A nurse practitioner model of care in the era of direct acting antiviral therapy for hepatitis C virus infection

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Abstract
Background and Aim: Direct-acting antiviral (DAA) therapy for hepatitis C virus (HCV) infection has resulted in high rates of successful disease cure; however, not enough healthcare providers are available to deliver treatment to the population living with chronic HCV. To demonstrate that a nurse practitioner (NP) model of care is non-inferior to specialist gastroenterologist (SG) management of HCV infection, as measured by sustained viral response at 12 weeks (SVR12) after initiation of DAA therapy.

Design: Retrospective cohort database study.

Setting: Single-center outpatient study, Central Coast Local Health District (CCLHD).

Participants: All patients with chronic HCV treated in the CCLHD Liver Clinic in the period 3rd March 2016 to 31st May 2019 were retrospectively analyzed. In this time period, a total of 1638 patients with chronic HCV had completed treatment. Seven hundred and thirty-four patients were excluded (733 pre-PBS listing for DAAs and 1 not treated with DAA). Nine hundred and four patients were eligible for the study, of which 541 were managed by an SG, and 363 managed by an NP.

Main outcome measures: Data were collected on patient demographics, genotype, fibrosis score, and presence of cirrhosis. Primary end point was number of patients achieving SVR12.

Results: Of the 904 patients treated with DAA, 764 (84.5%) achieved SVR12. There was no statistical difference ($P > 0.05$) in achieving SVR12 between patients treated by an SP ($n = 481$, 88.9%) and those treated by an NP ($n = 281$, 77.4%).

Conclusion: An NP model of care is non-inferior to SG management of HCV infection, as evidenced by equivocal success in achieving SVR12 between the two treatment groups. Therefore, an NP model of care is a viable option in the era of DAA therapy for HCV infection. Ongoing investment into the delivery of NP care could increase treatment uptake of HCV, with the aim of decreasing overall burden of disease.

Introduction
Hepatitis C virus (HCV), an infection of the liver with significant morbidity and mortality, is a major public health challenge for Australia. Approximately 75% of those infected will develop chronic HCV. Chronic HCV is associated with an increased risk of cirrhosis (20–30%), liver failure, and hepatocellular carcinoma (5% of those with cirrhosis). At the start of 2016 in Australia, an estimated 227 306 people were living with chronic HCV, representing almost 1% of the Australian population.

Although the burden of disease attributable to chronic HCV is large, the uptake of treatment remains low, with only 2% HCV-infected Australians starting treatment in any year. Since the introduction of the highly effective, well-tolerated direct-acting antiviral (DAA) therapy for HCV infection, the possibility of treatment expansion and widespread cure has been raised, with DAAs curing 70–80% of HCV infection. An estimated 74 600 individuals have initiated DAA treatment for chronic HCV infection in Australia (70 260 individuals through Pharmaceutical Benefits Scheme [PBS] during 2016–2018, and 4340 individuals through early DAA access pathways in 2014 and 2015). These numbers show that only 33% of those living with chronic HCV have accessed the available curative treatment. In order to improve treatment uptake, it is necessary to identify and overcome the barriers to accessing treatment. One such barrier is
availability of specialty services and healthcare providers able to prescribe DAA therapy.

During 2016–2017, most HCV treatments were prescribed by providers classified by Medicare as specialists (59.4%), approximately 25% were prescribed by general practitioner (GPs), and the remaining were classified as “other prescribers” (15.9%). “Other prescribers” included nurse practitioners (NPs) and other doctors not classified as specialists or GPs.

The current target in Australia is to achieve complete elimination of HCV by 2030.5 Achieving HCV elimination and incidence reduction targets in Australia relies on ensuring people who are diagnosed with chronic HCV access appropriate care, treatment, and cure. Although DAAs have a high cure rate, are tolerable, and available at low cost to Medicare-eligible Australians, the current specialist workforce is insufficient to meet the treatment demands of the Australian population living with chronic HCV infection. It is therefore imperative to find other viable models of care, which do not rely on the specialist system, in order to deliver DAA therapy to those infected with chronic HCV in an effective and safe manner.

Early studies have demonstrated the utility of the delivery of DAA therapy to wider populations via primary care physicians (PCPs) and NPs. In 2008, a specialist nurse-led HCV clinic established in England was found to be a safe and effective way to streamline management of patients with HCV. Patients were found to be highly satisfied with the locally available service and appreciated the continuity of care provided by the specialist nurse. Consequently, this led to increased uptake of HCV treatment locally and a reduction in the number of patients referred to tertiary units.6 Later in 2015, a non-randomized clinical trial conducted in America demonstrated that HCV treatment administered by nonspecialist providers was as safe and effective as that provided by specialists. The study found that NPs and PCPs armored with specialty HCV training could substantially expand the availability of community-based providers, in order to improve delivery of HCV therapy.7

Another study conducted in Australia assessed the safety and efficacy of a nurse-led outreach program for treatment of chronic HCV in the custodial setting. The study showed that 69% of inmates treated by NPs achieved sustained viral response at 12 weeks (SVR12), and therefore suggests that the nurse-led and specialist-supported treatment model for those with chronic HCV offers potential to substantially increase treatment uptake and reduce disease burden.8

In this study, we endeavor to show that the NP model of care is non-inferior to specialist gastroenterologist (SG) management of HCV infection, as measured by SVR12 after initiation of DAA therapy.

Methods

Between 3rd March 2016 and 31st May 2019, data were collected on all patients seen at the Liver Clinic in Central Coast Local Health District, who were initiated on treatment for chronic HCV. After confirmation of active HCV infection, patients were assessed with a detailed history, examination, and relevant investigations. Once they were deemed suitable, patients underwent treatment for chronic HCV. Patients were treated by either one of four SGs or one NP who worked in the practice. Within this time period, only patients treated with DAA after PBS listing for DAAs (904) were included in the study. Data were collected on patient demographics, genotype, fibrosis score, presence of cirrhosis, loss to follow-up, and relapse. Primary end point was number of patients achieving SVR12. SVR12 was defined as an undetectable HCV RNA viral load 12 weeks after treatment completion (Table 1).

Results

Inclusion and exclusion criteria. Between 3rd March 2016 and 31st May 2019, 1638 patients were seen at the Liver Clinic in Central Coast Local Health District and were initiated on treatment for chronic HCV. Seven hundred and thirty-four of these patients were excluded from the study as they were either treated with DAA pre-PBS listing for DAAs (n = 733) or they were not treated with DAA (n = 1).

Patients. The remaining 904 patients were treated with DAA, including 566 (62.6%) men and 338 (37.4%) women. Three hundred and thirty-nine (59.8%) men were treated by an SG, 227 (40.1%) men were treated by an NP (P = 0.969). Two hundred and two (59.2%) women were treated by an SG and 136 (40.2%) women were treated by an NP (P = 0.969).

Table 1: Summary of patient characteristics and results

| Total | Specialist gastroenterologist | Nurse practitioner | P-value |
|-------|-------------------------------|--------------------|---------|
| Number of patients | 904 | 541 | 363 |
| Median age | 56 | 57 | 54 |
| Gender | | | |
| Male | 566 | 339 | 227 | 0.969 |
| Female | 338 | 202 | 136 | 0.969 |
| Fibroscan score (% treated by each group) | | | |
| F0–F2 | 61.9 | 55.9 |
| F3–F4/cirrhosis | 17.7 | 28.4 |
| Not recorded (APRI <0.7) | 7.2 | 9.1 |
| Not recorded (cirrhotic) | 13.1 | 6.6 | 0.712 |
| Sustained viral response | 764 | 481 | 281 | 0.317 |
| Lost to follow-up | 140 | 59 | 82 | < 0.05 |

APRI, AST to Platelet Ratio Index.
median patient age was 56 years old across both treatment groups (SG = 57 years old, NP = 54 years old) (see Fig. 1).

**Fibroscan and cirrhosis.** The majority of patients treated by an SG (61.9%) and an NP (55.9%) had a fibroscan score of F0-2. Three hundred and five patients had a diagnosis of cirrhosis upon commencing DAA treatment. The proportion of patients with cirrhosis treated by an SG was 33.3% (n = 180) and an NP was 34.4% (n = 125) (P = 0.712) (see Fig. 2).

**SVR_{12}**. Nine hundred and four patients were treated with DAA by an SG (n = 541, 59.8%) or an NP (n = 363, 40.2%). Seven hundred and sixty-four of 904 patients were treated by an SG (n = 481, 62.9%), and an NP (n = 281, 36.7%) achieved SVR_{12}. Therefore, those treated by an SG achieved SVR_{12} at a rate of 88.9%, and those treated by an NP achieved SVR_{12} at a rate of 77.4% (P = 0.317) (see Fig. 3).

**Lost to follow-up.** One hundred and forty-one patients were lost to follow-up, with a greater proportion of patients lost to follow-up in the NP group (n = 81, 22.3%) versus SG group (n = 60, 11.1%). Of those, 57.4% were from the NP group and 42.6% were from the SG group (P < 0.05) (see Fig. 4).

Among patients with cirrhosis, 15.7% (n = 25) were lost to follow-up in the NP group, compared with 9.6% (n = 16) in the SG group (P = 0.0949). On the other hand, in patients without cirrhosis, 22.5% (n = 56) were lost to follow-up in the NP group, and only 11.7% (n = 44) were lost to follow-up in the SG group (P = 0.0001) (see Fig. 5).

**Patients treated per month.** Average number of patients treated per month by NP was 15.1 and by SG was 9.7.

**Discussion**

Our initial data support the hypothesis that an NP model of care is non-inferior to SG management of HCV infection, as evidenced by equivocal success in achieving SVR_{12} between the two treatment groups. Therefore, task-shifting DAA-based HCV therapy to an NP model of care is a viable and effective option to increase access to HCV treatment and assist the healthcare system currently strained by a paucity of SGs.
There was no significant difference in patient demographics between those treated by an SG and an NP, including no notable differences in age, gender, fibroscan results, and presence of cirrhosis.

A greater proportion of patients lost to follow-up were in the NP group. In subgroup analysis of those with cirrhosis, there was no difference in loss to follow-up between treatment groups. In those without cirrhosis, a significantly higher proportion of patients were lost to follow-up in the NP group. Reasons for this may be related to patients returning to their PCP for on-treatment and post-treatment care, or be reflective of selection bias, whereby patients in the NP group may have less significant medical comorbidities that require ongoing specialist physician care. The hepatocellular carcinoma (HCC) surveillance program in our center is also run by NP, which may also explain the higher loss of follow-up rate in those without cirrhosis in this study.

The strengths of this study are that the data were comprehensive and there was a large cohort of patients engaged in the service. No patients were excluded based on comorbid conditions; thus, the study population is generalizable to persons living with chronic HCV, where the prevalence of comorbid conditions is substantial.

The main limitation of this study is that it was a retrospective analysis. Furthermore, there was only one NP and four SGs on site involved in treating chronic HCV patients with DAA. It would be favorable to conduct a study with a larger group of healthcare providers to eliminate the variable of individual expertise and allow the data to be applicable for a greater majority of NPs and SGs. As this study was conducted in a single center, it would be beneficial to replicate the success of this study in other centers across Australia.

The primary outcome analysis was limited to ascertaining SVR12 and did not address other important aspects of HCV care, including treatment side effects and surveillance for hepatocellular carcinoma or reinfection. Following this group of patients over a longer period of time and assessing whether there was a difference in rates of complication and HCV relapse between treatment groups could be further studied. It would also be important to study whether there was any difference in safety outcomes and adverse events between treatment groups.

Nevertheless, the data illustrate the feasibility and efficacy of the NP model of care in treatment of chronic HCV patients. With an increase in availability of the NP model care, there will be an increase in accessibility to treatment and therefore the potential to markedly increase treatment uptake and reduce disease burden. Implementation of this model would allow other states and possibly, other nations to treat a greater number of patients infected with HCV than they are currently able to treat. Overall, this poises us in a better position to reach the goal of HCV elimination in Australia by 2030.

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References

1 Nazareth S, Piercey C, Tibbet P, Cheng W. Innovative practice in the management of chronic Hepatitis C: introducing the nurse practitioner model. Aust J Adv Nurs. 2008; 25(4): 107–13.
2 Burke M, Cabrie T, Cowie B, Dore G. HV, Viral Hepatitis & STIs: A Guide for Primary Care [Internet], 4th edn. Darlinghurst: Australasian Society for HIV Medicine, 2014 [cited 22 Mar 2020]. Available from URL: https://www.ashm.org.au/products/product/1976963411.
3 MacLachlan J, Thomas L, Cowie B. Viral Hepatitis Mapping Project: National Report 2017 [Internet]. Darlinghurst: Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine, 2019; 62–104 Available from URL: https://ashm.org.au/products/product/Viral-Hepatitis-Mapping-Project-2017.
4 NSW Ministry of Health. NSW Hepatitis C Strategy 2014–2020. North Sydney: NSW Ministry of Health, 2014; 1–34.
5 Burnet Institute and Kirby Institute. Australia’s Progress Towards Hepatitis C Elimination: Annual Report 2019 [Internet]. Melbourne: Burnet Institute, 2019; 22–36 Available from URL: https://kirby.unsw.edu.au/report/australias-progress-towards-hepatitis-c-elimination-annual-report-2019.
6 Mitra V, Soloman A, Cockside T, Kapur K. Safety and efficacy of a nurse-led hepatitis C service in a district general hospital. Gut. 2010; 59(Suppl 1): A155.1–A155.1.
7 Kattakuzhy S, Gross C, Emmanuel B et al. Expansion of treatment for hepatitis C virus infection by task shifting to community-based non-specialist providers. Ann. Intern. Med. 2017; 167(5): 311–18.
8 Lloyd A, Clegg J, Lange J et al. Safety and effectiveness of a nurse-led outreach program for assessment and treatment of chronic hepatitis C in the custodial setting. Clin. Infect. Dis. 2013; 56(8): 1078–84.