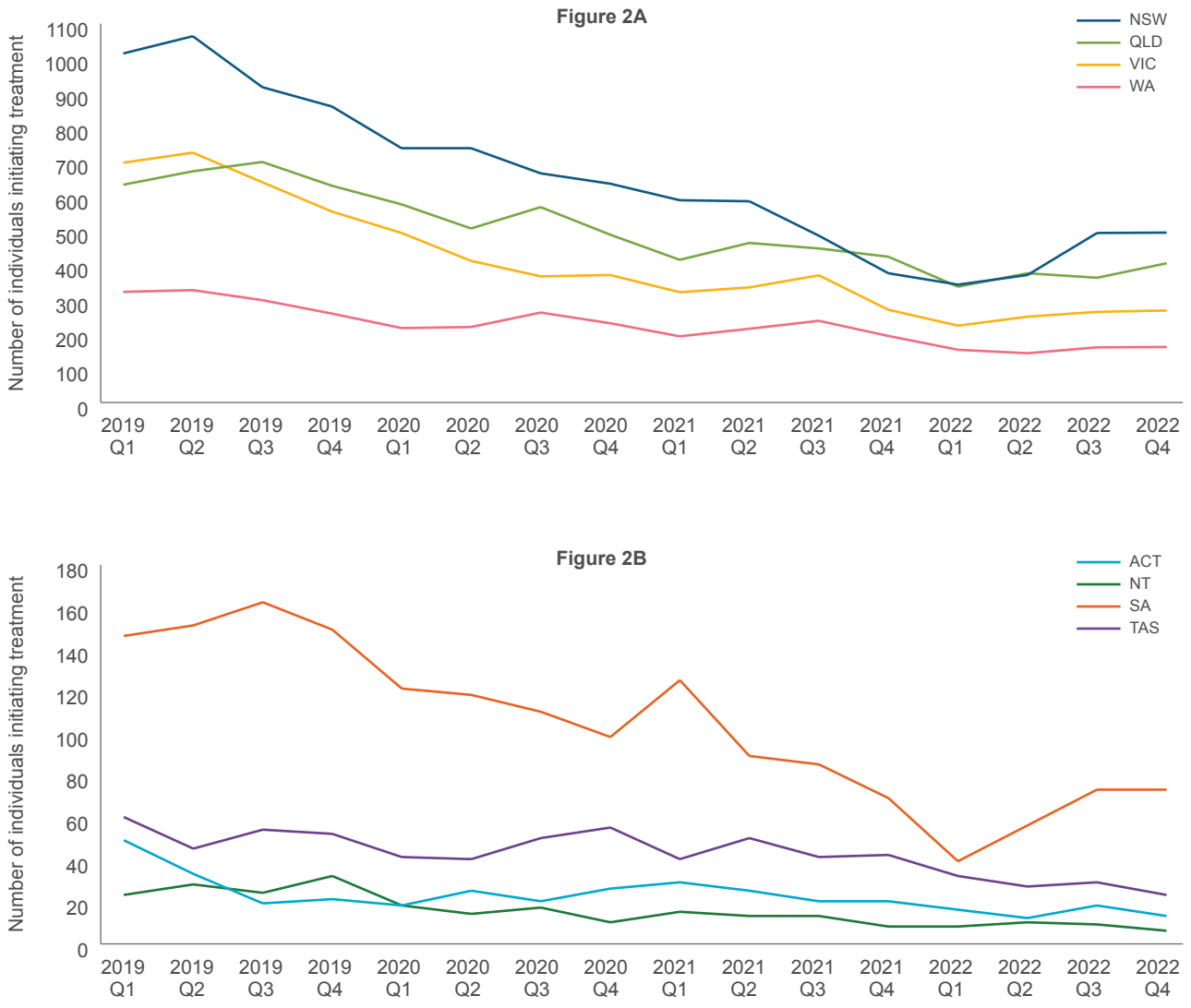
4. Yee J, Carson JM, Hajarizadeh B, Hanson J, O'Beirne J, Iser D, Read P, Balcomb A, Doyle JS, Davies J, Martinello M, Marks P, Dore GJ, Matthews GV. High Effectiveness of Broad Access Direct-Acting Antiviral Therapy for Hepatitis C in an Australian Real-World Cohort: The REACH-C Study. Hepatology Communications 2022; 6(3): 496-512.
5. Carson JM, Hajarizadeh B, Hanson J, O'Beirne J, Iser D, Read P, Balcomb A, Davies J, Doyle JS, Yee J, Martinello M, Marks P, Dore GJ, Matthews GV. Effectiveness of treatment for hepatitis C virus reinfection following direct acting antiviral therapy in the REACH-C cohort. International Journal of Drug Policy 2021; 96: 103422.
6. Carson JM, Hajarizadeh B, Hanson J, O'Beirne J, Iser D, Read P, Balcomb A, Davies J, Doyle JS, Yee J, Martinello M, Marks P, Matthews GV, Dore GJ. Retreatment for hepatitis C virus direct-acting antiviral therapy virological failure in primary and tertiary settings: The REACH-C cohort. Journal of Viral Hepatitis 2022; 29(8): 661–76.
7. Carson JM, Barbieri S, Matthews GV, Dore GJ, Hajarizadeh B. National trends in retreatment of HCV due to reinfection or treatment failure in Australia. Journal of Hepatology 2023; 78(2): 260-70.
8. 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
9. For a small number of individuals (n=16), data of jurisdiction of residence were not available.

The quarterly number of DAA treatment initiations in Australia is illustrated in Figure 1. In 2022, number of individuals initiating treatment increased from 1,141 in the first quarter to 1,432 in the last quarter. Despite this encouraging recent quarterly-based increase in 2022, annual treatment continued to decline. The annual number of individuals initiating DAA treatment included 33,202 in 2016, 20,969 in 2017, 15,209 in 2018, 11,314 in 2019, 8,228 in 2020, 6,557 in 2021, and 5,205 in 2022. It should be noted that these data included people who initiated DAA treatment for the first time (first course). The data of people who received re-treatment are presented later in this report.

DAA treatment uptake by jurisdictions

The trends of DAA treatment uptake (initial treatment) during 2019-22 by jurisdiction are illustrated in Figure 2. In all jurisdictions, the trend was decreasing during 2019-21. However, in 2022, the treatment uptake increased in several jurisdictions. In most of these jurisdictions, this increase could be reflective of enhanced HCV testing programs implemented in the community and prisons in late-2021 and 2022. It should be noted that these data included the initial DAA treatment (first course). The data of re-treatment are presented later in this report.

Figure 2: Quarterly number of individuals initiating DAA treatment during 2019 to 2022 in Australian jurisdictions



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 2016 and 2022, 68% were men and 32% were women. Median age was 47 years (quartiles 1-3: 38-57) with a similar age distribution between men and women (Figure 3).

The trend of DAA treatment uptake during 2019-22 by age is illustrated in Figure 4. Increasing trend in treatment uptake during 2022 was observed in all age group with the greatest increase in people ≤30 years old and those 41-50 years old. During 2016 to mid-2020, there has been a trend towards higher proportion of treatment initiations in younger individuals, particularly with a consistent increase in proportion of people ≤30 years old. Age distribution remained relatively consistent after mid-2020 (Figure 5).

Figure 3: Age distribution of individuals initiating DAA treatment during 2016 to 2022, by gender

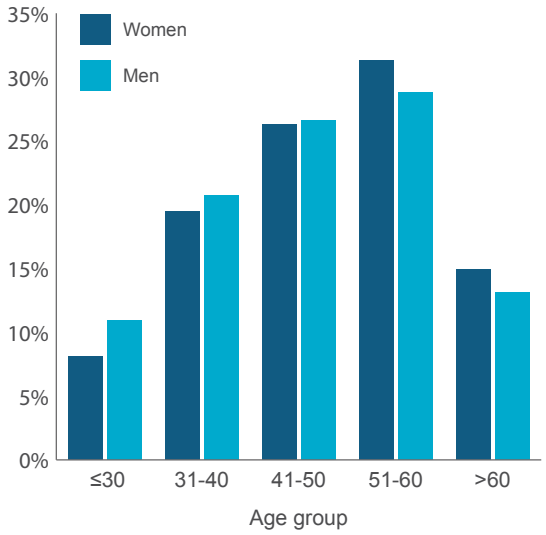


Figure 4: Quarterly number of individuals initiating DAA treatment during 2019 to 2022, by age group

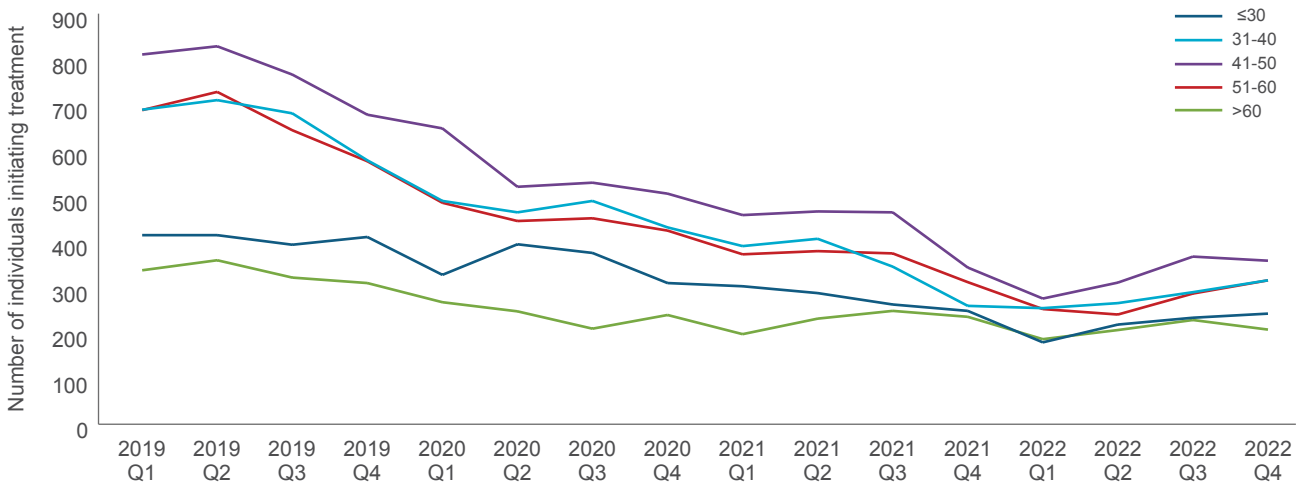
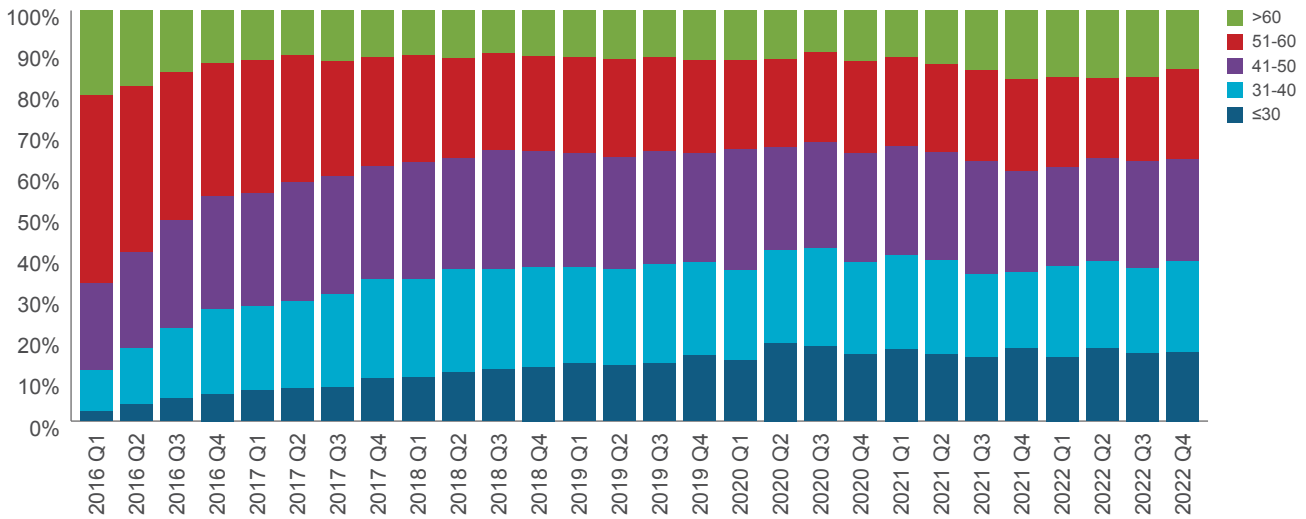


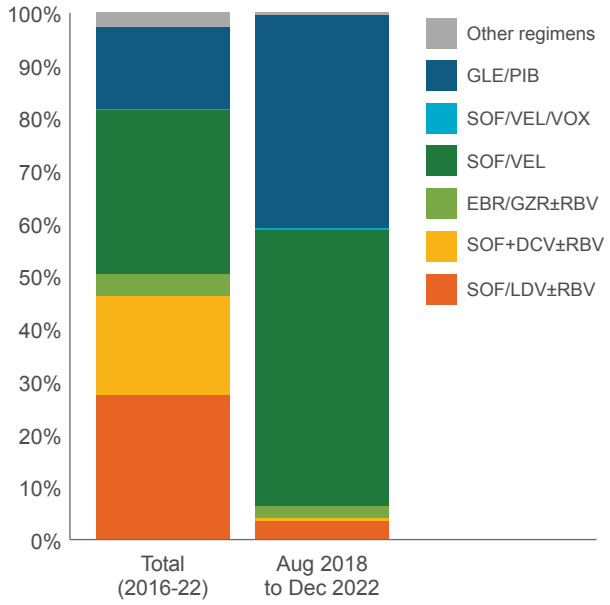
Figure 5: Quarterly proportion of individuals initiating DAA treatment during 2016 to 2022, by age group.



Distribution of DAA regimens prescribed for individuals initiating treatment

During 2016 to 2022 and among individuals initiating DAA treatment for the first time (first course), the most commonly prescribed regimens were sofosbuvir/velpatasvir for 31%, and sofosbuvir/ledipasvir±ribavirin for 27% of the patients. Sofosbuvir/velpatasvir and glecaprevir/pibrentasvir were PBS listed in August 2017 and August 2018, respectively. Since August 2018 (when all regimens were available through PBS), 53% of individuals initiating DAA treatment have been prescribed sofosbuvir/velpatasvir, and 41% have been prescribed glecaprevir/pibrentasvir (Figure 6).

Figure 6: Distribution of DAA regimens prescribed during 2016 to 2022 (overall), and August 2018 to December 2022 (all regimens where PBS-listed)



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

Distribution of health care providers prescribing for individuals initiating DAA treatment

Among individuals initiating DAA treatment during 2016 to 2022, the majority received their prescriptions from general practitioners (GPs; 46%), followed by gastroenterologists (35%). Overall, 52% of individuals were initiated on treatment by specialists, and 48% by non-specialists (i.e., GPs and nurse practitioners).

Distribution of prescriber types varied across jurisdictions (Figure 7). The proportion of individuals initiated on DAA treatment by GPs was highest in Western Australia (61%). The proportion of individuals initiated on treatment by specialists was highest in

Victoria (62%). The largest number of individuals initiated on treatment by nurse practitioners was from Queensland (n=1,260, 6%).

The quarterly number of DAA treatment initiations by prescriber types is shown in Figure 8. During 2022, the greatest increase was observed in treatment initiation by GPs.

During 2019-22, the number of individuals initiated on DAA treatment by nurse practitioners increased while treatment initiation by GPs and specialists decreased. Nurse practitioners have been authorised to prescribe DAA since June 2017. A total of 2,048 individuals were initiated on treatment by nurse practitioners, including 92 in 2017, 219 in 2018, 261 in 2019, 416 in 2020, 525 in 2021, and 535 in 2022.

Figure 7: Distribution of prescriber types for individuals initiating DAA treatment during 2016 to 2022, in Australia and by jurisdiction

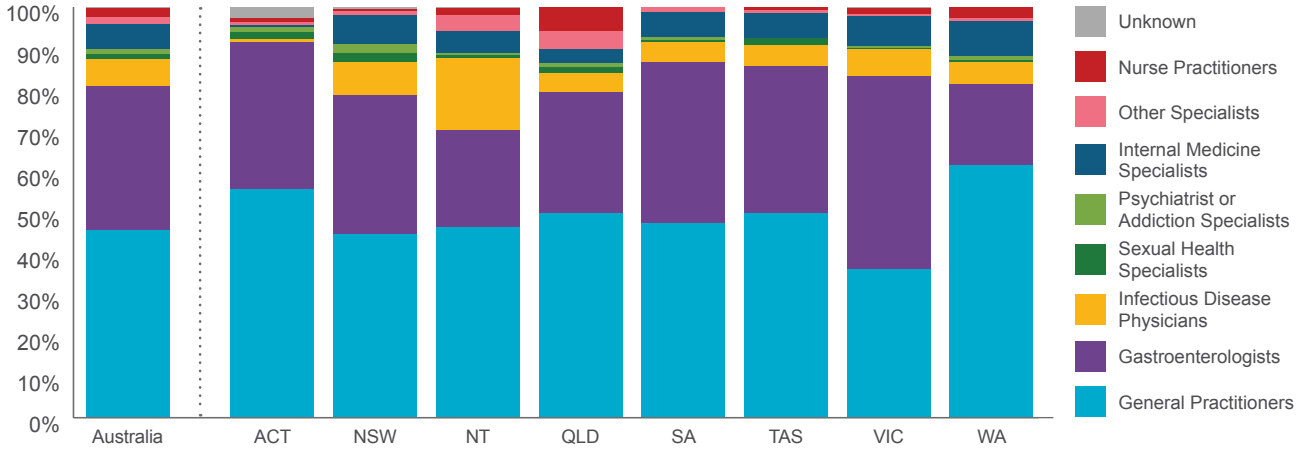


Figure 8: Quarterly number and proportion individuals initiating DAA treatment during 2019 to 2022, by prescriber type

Figure 8A

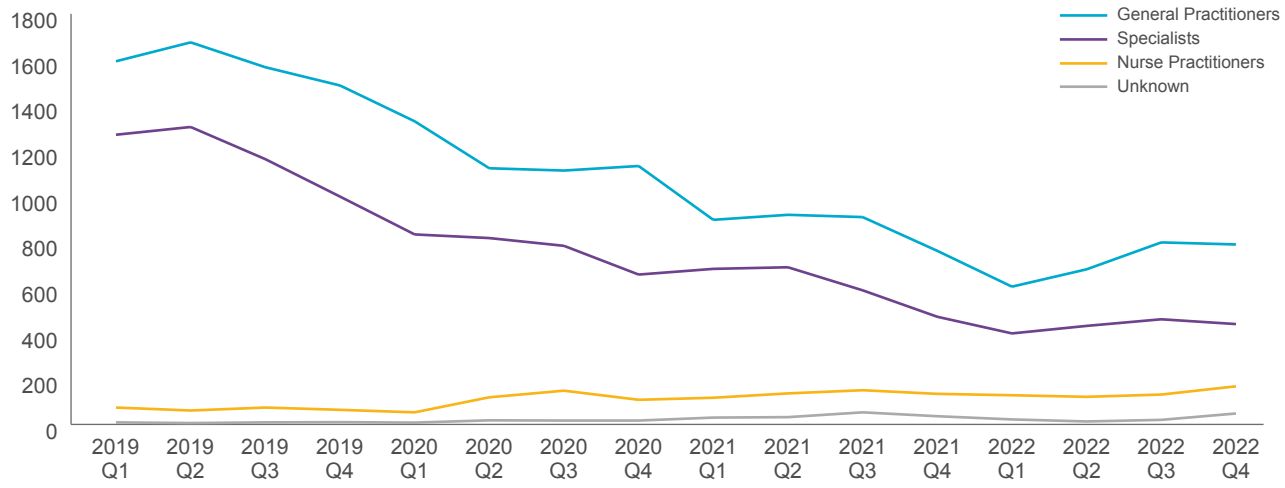


Figure 8B

DAA treatment discontinuation

Between March 2016 and September 2022, among 91,958 individuals who initiated DAA treatment,[10] 8.6% (n=7,942) discontinued treatment, including 4.0% (n=3,704) early discontinuation and 4.6% (4,238) late discontinuation. Among those who discontinued treatment (n=7,942), 26% (n=2,051) received re-treatment.

The trend in proportion of individuals who discontinued treatment during 2016 to 2022 is shown in Figure 9. Although the proportion of late treatment disconnection was relatively stable, the proportion of early discontinuation increased from less than 3% in 2016 to 9.6% in the last quarter of 2021, followed by a relatively stable trend during 2022.

10. After excluding individuals who were dispensed the whole treatment course at a single time. See Methodology section for more details.

The trend in the annual proportion of individuals who discontinued treatment by jurisdiction is shown in Figure 10. Increasing trends in treatment discontinuation over time were observed in most jurisdictions. The jurisdictional trends were presented annually (rather than quarterly) given the small numbers of treatment initiation and/or discontinuation in each quarter. However, in smaller jurisdictions (e.g., Australian Capital Territory and Northern Territory) the annual numbers in recent years were not large enough and thus the major changes observed in annual trends should be interpreted conservatively.

Figure 9: Quarterly proportion of individuals who discontinued DAA treatment before completion among those initiating DAA treatment during 2016 to 2022

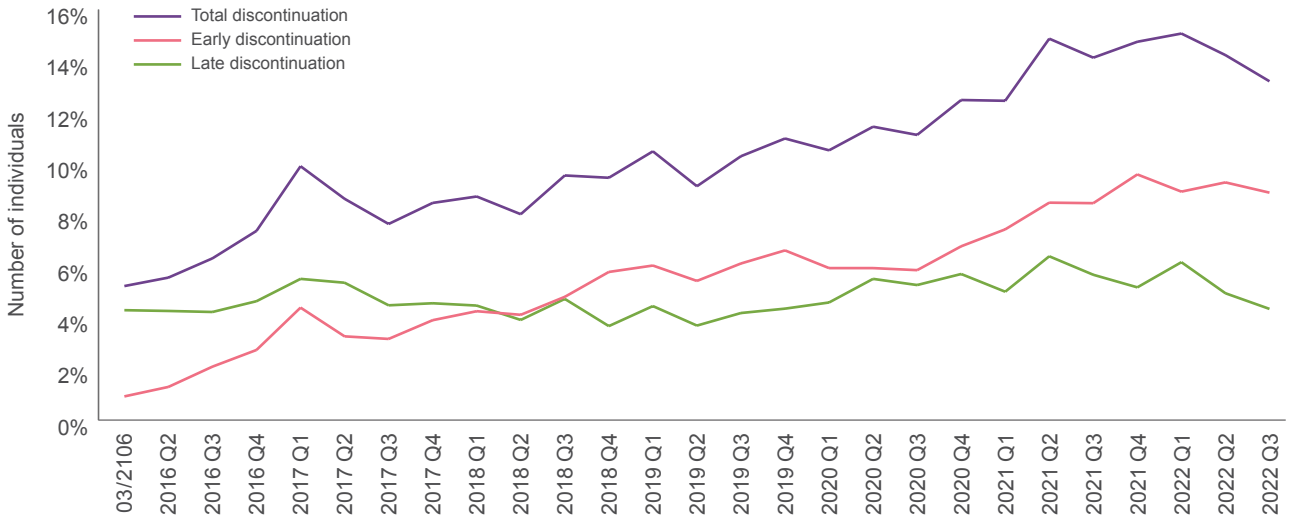
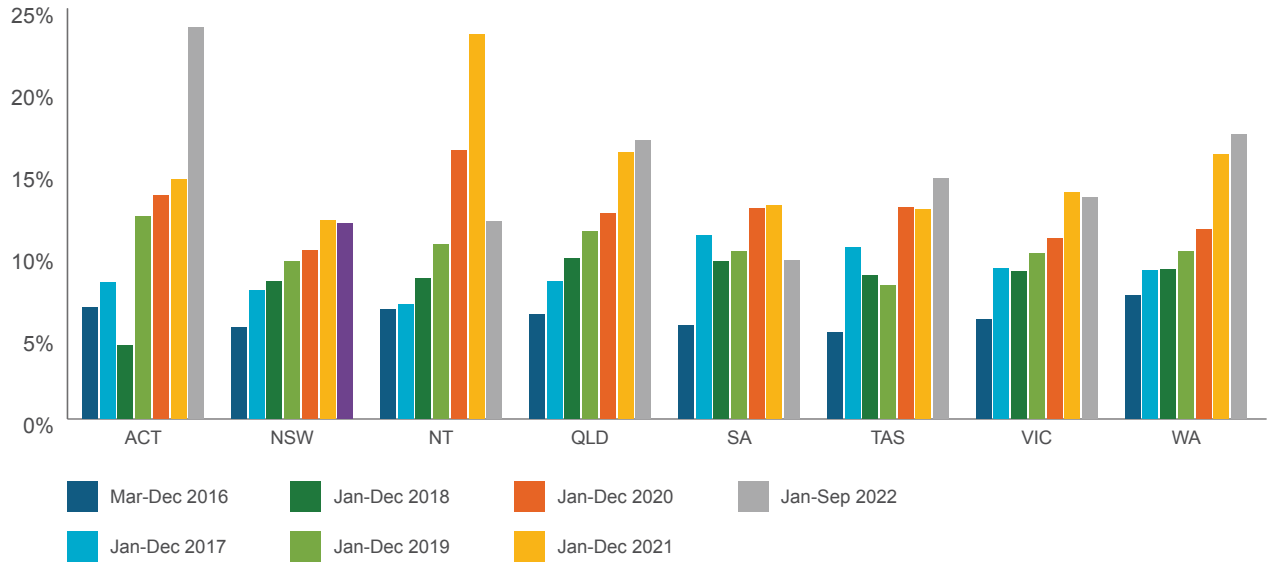


Figure 10: Annual proportion of individuals who discontinued DAA treatment before completion among those initiating DAA treatment during 2016 to 2022, by jurisdictions



DAA re-treatment uptake

Among 100,684 individuals who received treatment (first course), 8.5% (n=8,514) received at-least one course of re-treatment (second course), 1.5% (n=1,511) received at-least two courses of re-treatment (third course), and 0.3% (n=280) received more than two courses of re-treatment (fourth course or more).

Among a total of 10,385 re-treatment initiations, 57% (n=5,922) were for HCV re-infection and 43% (n=4,463) for treatment failure. The trend of re-treatment initiations in Australia is illustrated in Figure 11. Number of re-treatment initiations for treatment failure increased between the first and second quarters of 2019, corresponding to when sofosbuvir/velpatasvir/voxilaprevir became available through PBS in April 2019. Since mid-2019, the trend in number of re-treatment initiations for treatment failure has been decreasing.

The trend in the number of re-treatment initiations for HCV re-infection was increasing until mid-2020. After a plateau and then decreasing phase during 2020-21, the number of re-infection re-treatment initiations increased again in 2022. This latest increase, similar to the trend observed for initial treatment uptake, could be the result of enhanced HCV testing programs implemented in several jurisdictions through which many individuals with HCV re-infections were diagnosed and linked to clinical care.

The jurisdictional trends of re-treatment initiations for treatment failure and HCV re-infection are shown in Figure 12 and Figure 13, respectively. For smaller jurisdictions, the trends were presented annually (rather than quarterly) given the small numbers of re-treatment initiation in each quarter. In all larger jurisdictions (Figure 13A) the trends in re-treatment for re-infection in 2022 were increasing with the most significant increases observed in New South Wales and Queensland.

Figure 11: Number of DAA re-treatment initiations for HCV re-infection or treatment failure in each quarter during 2016 to 2022 in Australia

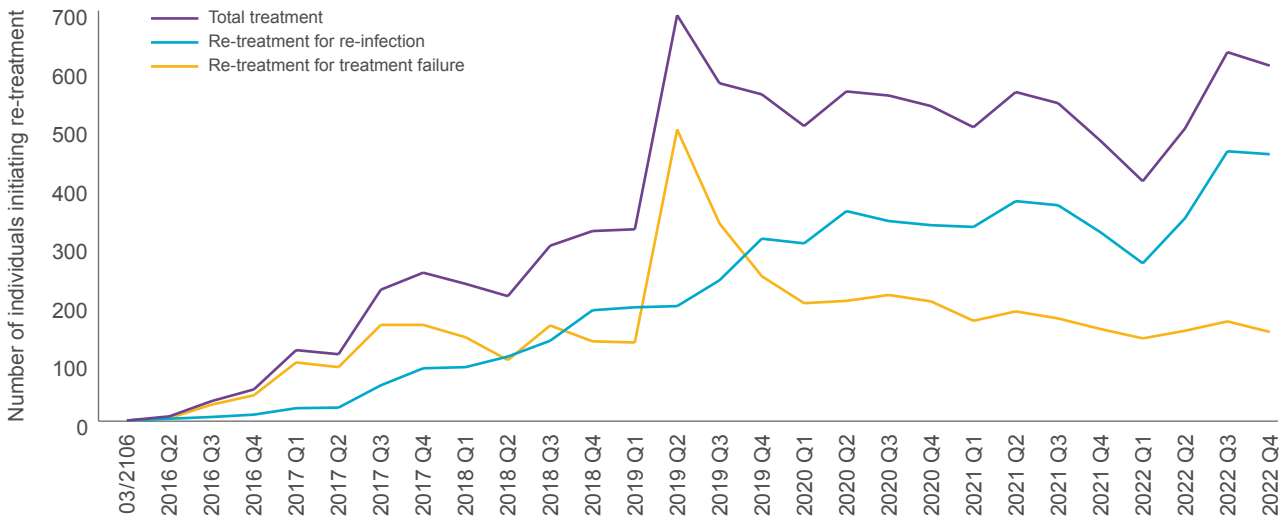


Figure 12: Number of DAA re-treatment initiations for treatment failure in each quarter (A) and year (B) during 2016 to 2022 in Australian jurisdictions

Figure 12A

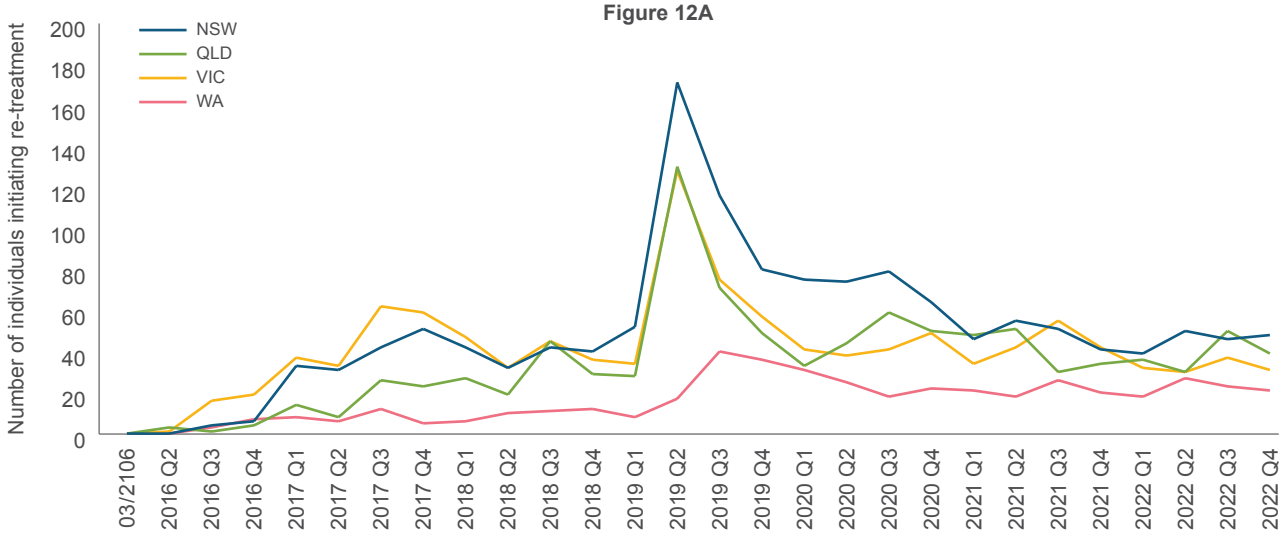
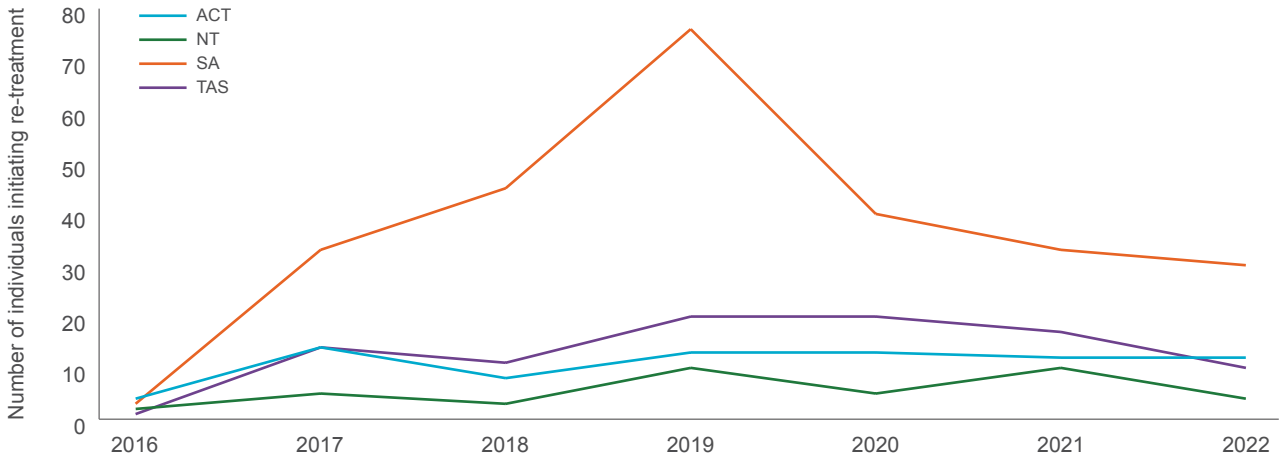


Figure 12B



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

Figure 13: Number of DAA re-treatment initiations for HCV re-infection in each quarter (A) and year (B) during 2016 to 2022 in Australian jurisdictions

Figure 13A

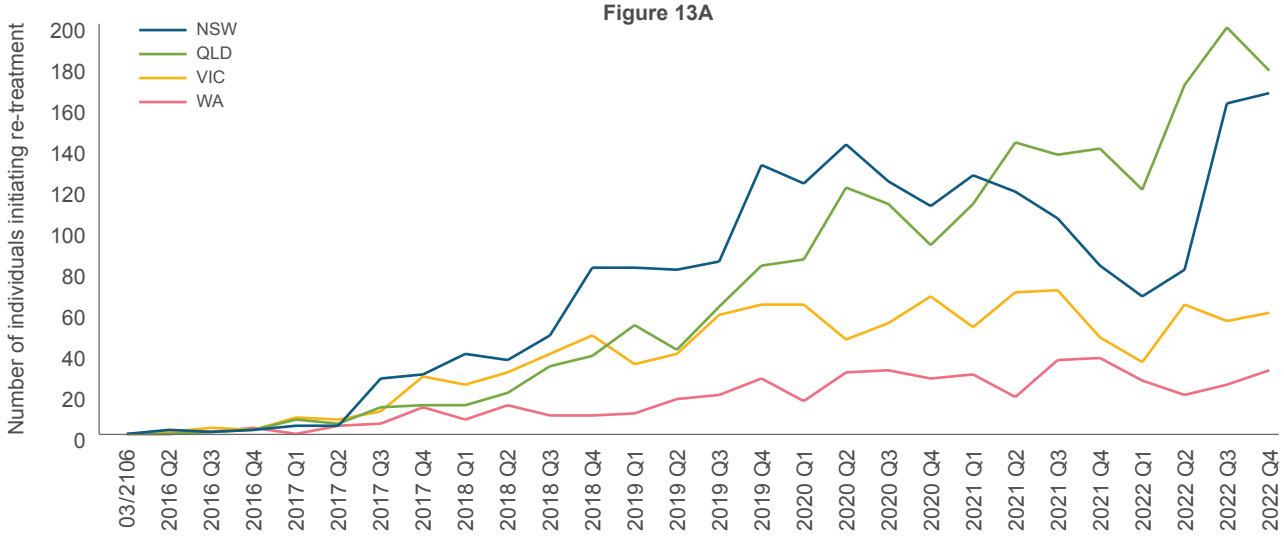
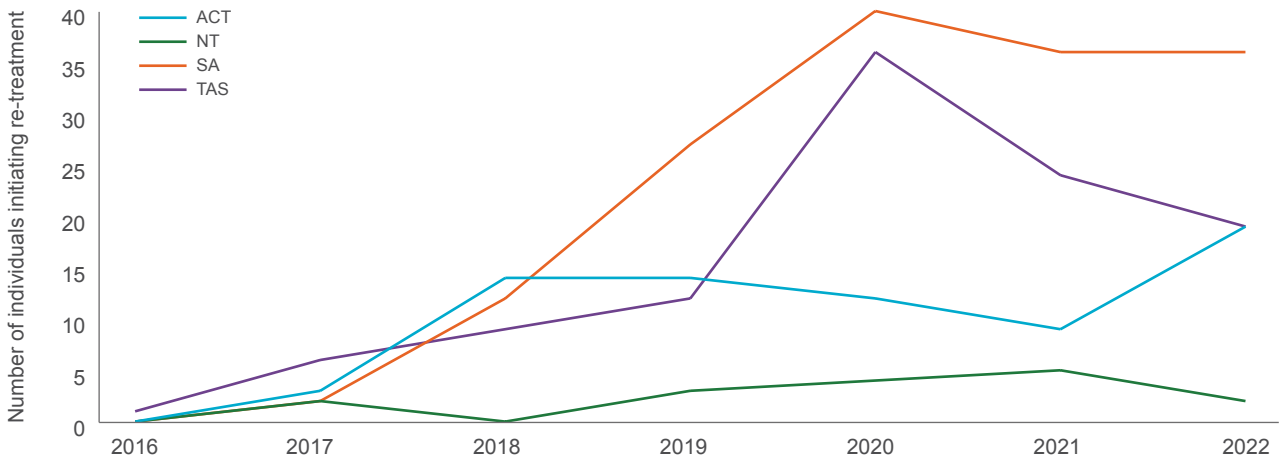


Figure 13B



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