Faculty of Health Sciences

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Treatment of hepatitis C in injecting drug users in the Perth metropolitan area

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Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

Signature: ………………………………………….

Date: ……………………

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Abstract

Chronic hepatitis C is a viral infection affecting 230,000 people in Australia that can lead to liver cirrhosis or liver cancer. Most Australians living with the hepatitis C virus (HCV) are current or former injecting drug users (IDUs). Despite the widespread availability of HCV treatment in Australia, and some studies estimating high levels of intention to uptake treatment, uptake remains low among IDUs. Several factors are responsible for IDUs' low rate of HCV treatment uptake; they include lack of treatment efficacy (low probability of viral clearance), debilitating treatment side effects, lengthy treatment duration and the stigma associated with HCV and IDU. To date, only a few studies have examined the intention of IDUs to undertake treatment and the factors that influence uptake. Consequently, this study was designed to explore the factors that influence intention to undertake HCV treatment, using data collected from HCV infected IDUs in the Perth metropolitan area.

A mixed-methods design consisting of semi-structured interviews, focus groups and a cross-sectional survey was selected for this study. In the qualitative phase, which ran from September 2012 until March 2013, IDUs were recruited through the Western Australian Substance Users' Association (WASUA) and HepatitisWA. Twenty-one HCV infected IDUs who had experienced treatment (the treatment group) and 25 who had not (the non-treatment group) were interviewed individually about the factors influencing their intention to undertake HCV treatment, their experiences of HCV stigma and their beliefs about HCV treatment. Five focus group discussions (with five IDUs in each group) were conducted over June–August 2013 to gain further insight into the perceptions of HCV-infected IDUs with no treatment experience about triple HCV therapy (pegylated interferon and ribavirin in combination with either boceprevir or telaprevir) and to confirm the themes that emerged from the one-on-one interviews. In the cross-sectional survey (December 2013 to November 2014), 336 HCV-infected IDUs with no treatment experience were recruited from WASUA, HepatitisWA and the WA AIDS Council (WAAC). Participants completed a purpose-designed

questionnaire about their socio-demographic characteristics, drug-use history, health-care-seeking characteristics, aspects of treatment, stigma, support and their intention to undertake treatment.

Analysis of the qualitative data has revealed the factors influencing HCV-infected IDUs' intention to undertake HCV treatment; treatment side effects; treatment effectiveness; treatment duration; concern about stigma; and lack of support. In addition to these factors, protecting family, increasing quality of life, and maintaining careers were reported by the treatment group, and unstable housing was reported by the non-treatment group, as important factors that influenced their treatment intention to undertake HCV treatment. Both groups reported that peers' experiences of treatment, both positive and negative, were an important influence on their intention to undertake HCV treatment.

The qualitative study was valuable in guiding development of the quantitative survey instrument. The survey confirmed most of the findings that emerged from the qualitative study. Analysis of survey data revealed significant associations between intention to undertake HCV treatment and the following factors: support; treatment side effects; treatment efficacy; stigma; not drinking alcohol in the past year; non-homeless status; and non-Aboriginal ethnicity. The study also found a high overall level of expressed intention to undertake HCV treatment, with 63% of participants responding positively.

This study was conducted when HCV treatment consisted of the standard combination of pegylated interferon and ribavirin, and triple therapy. However, new interferon-free HCV treatments – direct-acting antivirals (DAAs), which feature minimal side effects, shorter treatment duration and higher efficacy than the old treatments – were listed on Australia's Pharmaceutical Benefits Scheme (PBS) in March 2016. However, some other factors such as unstable housing, forgetfulness, lack of priority for treatment, lack of control in life, pre-existing psychiatric illness and stigma, could significantly influence intention of HCV- infected IDUs to undertake new HCV treatment.

Hence, the study results have ongoing utility for policymakers and service providers seeking to increase the uptake of HCV treatment among IDUs. Clinics offering HCV treatment in community settings, training on DAAs for relevant health care practitioners, training for health care practitioners about reducing stigma and discrimination relating to injecting drug use, and facilitation of family and other support for patients will bolster HCV treatment uptake and reduce the burden of HCV-associated disease in Australia. In addition, future research about intention to undertake treatment with DAAs using a cohort method with a large sample size is recommended to enrich and confirm the results of this study. This will enable a more accurate estimate of the rate of intention and factors that predict intention to undertake treatment.

Abbreviations

OR	Odds Ratio
AOR	Adjusted Odds Ratio
DAA	Direct-Acting Antiviral
IDUs	Injecting Drug Users
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
MSM	Men who have Sex with Men
NSEP	Needle and Syringe Exchange Program
NSP	Needle and Syringe Program
OR	Odds Ratio
PBS	Pharmaceutical Benefits Scheme
RR	Relative Risk
RNA	Ribonucleic Acid
SVR	Sustained Virological Response
TAFE	Technical and Further Education
US	United States
WAAC	WA AIDS Council
WASUA	West Australian Substance Users Association
WHO	World Health Organization

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Chapter 1: Introduction

This chapter includes the background to the study, the research questions, study aim and objectives and the perceived significance of the study.

1.1 Background of the study

The hepatitis C virus (HCV) is a significant public concern, affecting 170 million people worldwide (WHO 2015). In Australia, an estimated 230,000 individuals are currently infected (Sievert et al. 2014). The majority of cases of HCV in high income countries were acquired through injecting drug use (Grebely et al. 2008). HCV has six genotypes (1–6), but the most common genotypes in Australia are 1, 2 and 3. HCV is often asymptomatic and over decades can lead to cirrhosis and to hepatocellular carcinoma (HCC) (Sievert et al. 2014). In Australia, it is expected that the annual number of HCV-related HCC cases will increase by 245% between 2013 and 2030 (from 590 to more than 2000) and annual HCV liver-related deaths will increase by 230% (from 530 to more than 1700) (Sievert et al. 2014).

Until April 2013 HCV treatment for HCV genotypes 1,2 and 3 was based on a combination of pegylated interferon and ribavirin, known as standard combination treatment (Manns et al. 2001, Manns, Wedemeyer, and Cornberg 2006). It was subsidised by the Federal Government through the Pharmaceutical Benefits Scheme (PBS) (DOHAC 2000). This combination of drugs produced a sustained virological response (SVR) in almost 50% of people with genotype 1 and 70–80% of people with genotypes 2 and 3 (Manns et al. 2001, Manns, Wedemeyer, and Cornberg 2006). Standard combination treatment involved adverse side effects, such as physical, psychiatric, cognitive and dermatological side effects, and had to be given for a total of 48 weeks for genotype 1 and 24 weeks for genotypes 2 and 3 (Manns et al. 2001, Manns, Wedemeyer, and Cornberg 2006). In April 2013, the first direct-acting antivirals (DAAs) were listed on the PBS, including boceprevir and telaprevir, and were added to the standard combination therapy for HCV

genotype 1, called triple therapy (He´zode 2012). The study described in this thesis was conducted when standard combination treatment and triple therapy were the only options available for HCV-infected injecting drug users (IDUs).

New DAAs have revolutionised the treatment of HCV. They are interferon-free for most genotypes and require daily tablets, rather than weekly injections in combination with tablets (Poonsapaya et al. 2015). The treatments are also much shorter in duration New HCV treatments (Poonsapaya et al. 2015) were listed on the PBS in March 2016 (HepatitisAustralia 2016). Figure 2.1 summarises information on the new HCV treatment regimens; with more detailed information provided in Chapter 2. Despite the widespread availability of publicly funded HCV treatment in Australia, uptake among people with chronic HCV has been low with less than 2% of affected people receiving antiviral therapies per annum (Guy and McGregor 2015).

Moreover, the reported intention among IDUs to take up HCV treatment is low and actual uptake in this population remains very low (Sievert et al. 2014) Low uptake of treatment among HCV-infected IDUs has significant implications for the numbers of people progressing to cirrhosis and HCC in future years (Sievert et al. 2014). However, the introduction of the new HCV treatments (more detailed information is given in Chapter 2) could significantly increase the rate of HCV treatment uptake among HCV-infected IDUs.

Few researchers to date have examined the prevalence of reported intention to undertake treatment among IDUs and there has been no research conducted on this topic in metropolitan Perth, Western Australia. In recent Australian studies, the prevalence of reported intention of HCV-infected IDUs to undertake treatment ranged from 53% (Treloar et al. 2012 , Alavi et al. 2013) to 67% (Alavi et al. 2015). Several Australian studies have explored factors influencing IDUs' intention to undertake HCV treatment, identifying characteristics of treatment, social, personal and demographic factors as

strongly associated (Treloar et al. 2012 , Alavi et al. 2015, Alavi et al. 2014, McNally, Sievert, and Pitts 2006, Doab, Treloar, and Dore 2005). Experience or fear of encountering treatment side effects, lack of treatment efficacy (Fusfeld et al. 2013, Treloar, Newland, et al. 2010, Zeremski et al. 2014), lengthy treatment duration (Fusfeld et al. 2013, Berg et al. 2006) peers' experiences of treatment (Treloar et al. 2014, Swan et al. 2010) and lack of support (Evon et al. 2011, Wilson et al. 2010) have been associated with treatment refusal and discontinuation of treatment among HCV-infected IDUs. Stigma associated with HCV and IDUs (Harris 2009, Tinda, Cook, and Foster 2010), housing status (Harris, Rhodes, and Martin 2013, Treloar, Newland, et al. 2010), ethnicity, older age (35-45 years) (Alavi et al. 2015) and employment status (Grebely et al. 2008) have also been reported as influencing the intention of HCV-infected IDUs not to undertake treatment.

However, in Australia little attention has been given simultaneously to the factors influencing treatment intention and the predictors of intention to take up treatment. A few studies have been conducted in the Eastern States (Treloar et al. 2012 , Alavi et al. 2015, Doab, Treloar, and Dore 2005), but no study in the Perth metropolitan area has attempted either to examine or to provide a systemic review of factors that influence intentions of HCV-infected IDUs to take up treatment. This study was designed to fill this gap by collecting evidence for development of appropriate interventions for increasing intention to take up treatment and actual treatment uptake through discovering the associations between predictive factors and intention to take up HCV treatment among IDUs in the Perth metropolitan area.

1.2 Research aim and questions

The overarching aim of this study was to gain better understanding of what factors can influence the intentions of HCV-infected IDUs' uptake of HCV treatment.

1. What factors influence the intentions of HCV-infected IDUs in relation to the uptake of HCV treatment?

2. What is the prevalence rate of intention to undertake HCV treatment among HCV- infected IDUs in Perth metropolitan area?

3. What is the association between socio-demographic, drug use and health-care-seeking characteristics and intention to undertake HCV treatment?

4. What is the association between treatment side effects, treatment effectiveness, treatment duration, support, stigma and intention to undertake HCV treatment?

1.3 Objectives of the study

With respect to HCV-infected IDUs in the Perth metropolitan area:

1. Identify the determinants of treatment intention and the uptake of HCV treatment.

2. Measure the prevalence rate of intention to undertake HCV treatment.

3. Determine the socio-demographic characteristics, drug history characteristics and health-care-seeking characteristics associated with intention to undertake HCV treatment.

4. Determine the characteristics of treatment, support and stigma associated with intention to undertake HCV treatment.

5. Recommend strategies for increasing uptake of HCV treatment.

1.4 Significance

This study was designed to identify and explore the factors that influence the intention of HCV-infected IDUs to take up of HCV treatment. A recent study has suggested that the number of people living with chronic HCV in Australia is expected to increase to 255, 500 by 2025 and then decline to 251,970 by 2030 (Sievert et al. 2014). Despite improvements in HCV treatment, many HCV-infected individuals remain untreated or have been treated unsuccessfully (Razavi et al. 2014). The number of cases of decompensated cirrhosis and HCC are predicted to increase from 1430 to 4170 and from 590 to 2040 respectively over the period 2013–2030 (Sievert et al. 2014). This

will result in an increase in the number of deaths from HCV-related liver disease to 630 by 2030 compared with 250 in 2013, if the rate of treatment uptake does not increase (Razavi et al. 2014).

Although, some researchers have studied Australian IDUs' intention to take up treatment these studies have been conducted in the Eastern States and have not included Perth (Treloar et al. 2012 , Alavi et al. 2015, Doab, Treloar, and Dore 2005). Given the sample size of 85 (Treloar et al. 2012) and 100 (Doab, Treloar, and Dore 2005) and assessing study population by health care providers (Doab, Treloar, and Dore 2005, Alavi et al. 2015) could represent a study group who were more engaged in health services which could lead to higher estimation of HCV treatment intention. Therefore, the results of these studies were not generalisable to the populations of current IDUs in Perth. There is no data relating to the treatment intentions of IDUs for the Perth metropolitan area in either clinical or non-clinical setting. Perth is also the most remote city where access to health services is more limited. It is plausible that HCV-infected individuals in Perth have novel perspectives that are yet to be explored on why their intention to undertake treatment is low and why they struggle to complete the treatment regimen. Moreover, few studies of HCV treatment have used a mixed-methods approach, despite the obvious value of such a design for this sensitive and little-known topic. This study used exploratory sequential mixed methods, commencing with semi-structured interviews, then focus group discussions and finally a cross-sectional survey, to capture the perspectives of IDUs who had experienced HCV treatment and IDUs who had not experienced treatment. Conducting mixed-methods research in a complementary way strengthened the study, and added validity and reliability to the findings.

Focus groups enabled rich descriptions of IDUs' perceptions of triple therapy (standard treatment in combination with either boceprevir or telaprevir), providing detailed understanding from a user perspective. Despite the proven benefits of the triple treatment regime over the previous pegylated interferon and ribavirin treatment, including reduced treatment duration and improved SVR rate, there is no empirical evidence (Evon et al. 2013, Treloar et al. 2012

) showing how IDUs view triple treatment and whether or not they intend to undertake this treatment. Arguably this is because the treatment is novel and studies have almost invariably focused on evaluation of the safety and efficacy of triple therapy within a clinical trial framework (Hézode 2012, Pearlman 2012), with little attention to identifying how the triple regime is valued and perceived by IDUs, and what processes must be in place to enable IDUs to access treatment.

This study, by adding new information on IDUs' perspectives to the extant literature on factors influencing treatment intention, develops a more complete and comprehensive picture of the topic. The mixed-methods design of this study produced rich and varied data that is useful for developing relevant interventions that enable increased intention to undertake treatment. It is expected that the research presented in this thesis offers an improved understanding of the factors which influence intention of HCV-infected IDUs to undertake HCV treatment and adds valuable knowledge to the scholarly literature. The findings of this study will enable policymakers to develop HCV treatment strategies to increase rates of uptake, and represent a foundation for further research in the field.

1.5 Outline of the thesis

This thesis contains seven chapters. The current chapter (1) provides a brief background to HCV treatment and the likely factors related to low uptake of HCV treatment among IDUs. It also presents the research questions, objectives and outlines the significance of the study.

Chapter 2 contains a review of relevant literature, covering both the past situation and the recent changes in HCV treatment in Australia. Literature on the factors influencing HCV treatment intention among HCV-infected IDUs is examined in detail.

Chapter 3 describes the methods used in the study, including the research design, interview questions, sample size, recruitment of subjects, data collection, and analysis. Ethical considerations are also outlined.

Chapters 4 and 5 describe the findings of the qualitative and quantitative analyses.

Chapter 6 contains a detailed discussion of the findings presented in Chapters 4 and 5 with reference to the existing literature.

Chapter 7 presents the conclusion of the thesis, the limitations of the study, and recommendations for future research.

Information sheets, the consent form, interview questions, questionnaires and other relevant documents are provided as Appendices 1 to 14.

Chapter 2: Review of the Literature

This literature review provides a brief background to HCV, its clinical manifestations, disease progression, risk factors, prevalence and burden, followed by an overview of the history of HCV treatment. This chapter reviews the existing literature relevant to intention to undertake HCV treatment in Australia and few developed countries. This is because they are similar to Australia in terms of low rates of HCV treatment uptake among HCV-infected IDUs and the majority of HCV infections being associated with injecting drug use. Finally, the chapter presents the factors influencing intention of HCV-infected IDUs to undertake HCV treatment.

2.1 Hepatitis C

The hepatitis C virus, originally referred to as non-A,-non-B hepatitis, first came to the attention of clinicians in February 1963 when 50% of cases of post-transfusion hepatitis were found to be neither hepatitis B nor hepatitis A (Hampers, Prager, and Senior 1964). Accumulating evidence in the 1960s and 1970s revealed other features of non-A, non-B hepatitis, such as chronicity and progression towards cirrhosis (Alter et al. 1978). In 1989, non-A, non-B hepatitis–associated ribonucleic acid (RNA) was isolated using advanced molecular approaches and the new virus came to be known as hepatitis C (Choo et al. 1990). The genetic organisation of this enveloped, positive-strand RNA virus is considered similar to those of pestiviruses and flaviviruses (Choo et al. 1990, Barreiro et al. 2012).

2.1.1 Viral genotypes

HCV has six genotypes, each containing subtypes which are categorised based on viral nucleotide sequence heterogeneity (Kuiken and Simmonds 2009). The genotypes and subtypes differ by approximately 31–33% and 20–25% respectively at the nucleotide level (Kuiken and Simmonds 2009). HCV genotypes are important as they are strong predictors of the outcomes of HCV treatment: genotypes 2 and 3 were the most susceptible to the standard

combination of pegylated interferon and ribavirin treatment, while genotypes 1 and 4 were the least susceptible (Imhof and Simmonds 2011). However, with the advent of the new DAAs, genotypes 1, 2 and 3 are now the most susceptible to treatment (Sarrazin 2016). Genotype also plays a role in disease outcomes, particularly for those infected with genotype 1b and genotype 3, who are at higher risk for HCC and steatosis respectively (Rubbia-Brandt et al. 2000).

2.1.2 Clinical manifestations of hepatitis C infection

There are two phases in HCV infection: acute and chronic. The acute phase refers to the first six months following HCV infection (Busch and Shafer 2005). During this period, antibodies are developed and liver enzymes such as serum alanine aminotransferase are raised (Busch and Shafer 2005). Within this period, an estimated 20% of infected individuals clear the virus spontaneously (Zeuzem et al. 2011), which is referred to as a 'resolved infection'; the remaining 80% develop chronic HCV infection. During the acute phase, there can be significant elevation of liver enzymes in the first 2-8 weeks following exposure, reflecting acute hepatocellular damage (Chen and Morgan 2006). Nevertheless, symptoms of an acute HCV infection are often very general and may go unrecognised, with 70–80% of HCV-infected individuals not diagnosed during this period (Chen and Morgan 2006). An estimated 75-85% of acute infected cases who do not clear the virus within six months and develop chronic HCV infection (Chen and Morgan 2006).

Chronic HCV infection is characterised by HCV RNA persisting in the blood for at least six months after the acute phase and can progress to cirrhosis, HCC and liver failure over two to three decades (Cacouba et al. 2014). This stage of chronic HCV infection is frequently asymptomatic and can last as long as 40 years (Lee et al. 2012).

Chronic HCV infection can also lead to numerous extrahepatic manifestations, and 40–74% of HCV infected patients , develop at least one extrahepatic manifestations over the course of their disease (Cacouba et al.

2014). The most common extrahepatic manifestation associated with HCV is mixed cryglobulinemia (an abnormal blood protein), which is a systemic vasculitis. Mixed cryglobulinemia is often asymptomatic, but may present symptoms such as fatigue, muscle pain, rash, joint pain, kidney disease, numbness and tingling (Lee et al. 2012). Other conditions possibly associated with HCV, but which are less likely to occur include porphyria cutanea tarda, lichen planus (skin problems), non-Hodgkins lymphoma, autoimmune thyroiditis, Sjogrens syndrome (dryness of the mouth and eyes) and seronegative arthritis. Extrahepatic manifestations associated with HCV vary in severity, but HCV treatment often leads to resolution of these symptoms (Cacouba et al. 2014).

2.1.3 Disease progression

Liver disease has four stages, which are classified based on the variation in the degree of fibrosis (scarring) and inflammation. As the disease progress, liver function which may ultimately be inhibited (Goodman 2007). At stages 0, 1 and 2, the degree of fibrosis has little effect on liver function (Goodman 2007, Pinzani, Rossellia, and Zuckermanna 2011). Within this period, inflammation responds to HCV treatment and often resolves infection, preventing progression to the more serious stages of liver disease (Pinzani, Rossellia, and Zuckermanna 2011).

By stages 3 or 4 of fibrosis, liver function is affected due to obstruction of blood flow though the liver (Davis et al. 2010). In the final stage, called cirrhosis, the liver architecture is disrupted by irreversible scarring and it is not possible to return liver function to normal even after successful virological treatment (Davis et al. 2010). In spite of this, HCV treatment for people with advanced fibrosis and cirrhosis is important to limit progression to decompensated cirrhosis (see below), HCC and liver failure (Morgan et al. 2013). The progression from acquisition of HCV to cirrhosis may take at least 10 to 20 years (Hoofnagle 1997).

There are two types of cirrhosis: compensated and decompensated cirrhosis. Compensated cirrhosis is marked by severe scarring of the liver, which nonetheless remain capable of performing many vital bodily functions (Pinzani, Rossellia, and Zuckermanna 2011). Decompensated cirrhosis is defined as extensive scarring of the liver to the extent that it is incapable of functioning properly, leading to complications (Zipprich et al. 2012). Symptoms of decompensated cirrhosis include tiredness, loss of appetite, vomiting, jaundice, weight loss, abdominal pain and bleeding (Zipprich et al. 2012). Not all people with cirrhosis experience symptoms until the occurrence of severe complications such as oedema (accumulation of fluid in the extremities, particularly the feet and legs), enlargement of the spleen and portal hypertension (Pinzani, Rossellia, and Zuckermanna 2011). Individuals who experience such complications are likely to progress to the final stage of liver disease, where the liver is no longer capable of performing its functions. Liver transplantation is the only treatment for this final stage.

People with chronic HCV initially develop chronic inflammation, leading to cirrhosis in some (20–40%), and of these 4–6% develop HCC within 10–40 years of infection (Castelloa et al. 2010). It is estimated that 350,000 to 500,000 people die globally per annum from HCV-related complications, mainly cirrhosis and HCC (WHO 2015). Progression to HCC occurs more quickly among chronically infected individuals who have alcoholic liver disease (Mueller, Millonig, and Seitz 2009).

2.1.4 Risk Factors for HCV

HCV is a blood-borne virus; the most efficient means of transmission is through percutaneous exposure to contaminated blood (Lavanchy 2009). Well-documented means of transmission (with widely varying degrees of efficiency) include: sharing of contaminated needles or equipment for drug use; reuse of needles in health care; contaminated blood transfusions or blood products (in countries where the blood supply is not screened); vertical transmission from mother to child; sharing of personal items such as razors

and toothbrushes; and tattooing and body piercing. These transmission routes and their importance for the HCV epidemic are described below.

2.1.4.1 Injecting drug use

Injecting drug use is considered to be the predominant mode of HCV transmission in most countries (Backmund et al. 2005, Alter 1997, Xia et al. 2008). Major factors which influence HCV transmission in IDUs include the fact that parenteral transmission of hepatitis C is highly effective, the size of the vulnerable population, and the prevalence of risk behaviours (Maher et al. 2006). HCV risk is highly correlated with the sharing of needles, syringes and other injecting equipment, as well as the duration of injecting; the longer an individual has been injecting, the more likely they are to have been exposed to hepatitis C (Hagan et al. 2006b, Brewer et al. 2006, Shannon et al. 2008).

Although the sharing of needles is the highest risk factor for IDUs, sharing or reusing other equipment such as swabs, cottons, spoons, water vials, tourniquets and fingers are also implicated the spread of HCV (Crofts, Aitken, and Kaldor 1999). For example, Koester et al. indicated that if a contaminated needle is used in a cooker (a container for mixing drugs using heat), the cooker becomes contaminated and even two or three days later a pathway for HCV transmission could be created (Koester, Booth, and Zhang 1996).

Injecting drug use is the primary route of HCV transmission in Australia (Grebely et al. 2008, Treloar et al. 2014, Dore et al. 2003), but it is not in itself a risk factor for HCV if sterile equipment and aseptic techniques are used. Harm-reduction strategies such as needle and syringe programs (NSP) have been highly effective in reducing transmission of HCV, preventing an estimated 97,000 new HCV infections in Australia over the decade 2000–2009 (Middleton et al. 2013). Transmission can occur when people who have HCV are unaware they are infected and pass it on unknowingly through the sharing of injecting equipment (Pugh 2008). Transmission risk of HCV is high (2.5–5.0%) when unsafe injecting practices are employed (Grebely and Dore 2011). Unsafe injecting practices account for nearly 80% of all current HCV infections and more than 90% of all new infections (Razalia et al. 2007).

Australian NSP surveys have found that the prevalence of reported re-use of syringes, including reuse of one's own syringe, reduced from 31% to 21% over the period 1997–2014, but remained stable from 2010 to 2014 (Iversen and Maher 2015). There was also a reduction in the proportion of participants reporting receptive sharing of drug-preparation equipment from 45% to 30% between 1999 and 2014. In all survey years, spoons and water were the most commonly shared drug-preparation items (Iversen and Maher 2015).

2.1.4.2 Blood transfusion and its products

Prior to the development of a laboratory detection method for HCV, blood transfusion was a major mode of transmission (Donahue et al. 1992). People with thalassaemia or haemophilia were at high risk of acquiring HCV due to receiving multiple transfusions (Brettler et al. 1990). A study in a large US haemophilic population indicated that almost 89% had active HCV infection (Troisi et al. 1993). A British study estimated the frequency of infectious donations entering the blood supply at one in 520,000 over 1993–1998, decreasing to one in 30 million between 1999 and 2001, when all donations started being tested for HCV RNA (Soldan et al. 2003). Universal screening of blood donations for HCV was introduced in 1990 in Australia (Donahue et al. 1992), resulting in a significant decrease in the number of cases of transfusion-acquired HCV (Humphery et al. 2004). The number of cases of HCV acquired through blood transfusion reduced significantly in Australia from 13 in 1995 to zero in 2000 (Humphery et al. 2004). There were no transfusion-acquired HCV infections between 2005 and 2014 in Australia (Ismay et al. 2015).

Although screening of the blood supply for HCV has almost eliminated this mode of transmission in developed countries (Busch et al. 2005), the risk of HCV infection through blood transfusion remains an important risk factor in some developing countries due to lack of resources for screening blood donors and use of commercial donors (Liu et al. 2010, Hladik et al. 2006, Luby et al. 2000). For example in Africa, the recent risk of HCV infection via

blood transfusion was estimated to be one in 100,000 transfusions (Rerambiah et al. 2014).

2.1.4.3 Mother-to-child transmission

The risk of HCV transmission from pregnant mother to infant is around 4% (McMenamin et al. 2008, Dienstag 1997). This risk is increased when the mother is co-infected with HIV or hepatitis B (Ferrero et al. 2003, Thomas et al. 1998). The vertical transmission rate has been estimated at 5.4% in human immunodeficiency virus (HIV) co-infected women, compared to 2.0% in HIV-negative women (Ferrero et al. 2003). The risk of vertically transmitted HCV infection was 3.2 times higher in HIV-infected infants than non-HIV-infected infants (Thomas et al. 1998). Eight studies that were part of a single meta-analysis conducted among HIV-positive and HIV-negative women reported crude rates of mother-to-infant transmission of 22.1% and 4.3% respectively (Maccabruni et al. 1995, Granovsky et al. 1998, Zuccotti et al. 1995, Tovo et al. 1997, Zanetti et al. 1998, Paccagnini et al. 1995, Mazza et al. 1998, Gussetti et al. 1998). There is no evidence of HCV transmission via delivery or breastfeeding (Ferrero et al. 2003, McMenamin et al. 2008), but some studies have suggested the risk of transmission from mother to baby could increase with an increasing viral load at the time of delivery (Schwimmer and Balistreri 2000, McMenamin et al. 2008, Tosone et al. 2014, Ferrero et al. 2003). Pregnancy has been shown to affect HCV viral loads, with a reduction in the first and second trimesters and an increase in the third trimester, which could increase the risk of transmission at birth (Wejstål, Widell, and Norkrans 2001, Paternoster et al. 2001, Tosone et al. 2014).

2.1.4.4 Sexual contact

The risk of transmission of HCV through sexual activity is not clear. Some studies have identified HCV RNA in the saliva and semen of HCV-infected individuals, suggesting that sexual contact is a potential route of HCV exposure (Liou et al. 1992, Briat et al. 2005). Several researchers who examined the association between sexual contact and HCV transmission among high-risk groups such as men who have sex with men (MSM), HIV-

positive people and serodiscordant monogamous couples have suggested that the risk of HCV transmission is positively associated with the number of sexual partners as well as when the sexual partner is co-infected with HIV/HCV (Leruez-Ville et al. 2000, Nyamathi et al. 2002, Workowski and Berman 2010).

Sexual HCV transmission has been supported in a study which reported that 15% of non-IDU women having unprotected sex with an HCV-infected injecting partner became HCV positive (Goldberg et al. 2001). However, a 10-year prospective study of 895 monogamous spouses of chronically infected partners showed a rate that was very low or even nil (Vandelli et al. 2004). Sexual HCV transmission varies by the type of sexual relationship. Incidence of HCV was reported to be 0–0.6% per year among long-term monogamous heterosexual relationships, while among heterosexual relationships with multiple partners or a history of sexual transmitted diseases it was 0.4–1.8% per year (Terrault 2002). Overall, sexual transmission of HCV is thought to be uncommon, but less so in high-risk populations (Terrault et al. 2013).

2.1.4.5 Sharing of personal items

Other documented means of transmission include sharing personal care items like toothbrushes, razors, nail clippers and other items that may come into contact with blood from HCV-infected individuals (Janjua et al. 2010, Lock et al. 2006). These routes of HCV transmission are not regarded as efficient and there is insufficient data to indicate their contribution to the transmission of HCV (Janjua et al. 2010, Lock et al. 2006). However, researchers who tested the toothbrushes of HCV-infected individuals have found that 40% had detectable HCV RNA (Lock et al. 2006). In addition, a cross-sectional study conducted in a psychiatric institution indicated that razor-sharing was a plausible route of HCV transmission, after adjusting for age, duration of hospitalisation and history of surgery (Sawayama et al. 2000).

2.1.4.6 Tattooing and body piercing

Although tattooing and body piercing involve potential percutaneous exposure, the risk of HCV transmission via these activities is very low provided that adequate infection control measures are in place (Jafarib et al. 2007). However, non-professional tattooing and multiple tattoos have been associated with increased probability of HCV transmission (Haley and Fischer 2003, Nishioka et al. 2002). The relative contribution of body piercing as an independent risk factor for HCV is poorly defined, particularly in developed countries (Kim 2002, Shepard, Finelli, and Alter 2005).

2.1.5 Prevalence of HCV

HCV is a disease of global importance that requires multiple interventions for its prevention and control (Lavanchy 2011). The prevalence of HCV infection is approximately 2.2–3.0% worldwide, which equates to 185 million people infected with chronic HCV (WHO 2014). In developed countries, the highest prevalence of HCV is among IDUs (Aceijas and Rhodes 2007). There are an estimated 10 million active IDUs worldwide (Nelson et al. 2011) and 8 million have chronic HCV (Hagan et al. 2008).

In Australia, the estimated prevalence of HCV is published in an annual surveillance report (Iversen and Maher 2015). This surveillance activity has been conducted every year since 1997 (Iversen and Maher 2015). However, notification rates of HCV in Australia do not necessarily reflect the number of recently infected individuals because the infection is often asymptomatic and people are unlikely to present for testing until sometime following exposure (Middleton et al. 2013). It has been estimated that 40,000–50,000 Australians remain unaware that they are infected with chronic HCV (Middleton et al. 2013).

The most recent estimate of the number of Australians who are anti-HCV antibody-positive is 308,110, a national prevalence of 1.3% (Sievert et al. 2014). Of these, an estimated 80,000 individuals have cleared HCV naturally (Sievert et al. 2014). It has been reported that 230,470 Australians had chronic

HCV at the end of 2014 (Guy and McGregor 2015), giving a prevalence of HCV viraemia of 1.05% (Sievert et al. 2014). New South Wales had the highest number of reported chronic HCV infections (81,940), followed by Victoria (55,760), Queensland (47,950) and Western Australia (20,510) (Guy and McGregor 2015).

According to recent Australian NSP surveys, the prevalence of HCV among IDUs was highest at 60% from 1995 to 2008, declining to 53–54% the over period 2010–2014 (Iversen and Maher 2015). The rate of new diagnoses of HCV in Australia has declined from 61 to 46 per 100,000 between 2005–2014 (Guy and McGregor 2015). This decline has occurred in most age groups but is most noticeable among people aged 25–29 and 20–24 years (49% and 44% respectively) (Guy and McGregor 2015). However, these two age groups still had the highest rates of newly acquired HCV infections. Rates of HCV diagnosis in 2014 were almost five times higher in the Indigenous population than in the non-Indigenous population (Guy and McGregor 2015). Overall, it is predicted that the number of people with chronic HCV in Australia will reach 255,500 by 2025, then decline to 251,970 by 2030 (Sievert et al. 2014).

HCV prevalence is estimated at 3.5% in Central and East Asia and in North Africa and the Middle East, and 1.5–3.5% in South and Southeast Asia, sub-Saharan Africa and Latin America (Lavanchy 2011). The Asia-Pacific region and North America have an estimated prevalence of less than 1.5% (Lavanchy 2011). The prevalence of HCV in Northern Europe ranges from 0.1% to 1%, in Central Europe from 0.2% to 1.2% and in Southern Europe from 2.5% and 3.5% (Esteban, Sauleda, and Quer 2008).

In Sub-Saharan Africa an estimated 28 million people are infected (Lavanchy 2011), giving an HCV seroprevalence of 3%, ranging from 2.1% in Southeast Africa to 2.8% in West Africa to 7% in Central Africa (Hanafiah et al. 2013). The primary mode of HCV transmission in Africa has not been documented (Layden et al. 2014). Unsterile needles, unsafe transfusions of blood products and co-infection with HIV are plausible reasons, but lack of both primary data and population-based studies in Sub-Saharan Africa prevent determination of

the routes of HCV transmission (Layden et al. 2014). In Southern, East, West, and Central Africa the estimated prevalence of HCV is 1.8% in blood donors, 2.5% in pregnant women, 3.5% in individuals with comorbid HIV, 5.4% in individuals from the general population, 8% in those with a chronic illness (diabetes and liver disease) and 10.2% in those at high risk of infection (prisoners, IDUs, sex workers, hemodialysis patients, hospital workers and adults and children with sickle cell anaemia) (Mora et al. 2016).

Egypt has the highest national prevalence of HCV. Frequent reuse of syringes during a schistosomiasis suppression program in the 1960s and 1970s spread HCV widely (Frank et al. 2000) and it is also associated with unsafe injection practices, lack of infection control in tertiary hospitals and use of unscreened blood for transfusions (Miller and Abu-Raddadb 2010). Older age groups have higher prevalence of HCV than younger groups (Umar et al. 2013): prevalence of chronic infection was 22.1% among people aged 55–59 years and less than 1% among people aged below 20 years in 2009 (Umar et al. 2013). Also, social determinants of health, including education level, socioeconomic status, and place of residence can impact on HCV prevalence (El-Zanaty and Way 2009). For instance, HCV prevalence is higher in rural (5.1%) and illiterate people (14.5%) than in urban areas (3.1%) and among those who have completed secondary education or higher (4.1%) (El-Zanaty and Way 2009). Exposure to HCV information (therapeutic and preventive) through the media (Chemaitelly, Abu-Raddad, and Miller 2013) and engaging in health education programs (Mohamoud et al. 2013) might also explain the disparity in HCV prevalence among urban versus rural residents and more educated versus less educated people.

2.1.6 Burden of HCV disease

The burden of HCV disease affects many countries, but differs widely between them (Mathurin 2013) depending on HCV prevalence, mean duration of infection, age, alcohol intake, and uptake and success of HCV treatment (Mathurin 2013). HCV is the most common cause of chronic liver disease, particularly in Australia, the USA, and Europe (Hanafiah et al. 2013).

As noted earlier, an estimated 2.8% of the world's population suffer from HCV and a significant proportion of these people will develop liver complications. It is estimated that 350,000 to 500,000 people die per annum from HCV-related complications, mainly liver cirrhosis and HCC (WHO 2015). The WHO has estimated that 27% of cirrhosis and 25% of HCC can be attributed to HCV worldwide (WHO 2015).

Globally, the burden of HCV disease associated with HCC and cirrhosis is 15–20 times higher among cases with chronic HCV infection compared to HCV RNA–negative but HCV antibody positive individual (El-Serag 2012). HCC is the fifth most common carcinoma and the third most common cause of cancer deaths globally (Parkin et al. 2005). HCC develops after 20 years of HCV infection and its risk increases among patients with cirrhosis or advanced fibrosis (Hanafiah et al. 2013).

Epidemiological capacity varies greatly, so the HCV disease burden is not well understood in many countries (Averhoff, Glass, and Holtzman 2012). In some countries the burden of HCV disease is derived from serological surveys, but this method is too expensive for others, where the burden is estimated from other sources, such as surveys of blood donors, high-risk populations and pregnant women, and so is not generalisable to a wider population (Averhoff, Glass, and Holtzman 2012). A recent global assessment of HCV estimated that 195,700 people died from HCV-related HCC in 2010 (Razavi et al. 2014). Egypt has the highest burden of HCV disease, including an estimated 770,000 people with HCV-related cirrhosis and 16,000 with HCV-related HCC, and 33,000 HCV-related deaths from liver failure in 2013 (Razavi et al. 2014). Brazil has the next highest level of HCV related-HCC with 8,400, followed by Turkey with 2,200 infected people (Dore, Ward, and Thursz 2014). Denmark with 80 HCC cases and the Czech Republic with 70 have the lowest burden of HCV disease as measured by the incidence of HCV-related HCC, due to a very low HCV prevalence and young age distribution respectively (Dore, Ward, and Thursz 2014).

In Australia, HCV represents a major burden on the health system (Sievert et al. 2014). There was a high incidence of HCV infection among IDUs in the 1980s and 1990s, and it is expected that, as the population ages, cases of HCC and HCV-related cirrhosis will increase considerably over the next two decades, inflating health costs (Sievert et al. 2014). The most recent data shows that there were 1430 cases of decompensated cirrhosis in Australia in 2013 (Razavi et al. 2014) and 590 cases of HCV-related HCC in the same year. It is projected that these numbers will almost triple by 2030 (Razavi et al. 2014).

HCV is the most common indication for liver transplantation in adults in Australia, which reflects the increasing burden of end-stage liver disease (HCC and liver failure) due to HCV (Sievert et al. 2014). Gidding and her colleagues collected data from all transplant units in Australia on all patients listed for liver transplantation over 1997–2006, finding that 30% had HCV-related cirrhosis and 50% of recipients had HCC related to HCV (Gidding et al. 2009). The number of liver transplants attributable to HCV infection increased from 63 (33% of all liver transplants) to 81 (36%) between 2012 and 2014 (Guy and McGregor 2015). In Australia, annual liver-related deaths increased from 250 to 630 over 2003–2013 (McDonald et al. 2014) and are forecast to increase to more than 1700 by 2030 (Sievert et al. 2014).

2.1.7 History of HCV treatment

The aim of HCV treatment is to eradicate the virus from the body, thus avoiding progression to liver damage and extrahepatic disease. Major advances in the treatment of HCV have occurred over the past two decades (Figure 2.1). Interferon treatment for non-A, non-B hepatitis was first introduced in 1986; administered for 24 weeks, it achieved normalisation of liver enzymes among 6–10% of those who were treated (Davis et al. 1989, Bisceglie et al. 1989). With the addition of ribavirin (which increases the antiviral action of interferon, as well as reducing the risk of relapse after completion) to interferon in the 1990s, SVR rates improved to 30% for genotype 1 (48 weeks' treatment) and 62% for genotypes 2 and 3 (24 weeks)

(Poynard et al. 1998, McHutchison et al. 1998). The combination of interferon and ribavirin was adopted as the standard treatment in 1998, with ribavirin administered orally twice a day and interferon injected three times per week (McHutchison et al. 1998).

Pegylated interferon was introduced in 2001 and again the SVR increased considerably, reaching up to 80% for genotypes 2 or 3 (24 weeks' treatment) and 50% for genotype 1 (48 week) (Manns et al. 2001, Manns, Wedemeyer, and Cornberg 2006). Pegylated interferon was administered as a single injection once a week, along with ribavirin tablets taken twice daily. However, HCV treatment with either interferon or pegylated interferon had significant side effects such as flu-like symptoms (fever, fatigue, headache and muscle pain), lack of appetite, nausea and vomiting, injection site reactions and psychiatric side effects (depression, anxiety irritability and in some cases suicidal ideation and insomnia), compounded by ribavirin side effects including anaemia and skin rashes (Manns et al. 2001, Manns, Wedemeyer, and Cornberg 2006).

Until 2011, pegylated interferon and ribavirin combination therapy with a duration of 24–48 weeks (depending on genotype) was considered the gold standard of HCV treatment. However, in 2011 a third drug, the first DAA (a combination of boceprevir and telaprevir), was added to the standard combination therapy for treatment of genotype 1 (Bacon et al. 2011, Poordad et al. 2011). These drugs were approved for use in Australia in 2012 and were listed on the PBS from April 2013 (HepatitisAustralia 2016) These first-generation DAAs had additional side effects such as severe skin reactions (Lawitz 2011) and more marked anaemia (Poordad et al. 2011, Bacon et al. 2011), but this triple therapy achieved SVR rates of 66–69% among treatment-naïve individuals with genotype 1 over 22–48 weeks. In treatment-experienced cases, SVR rates reached 83% for those who had previously relapsed and 59% among partial responders (Ghany et al. 2011). Generally, SVR rates for patients with HCV genotype 1 infection reached 70%, significantly higher than the 50% achieved with pegylated interferon and

ribavirin (Poordad et al. 2011). Among those with cirrhosis, SVR rates were around 50% (Poordad et al. 2011, Bacon et al. 2011, Zeuzem et al. 2011).

In 2013, a second-generation HCV-specific protease inhibitor known as simeprevir was released and approved for treatment of HCV genotypes 1 and 4 (Manns et al. 2013). However, in Australia this preparation was not listed on the PBS until late 2014 (Thompson and Holmes 2015). Unlike telaprevir and boceprevir, this protease inhibitor did not cause additional side effects (Manns et al. 2013, Jacobson et al. 2013). SVR rates for simeprevir in combination with pegylated interferon and ribavirin among naïve patients with genotype 1 and 4 were around 80% after only 24 weeks (Manns et al. 2013, Jacobson et al. 2013). However, prior to commencing treatment with simeprevir, HCV-infected individuals with genotype 1a should be screened for a genetic mutation known as Q80K polymorphism, which reduces the efficacy of simeprevir-containing triple treatment (Izquierdo et al. 2014). The frequency of Q80K varies by country and it is more common where HCV genotype 1a is predominant, such as in Europe and North America (Sarrazina et al. 2015). An SVR rate of 85% has been recorded in cases without the Q80K variant, compared to 50% in those with it (Jacobson et al. 2014). However, simeprevir is not recommended for patients who have previously been treated with pegylated interferon and ribavirin, with or without boceprevir/telaprevir (Izquierdo et al. 2014).

The greatest development in HCV treatment to date occurred with the release of sofosbuvir in 2013. Sofosbuvir is a polymerase inhibitor and has pan-genotypic activity (Lam et al. 2012). The addition of sofosbuvir to pegylated interferon and ribavirin resulted in SVR rates of 90% for patients with HCV genotype 1; 97% for genotypes 4, 5 and 6 among both naïve and treatment-experienced patients within 12 weeks; 93% for patients with genotype 2 with cirrhosis; 85% for patients with genotype 3 with or without cirrhosis; and 100% for patients with genotype 2 without cirrhosis (Lawitz et al. 2015). For genotypes 2 and 3, sofosbuvir and ribavirin without pegylated interferon achieved 93% and 85% SVR over 12 weeks and 24 weeks among naïve and

treatment-experienced cases respectively (Lawitz et al. 2015). Due to the success of these new anti-HCV drugs, sales and distribution of telaprevir was discontinued in 2014 and Merck announced that it planned to stop selling boceprevir by the end of 2015 (Jie and Douglas 2014).

In 2014, new DAAs consisting of Harvoni, Viekira Pak (3D therapy) and daclatasvir were approved for treatment of HCV genotype 1. Harvoni is a pill with a combination of sofosbuvir and ledipasvir, and requires treatment for 8 weeks for people with no treatment experience and no cirrhosis, 12 weeks for people with no treatment experience and cirrhosis, and 24 weeks for people with treatment experience and cirrhosis (Jensen and Holle 2016). Viekira Pak contains four antiviral drugs – paritaprevir, ombitasvir, ritonavir and dasabuvir – and is used for both treatment-naïve and treatment-experienced patients. Treatment duration and addition of ribavirin depend on whether cases are cirrhotic or non-cirrhotic and on genotype 1 subtype (Carrion, Gutierrez, and Martin 2014, Guido 2014, Kati et al. 2015). This medicine is given over a period of 12 weeks for genotype 1b with or without cirrhosis and 1a without cirrhosis, and 24 weeks for 1a with cirrhosis (Ferenci et al. 2014, Poordad et al. 2014). Reported SVR rates with Harvoni and Viekira Pak are 90–100% among naïve and previously treated cases (Lam et al. 2015, Ferenci et al. 2014, Esteban et al. 2014).

Daclatasvir is given in combination with sofosbuvir, and achieves SVR rates of 95% among naïve and treatment-experienced patients with genotype 1. They are given for 12 weeks for people with both no treatment experience and no cirrhosis and 24 weeks for others (Sulkowski et al. 2014). The advantages of these DAA treatments over their predecessors are shorter duration of treatment, fewer side effects, and higher success rates in clearing the virus. Harvoni, sofosbuvir/daclatasvir, sofosbuvir/ribavirin and sofosbuvir/pegylated interferon and ribavirin were listed on listed on the PBS in March 2016, followed by Viekira Pak in May 2016 (DOH 2016). These new medications (interferon-free) are available for treatment of genotypes 1, 2 and 3, the most common genotypes in Australia, and involve single oral

doses (Hepatitis Australia 2016). However, genotypes 4, 5 and 6 still require treatment with pegylated interferon and ribavirin in conjunction with one of these new medications (Hepatitis Australia 2016).

The recommended treatment regimens for these new DAAs range from 8 to 24 weeks and depend on HCV genotype, treatment history and the presence of cirrhosis, as indicated in Figure 2.1. In Australia, the actual cost of new DAAs is estimated around $100,000, however, Australian government has approved new dispensing cost. HCV treatment on the PBS and are available for the cost of a pharmacy. Treatment costs to general patients and concessional patients are $38.30 and $6.20 only for the pharmacy co-payment paid for a monthly prescription, respectively (Hepatitis Australia 2016). In addition, these new DAAs can be prescribed by general practitioners (GPs, who must consult a specialist) (Hepatitis Australia 2016). However, these new DAAs antiviral drugs require strict adherence in order to achieve successful outcomes of HCV treatment (Colpitts and Baumert 2016). Other DAAs are in the pipeline. Velpatasvir is currently under evaluation in various combinations in clinical trials (Gane et al. 2015). Other DAAs will undoubtedly become available in the near future.

Figure 2.1 Recommended treatment regimens for the new DAAs

Source: Hepatitis Australia (2016)

Genotype	No Previous Treatment (naïve)		Previously Received Treatment (experienced)	
	No cirrhosis	With cirrhosis	No cirrhosis	With cirrhosis
1 a/b	Ledipasvir/sofosbuvir [8 or 12 weeks]	Ledipasvir/sofosbuvir [12 weeks] or Sofosbuvir and Peg-Interferon alfa-2a/ribavirin [12 weeks]	Ledipasvir/sofosbuvir [12 weeks] or Sofosbuvir and Peg-Interferon alfa-2a/ribavirin [12 weeks]	Ledipasvir/sofosbuvir [24 weeks] or Sofosbuvir and Peg-Interferon alfa-2a/ribavirin [12 weeks]
1 a/b	Daclatasvir and sofosbuvir [12 weeks]	Daclatasvir and sofosbuvir and ribavirin [12 weeks] or Daclatasvir and sofosbuvir [24 weeks]	Daclatasvir and sofosbuvir [12 or 24 weeks]	Daclatasvir and sofosbuvir and ribavirin [12 weeks] or Daclatasvir and sofosbuvir [24 weeks]*
1a	Paritaprevir-ritonavir, ombitasvir, dasabuvir and ribavirin (12 weeks)	Paritaprevir-ritonavir, ombitasvir, dasabuvir and ribavirin (12 weeks)	Paritaprevir-ritonavir, ombitasvir, dasabuvir and ribavirin (12 weeks)	Paritaprevir-ritonavir, ombitasvir, dasabuvir and ribavirin (12 or 24 weeks)
1b*	Paritaprevir-ritonavir, ombitasvir and dasabuvir (12 weeks)	Paritaprevir-ritonavir, ombitasvir and dasabuvir (12 weeks)	Paritaprevir-ritonavir, ombitasvir and dasabuvir (12 weeks)	Paritaprevir-ritonavir, ombitasvir and dasabuvir (12 weeks)
2	Sofosbuvir and ribavirin [12 weeks]	Sofosbuvir and ribavirin [12 weeks]	Sofosbuvir and ribavirin [12 weeks]	Sofosbuvir and ribavirin [12 weeks]
3	Daclatasvir and sofosbuvir [12 weeks] or Sofosbuvir and ribavirin [24 weeks]	Daclatasvir and sofosbuvir [24 weeks] or Sofosbuvir and ribavirin [24 weeks]	Daclatasvir and sofosbuvir [12 weeks] or Sofosbuvir and ribavirin [24 weeks]	Daclatasvir and sofosbuvir [24 weeks] or Sofosbuvir and ribavirin [24 weeks]
4, 5, 6	Sofosbuvir and Peg-Interferon alfa-2a/ribavirin [12 weeks]	Sofosbuvir and Peg-Interferon alfa-2a/ribavirin [12 weeks]	Sofosbuvir and Peg-Interferon alfa-2a/ribavirin [12 weeks]	Sofosbuvir and Peg-Interferon alfa-2a/ribavirin [12 weeks]

2.2 Intention to take up treatment

Treatment intention refers to the intention to undertake treatment for active HCV. Intention to undergo HCV treatment is the result of an individual's evaluation of their ability to cope with treatment and consideration of alternative treatment options. Intention to undertake HCV treatment is viewed in some studies as willingness or readiness to undertake treatment (Stein, Maksad, and Clarke 2001, Fischer et al. 2005). Despite the variation in measurement methods of treatment willingness, most studies have reported high levels of intention to undertake treatment. A cross sectional study in the USA has found that nearly 81.5% of treatment-naïve HCV-infected IDUs aged 18-35 years intend to undertake treatment, particularly those who had a high perceived risk of developing liver disease and higher willingness to stop injecting drugs (Strathdee et al. 2005).

An opioid use cohort study in a community setting in Sothern Canada reported that 80% of IDUs indicated willingness to participate in HCV treatment (Fischer et al. 2005). However, in the pre-DAA era, most IDUs

emphasised the low efficacy of HCV treatment, indicating willingness to undertake treatment, but only if it could guarantee they would clear the virus (Fischer et al. 2005). A similar level of to receive HCV treatment (77%) was reported by IDUs in two inner-city community health clinics in Vancouver and British Columbia (Grebely et al. 2008).

An early Australian exploratory study of IDUs' intentions and barriers with respect to HCV treatment in a primary health facility and methadone clinic in inner Sydney, reported that 70–80% of IDUs intended to be treated for HCV infection (Doab, Treloar, and Dore 2005). The most recent Australian cohort studies, which were conducted in opioid substitution treatment clinics and community health centres in New South Wales, indicated that 67% of participants were intending to receive treatment (Alavi et al. 2015). A cross-sectional survey among clients of opioid substitution therapy clinics and the medically supervised injecting centre in Sydney reported that 53% of participants expressed willingness to undertake HCV treatment (Treloar et al. 2012). The findings of high levels of treatment willingness in these studies could be due to recruiting of participants from community settings, where better opportunities for delivering HCV care to IDUs are provided, and/or due to the self-reporting of treatment willingness.

Despite reporting high levels of intention to undertake treatment in the above studies and widespread availability, actual treatment uptake remains low among HCV-infected IDUs (Volk 2010, Grebely et al. 2009, Guy and McGregor 2015, Sievert et al. 2014). However, little recent data exists on the proportion of IDUs who have ever received treatment. A Canadian study reported that among 2118 HCV-infected IDUs, only 1.1% initiated treatment between 2003–2004; the rate of new HCV seroconversions in this cohort was 25 times the rate of HCV treatment uptake (Grebely et al. 2009). One study collected launch and sales data from 21 European countries and estimated that 3.5% of HCV-infected of individuals had been treated, ranging from 16% in France to 1% in Poland, by the end of 2005 (Lettmeier et al. 2008). Similarly in the USA 663,000 of an estimated 3.2 million HCV-infected people

received HCV treatment over 2002–2007 (Volk et al. 2009). A large retrospective study in the USA reported the treatment rate was low in Veterans Affairs at 13% (251 of 1929 patients), which was similar to the 14% rate in HCV specialist clinics (3537 of 24,853 patients) over the period 2004–2009 (Kramer et al. 2011).

A recent Australian cross-sectional study which examined trends in HCV treatment uptake among HCV-infected IDUs who attended NSPs from 1999 to 2011, reported that the proportion of participants who were on HCV treatment increased from 1.1% to 2.1% over this period. Likewise, the proportion of participants who had a lifetime history of HCV treatment increased from 3.4% to 8.6% between 1999 and 2011 (Iversen et al. 2014). Despite increases in the uptake of HCV treatment among IDUs in Australia over the period 1999–2011, rates of treatment among IDUs in Australia range from 1–2% per year (Guy and McGregor 2015, Sievert et al. 2014). Likewise, the rate of treatment uptake was less than 1% per year in the USA (Volk 2010) and Canada (Grebely et al. 2009). These low rates of treatment uptake reported by researchers may be accurate, but there are various factors associated with these low rates. The following section goes into deeper explanation of these factors.

2.3 Factors influencing intention to undertake treatment

2.3.1 Treatment characteristics

HCV treatment in the pre-DAA era was associated with a wide range of physical and psychiatric side effects (Zickmund et al. 2006, Manns, Wedemeyer, and Cornberg 2006, Keating and Curran 2003) and on average individuals could expect to experience at least eight side effects during the course of treatment (Zucker and Miller 2001). An early study among those who experienced treatment showed that 10–50% of patients on HCV treatment discontinued it due to fatigue (Bernstein et al. 2002), while recent studies show that 10–14% of patients withdraw from treatment due to depression, anxiety, fatigue and/or headache (Ghany et al. 2009).

As noted earlier, physical and psychiatric side effects of HCV treatment, include flu-like symptoms (fatigue, headaches, muscle pain), depression, suicidal ideation, mood disorders, anxiety, nausea, hair loss, skin rash, anaemia, anorexia, lack of concentration and insomnia (Hopwood and Treloar 2005, Russo and Frie 2003, Grebely et al. 2016, Grebely, Matthews, et al. 2011a, McGowan and Fried 2012). These side effects debilitate patients and weaken their capacity to function normally (Sgorbini, O'Brien, and Jackson 2009, Hopwood and Treloar 2005). Some patients undergoing treatment are unwilling to continue due to these side effects (Grebely et al. 2016, Grebely, Matthews, et al. 2011a, McGowan and Fried 2012). Pegylated interferon exacerbates pre-existing psychiatric problems such as depression, anxiety and mood disorders, which are common among HCV-infected IDUs (Alavi et al. 2012, Sylvestre et al. 2004, Schaefer and Mauss 2008). It is reported that IDUs have higher prevalence of psychiatric disorders (22–49%) than the general population(17%) (Kessler et al. 2005).

However, maintaining optimism before treatment (Treloar and Hopwood 2008) and applying adaptive approaches such as learning from past experiences of drug dependence, living with chronic disease and coping with depression (Hopwood and Treloar 2008) enable some IDUs to manage treatment side effects. Numerous studies show that fear or concern about treatment side effects is one of the main reasons IDUs refuse to undertake HCV treatment when it is offered (Grebely et al. 2009, McNally, Sievert, and Pitts 2006, Fischer et al. 2005, Grebely et al. 2008, Doab, Treloar, and Dore 2005, Treloar et al. 2014, Cooper and Mills 2006, Hopwood, Treloar, and Redsull 2006, Alavi et al. 2013).

As discussed earlier, the standard pre-DAA HCV treatment, based on pegylated interferon and ribavirin, had relatively low efficacy in HCV-infected people, particularly those with genotype 1 (Grebely et al. 2009, Manns, Wedemeyer, and Cornberg 2006, Mehta et al. 2008), and the overall efficacy of HCV treatment among IDUs was low (Doab, Treloar, and Dore 2005, Stoove, Gifford, and Dore 2005, Fleming et al. 2003). A study

conducted in the USA among IDUs reported that of 418 participants who had heard of HCV treatment, 30 participants (7.2%) refused treatment, 76 (18.8%) were not interested and 20 (4.7%) deferred their treatment. Of the 292 remaining participants, who indicated interest in treatment, only 55 agreed to commence treatment and of these only 5 participants cleared their HCV (Mehta et al. 2008). This study reported that low treatment effectiveness in achieving SVR was one of the main reasons that discouraged participants from undertaking HCV treatment (Mehta et al. 2008).

An Australian study that evaluated IDUs' attitude towards HCV treatment at different levels of efficacy reported that willingness to consider treatment increased with treatment efficacy, ranging from 36% to 93% for 20% and 70% efficacy respectively (Doab, Treloar, and Dore 2005). In other studies, HCV patients stated that they would prioritise HCV treatment if they had a guarantee of clearing the virus (Fischer et al. 2005). Therefore, perceptions of and concerns about treatment effectiveness were significant barriers to HCV treatment uptake (McNally, Sievert, and Pitts 2006, Treloar, Newland, et al. 2010, Khokhar and Lewis 2007, Parkes et al. 2006).

In addition to treatment side effects and efficacy, treatment duration is a concern for those considering HCV treatment (Falck-Ytter et al. 2002, Khokhar and Lewis 2007, Parkes et al. 2006). Lengthy treatment duration has led to low intention to undertake treatment and high dropout rates (Berg et al. 2006, Fusfeld et al. 2013). Adherence is crucial, as IDUs who take more than 80% of antiviral therapy for more than 80% of the required treatment duration are significantly more likely to eradicate the virus than those who do not (McNally, Sievert, and Pitts 2006). Nevertheless, treatment of 24 to 48 weeks duration with significant side effects can seriously interrupt the work and family life of IDUs (Hopwood and Treloar 2005, Hopwood, Treloar, and Bryant 2006). An abbreviated treatment duration of 12–24 weeks is reportedly more appealing to IDUs (Kamal et al. 2006, Rosa et al. 2006, Jaeckel et al. 2001, Wiegand et al. 2006). In particular, shorter treatment would be an advantage for IDUs who have comorbid psychiatric illness and

may lead to an increase in the number of patients interested in undertaking treatment (Grebely et al. 2010). For example, one study indicated that adherence to HCV treatment among patients with genotypes 1 and 2 was high for the first three and six months then after three and six months period after which individuals became reluctant to continue the treatment course (Kamal et al. 2006). Doubts about being able to complete treatment duration were reported in a study by Fusfeld et al. and participants in this study indicated that they would have been more willing to tolerate treatment side effects if treatment duration was shorter (Fusfeld et al. 2013).

Each of the described studies demonstrates that factors such as lack of treatment efficacy, lengthy treatment duration and fear of treatment side effects can create a challenging treatment experience for IDUs. When this population is considered for such treatment, it is clear that there are also other significant factors that can make seeking treatment difficult for IDUs. The next section reviews the literature on social and personal factors in relation to the uptake of HCV treatment.

2.3.2 Social and personal factors

2.3.2.1 Stigma

Researchers have suggested that the stigma associated with HCV and IDU can strongly influence IDUs' intention to undertake HCV treatment. Stigma occurs within general society, the health care system and family/personal relationships (Grebely et al. 2009, Harris and Rhodes 2013, Swan et al. 2010, Treloar, Rance, and Backmund 2013). The experience of stigma often leads to self-isolation, which decreases the intention to seek HCV treatment (Grebely et al. 2009). Harris, who conducted qualitative interviews with 40 HCV-positive IDUs in New Zealand and Australia, noted that due to internalising the social stigma of HCV, some participants considered their HCV a lower priority than other health issues; they viewed HCV not only as a health issue, but also as a moral issue (Harris 2009).

The main cause of stigmatisation is society's association of HCV with IDU (Nguyen et al. 2007), even for those who have contracted HCV through blood transfusion (Sgorbini, O'Brien, and Jackson 2009, Feiring, Taska, and Lewis 1996). This assumption also exists in health care settings, where IDUs can be treated differently from others with chronic disease (Sgorbini, O'Brien, and Jackson 2009). A lack of knowledge and awareness of HCV within health care settings as well as lack of interaction between health care providers and patients, in particular GPs, some of whom are not interested in providing care to IDUs can lead to stigmatisation (Hopwood and Southgate 2003, Zickmund et al. 2003, Sgorbini, O'Brien, and Jackson 2009).

When disclosing their HCV status and/or drug use status, HCV-positive individuals often experience stigma from friends and family in the form of shame (Corrigan, Watson, and Miller 2006, Zickmund et al. 2003). Fear of being left alone, negative reactions, deterioration of relationships and being pushed aside or abandoned by their family prevents many from disclosing their status (Tinda, Cook, and Foster 2010). This can render people unable to cope with HCV treatment and its side effects (Zickmund et al. 2003). Therefore, stigmatisation of HCV and its association with IDU can reduce willingness to undertake HCV treatment (Grebely et al. 2009). Moreover, this stigma can limit the network of families and friends who could provide support during HCV treatment (Phillips and Barnes 2016). HCV-infected individuals have reported that their friends physically moved away from them, refused to approach them and reduced or stopped communication with them (Moore, Hawley, and Bradley 2009).

Social support is a key factor in undertaking HCV treatment (Bangsberg 2008 , Phillips and Barnes 2016 , Sylvestre and Zweben 2007, Grebely, Bryant, et al. 2011, McNally, Temple-Smith, and Pitts 2004), through the integration of partners or other important family members into HCV treatment (Sgorbini, O'Brien, and Jackson 2009). A supportive environment can assist individuals to cope with the emotional and physical side effects of HCV treatment (Fraenkel et al. 2006) and improve treatment outcomes in general (Sgorbini,

O'Brien, and Jackson 2009). HCV patients who attended support groups benefited from talking with peers, who enabled them to validate the quality and severity of their symptoms (Fraenkel et al. 2006) maintain motivation in the face of adverse effects and share coping strategies (Rifai et al. 2006). It has been reported that individuals who have social support, live with family and/or friends (Alavi et al. 2013 , Alavi et al. 2015, Grebely, Bryant, et al. 2011) and/or have peer support (Treloar et al. 2014, Grebely et al. 2007, Crawford and Bath 2013, Norman et al. 2008) are more likely to be assessed for HCV treatment and are best equipped to undertake it.

The research outlined above demonstrates that significant stigmatisation and lack of social support exist in various forms and from several sources, and foster feelings of isolation within HCV-infected IDUs, thereby decreasing their intention to engage with health care settings, especially in seeking HCV treatment. A significant factor in eliminating stigma, highlight the importance of social support and so increasing the uptake of treatment is the identification of the sources and experience of both stigma and lack of support for IDUs.

2.3.2.2 Housing status

Unstable housing has been identified as one of the main factors that deter IDUs from undertaking HCV treatment (Mehta et al. 2008, Harris and Rhodes 2013, Cooper 2008). IDUs are more likely to experience unstable housing than members of the non-IDU population and this fundamental disadvantage reduces their ability to undergo HCV treatment (Harris and Rhodes 2013). A strong association exists between unstable housing and low HCV treatment uptake (Strathdee et al. 2005, Charlebois et al. 2012, Grebely, Bryant, et al. 2011).

A US study found that homeless IDUs reported drug treatment was ineffective in promoting abstinence because of their lack of stable accommodation after treatment (Freund and Hawkinsb 2004). Homeless IDUs are more likely to suffer from physical and mental health problems (Fischer et al. 2006, Gundlapalli et al. 2015), be involved in illegal activities for the purpose of income generation (Fischer et al. 2006), share needles

(Jarlais, Braine, and Friedmann 2007), and consume alcohol in a risky manner than those who are stably housed (Gundlapalli et al. 2015 , Charlebois et al. 2012, Cooper and Mills 2006, Stein et al. 2002). Lack of a permanent address and telephone number make it difficult to make and keep doctors' appointments, register with health care services, safely store medications, cope with treatment side effects and meet basic needs during treatment (Harris and Rhodes 2013).

A study assessing the factors affecting care-provider decisions to initiate HCV treatment for HIV/HCV co-infected homeless and marginally housed people found that the most common reasons for not offering HCV treatment were likelihood of poor medication adherence, depression, being a current IDU, and lack of patient interest in treatment (Thompsona et al. 2005). However, many clinicians were unwilling to recommend pegylated interferon and ribavirin for homeless HCV-positive people due to the drugs' side effects (Gundlapalli et al. 2015). An Australian study of the uptake of HCV treatment among clients of an opiate substitution program reported that a homelessness and unstable housing as barriers to engage with HCV treatment (Treloar, Newland, et al. 2010). Hence, homeless HCV sufferers are less likely to be treated than stably housed patients (Gundlapalli et al. 2015). Likewise, Charlebois et al. (2012) reported housing status was significantly associated with commencement of treatment: 87.5% of those who underwent treatment had stable housing compared to 62.8% of those who did not. This is confirmed by previous studies showing that provision of housing and housing improvement result in better health behaviours and outcomes (Fitzpatrick-Lewis et al. 2011, Thomson et al. 2009). Beyond, the characteristics of treatment, stigma, lack of social support and homelessness status, there is another significant factor that influence whether IDUs to accept or refuse HCV treatment. This factor, peer experience, which is discussed in the following sub section.

2.3.2.3 Peer experience

Circulation of positive information among peers can encourage HCV-infected IDUs to undergo treatment, but the reverse is also true. For example, a study showed that peer-delivered information about adverse effects, including depression, mood swings, weight loss, hair loss and experiences similar to heroin withdrawal, aroused fear among HCV-positive IDUs and made them reluctant to engage with HCV treatment (Swan et al. 2010). However, the same study showed that observing peers and family members who completed HCV treatment (even with unpleasant side effects) and obtained successful outcomes motivated IDUs to undergo treatment (Swan et al. 2010). Similarly, other research shows that many HCV-positive people are discouraged from undertaking treatment due to hearing negative comments about HCV medications (Munoz-Plaza et al. 2008, Treloar and Holt 2008).

Participants in one study reported that their attitudes about undertaking HCV treatment were based on either seeing peers going through treatment or hearing positive stories about treatment (Bova, Ogawa, and Sullivan-Bolyai 2010). An Australian study found that HCV-positive IDUs who engaged with HCV treatment were motivated by seeing friends become well and hearing positive stories of treatment (Treloar et al. 2014). A national study reported that participants obtained benefits from hearing about peers' experiences in support groups or through knowing peers who completed treatment, in particular for coping with treatment side effects (Hopwood, Treloar, and Redsull 2006). Previous studies have highlighted that oral messages spread among HCV-positive IDUs can be effective in promoting HCV treatment (Swan et al. 2010, Carriera, Laplanteb, and Bruneau 2005, Munoz-Plaza et al. 2008, Treloar, Byrona, et al. 2010). Along with peer experience, there are several personal factors that have also been shown to motivate treatment uptake. The following sub section describes some personal motivating factors associated with HCV treatment intention.

2.3.2.4 Encouraging factors

The literature on IDUs' experience of motivating factors for uptake of HCV treatment is sparse. However, there are findings from a few studies that highlight some facilitating factors, but not specifically among HCV-infected IDUs. For example, a US qualitative study conducted among HCV/HIV co-infected individuals where 95% of participants had a history of substance abuse reported four facilitators for HCV treatment uptake: experience in disease management; strong patient–provider relationships; gaining sober time; having a 'just get it done' attitude; and facing treatment head-on (Bova, Ogawa, and Sullivan-Bolyai 2010). Taking responsibility for children, obtaining information from health care professionals, the influence of trusted health professionals and reading material were shown to increase IDUs' interest in taking up HCV treatment in Dublin, Ireland (Swan et al. 2010). In particular, information from health care professionals can change perceptions of treatments and side effects, and relieve fears (Swan et al. 2010). The availability of HCV care and readiness to stop using drugs have also been associated with heightened uptake of HCV treatment among IDUs (Strathdee et al. 2005). A recent US study identified five motivating factors for initiation and completion of HCV treatment: possible future health problems due to HCV; patients' willpower; the stage of liver disease; availability of emotional support; and doctors' advice (Fusfeld et al. 2013).

Becoming symptomatic, having physical health problems, a diagnosis of liver damage (Swan et al. 2010, Strathdee et al. 2005, Grebely et al. 2008) and the desire to promote one's own health (Lally et al. 2008) and improve life overall (Swan et al. 2010) were identified as motivators by HCV-infected IDUs for receiving HCV treatment. Australian studies conducted in an opioid substitution therapy setting reported the desire to live longer and carry on with family responsibilities (Treloar et al. 2014) and encouragement from a trusted health professional (Treloar et al. 2014, Treloar, Newland, et al. 2010, Grebely, Bryant, et al. 2011) motivated IDUs to undergo HCV treatment. Another qualitative study of Australian prisoners who took up treatment in prison found the most common motivating factors were: protection of family,

partners, children and grandchildren; health and wellbeing; career; drug use cessation; and life-changing events (Yap et al. 2014). Swan et al. (2010) found that individuals who undertook HCV treatment or were interested in undertaking it in the future were usually motivated by emotional bonds with partners and children and responsibilities for family, and a desire to move on from injecting drugs (Mehta et al. 2008). In addition to the treatment facilitators earlier discussed, it is important to understand what other characteristics can influence treatment intention. Some of other characteristics are discussed briefly in the sub section below.

2.3.2.5 Additional factors

Although there is a lack of evidence on the associations between socio-demographic and drug-history characteristics, awareness of HCV genotype and HCV treatments and intention to take up treatment, several researchers have documented the relationship between specific demographics and intention to uptake treatment. For HCV genotype, a few have studies found that IDUs with non-1 HCV genotypes had higher intention to undertake HCV treatment (Alavi et al. 2015, Alavi et al. 2013). Other studies from the USA also reported that patients were less likely to undergo HCV treatment if they had genotype 1 (Kramer et al. 2011, Kanwal et al. 2007).

IDUs with better knowledge of HCV treatment were more likely to report higher intention to have HCV treatment (Treloar et al. 2012). In other research, injection of illicit drugs and alcohol intake influenced the uptake of HCV treatment more than clinical factors (Gidding et al. 2011) and were significantly associated with deferral of HCV treatment (Grebely et al. 2009, Grebely, Bryant, et al. 2011, Gidding et al. 2011, Kramer et al. 2011, Grebely et al. 2008). Similarly, a study by Butt et al. reported that intake of both alcohol and illicit drugs were predictive of non-treatment for HCV (Butt et al. 2007). Heroin use has been independently associated with decreased uptake of HCV treatment (Grebely et al. 2008, Kramer et al. 2011) and methamphetamine use marginally associated with higher intention to undertake HCV treatment (Alavi et al. 2015).

A Canadian survey of IDUs revealed that male IDUs showed greater intention to undertake HCV treatment compared to their female counterparts (Grebely et al. 2009). However, a US study reported that males, both IDUs and non-IDUs, were less likely to undergo HCV treatment(Kramer et al. 2011). In an Australian study, there was no significant difference in the intention to undertake HCV treatment between genders, with 47% of female IDUs expressing intention to take up treatment compared to 53% of male IDUs (Alavi et al. 2015).

The importance of ethnicity on treatment intention is also discussed in the literature, indicating a relationship between ethnicity and intention to take up treatment. For instance, Indigenous Australians struggle to undertake HCV treatment compared to non-Indigenous people (Alavi et al. 2015, Grebely et al. 2009, Alavi et al. 2014). US studies have also found African-American were less likely to undergo HCV treatment compared to Caucasians (Butt et al. 2007, Kramer et al. 2011). Other demographic characteristics reported to be associated with HCV treatment intention include older age – 35–45 years (Alavi et al. 2015) and ≥ 65 years old (Kramer et al. 2011) – and living with a spouse or other relatives/friends (Alavi et al. 2015, Alavi et al. 2013).

2.4 Summary of the literature

The hepatitis C virus was cloned and named in 1989. Although up to 25% of acute cases of HCV infection resolve spontaneously and infection is often asymptomatic for many years, the majority of acute infections, 75%, progress to chronic infection and can cause severe and even life-threatening complications in the long term. Development of liver disease is often measured over decades and is characterised by hepatocellular damage, inflammation and fibrosis. Worsening hepatic fibrosis may ultimately lead to cirrhosis, decompensated liver disease, HCC and end-stage liver disease, which requires liver transplantation. HCV is transmitted through blood-to-blood contact and sharing drug-injecting equipment is the dominant mode of transmission. Other forms of transmission (blood transfusions from infected

donors, tattooing and body piercing, sexual intercourse and vertical transmission during childbirth) are less common and pose smaller risks.

HCV prevalence in Australia is estimated to decrease by 2030, but if treatment uptake remains low, the numbers of HCV-associated cases of cirrhosis and HCC will increase, leading to substantial health care costs. Despite the widespread availability of HCV treatment in Australia, uptake remains low, particularly among IDUs – the population group with the greatest future disease burden. The literature shows that several factors influence the intention of HCV-positive IDUs to undertake treatment: treatment side effects; low treatment efficacy; lengthy treatment duration; lack of support; peers' experiences of treatment; stigma associated with IDU and HCV; unstable housing; and the desire to protect family, increase quality of life and maintain a career. The next chapter describes the research methodology and study design to address the research objectives.

Chapter 3: Methods

This chapter describes the methodology used in this study, this study design and site, the procedures used for the data collection, the data cleaning, analysis and storage. Methods employed to ensure reliability of the data are also presented. Furthermore, this chapter describes the ethical considerations related to the study.

3.1 Mixed-methods research

A mixed-methods approach enables the researcher to capture the details of a situation by providing rich and meaningful data that reflects participants' views at the individual level (Bryman 2015). This method consists of a two-phase design in which the qualitative research is conducted first and informs the following quantitative research. This design is particularly helpful when the variables of interest are unidentified (Creswell and Clark 2007).

The central principle of mixed-methods research is combining quantitative and qualitative approaches, rather than using each method in isolation (Creswell and Clark 2007). Creswell (2003) classified mixed-methods research into six groups: sequential explanatory; sequential exploratory; sequential transformative; concurrent triangulation; concurrent nested; and concurrent transformative (Creswell 2003). The sequential explanatory category refers to the researcher collecting quantitative data then qualitative data, while in the sequential exploratory category the qualitative data is collected first (Creswell 2003). Combining quantitative and qualitative data in a single study allows the researcher to gain better understanding of complex phenomena (Creswell and Clark 2007). Johnson and Onwuegbuzie (2004) asserted that "*researchers should collect multiple data using different strategies, approaches, and methods in such a way that the resulting mixture or combination is likely to result in complementary strengths and non-overlapping weakness*" (Johnson and Onwuegbuzie 2004,18).

Although the two types of data can be combined effectively, there are considerable theoretical differences between qualitative and quantitative research paradigms. Quantitative researchers have a positivist or empiricist ideology, which highlights observable phenomena. Bryman (1984) stated that *"the paraphernalia of positivism are characterized typically in the methodological literature as exhibiting a preoccupation with operational definitions, objectivity, replicability, causality, and the like"*(Bryman 1984,77). Through forms of random sampling, quantitative methods enable the researcher to generalise from the data collected from the sample to the entire population. Quantitative research typically involves a greater number of participants than qualitative research. It focuses on describing the concepts at hand and the relationships between them. *"Quantitative researchers seek explanations and predictions that will generate to other persons and places. The intent is to establish, confirm, or validate relationships and to develop generalizations that contribute to theory"* (Leedy and Ormrod 2005, 102).

In contrast, qualitative researchers *"argue for the superiority of constructivism, idealism, relativism, humanism, hermeneutics, and, sometimes, postmodernism"*(Johnson and Onwuegbuzie 2004,14). Qualitative research attempts to achieve understanding of the meanings that people depict from the conditions and actions in which they are involved (Creswell 2009). This is useful method when there is a need to explore a phenomenon involving people whose voices have been inaudible and should be heard, as well as when a problematic condition needs to be explored in more detail (Creswell 2009). Having direct contact with an individual experiencing the phenomenon in their natural surroundings, where they can tell their hidden stories, plays a significant role in achieving the detailed understanding possible with qualitative research (Creswell 2007).

Qualitative data collection can be sensitive and informative, and its analysis can create patterns or themes which reflect participants' opinions and the researcher's reflexivity (Creswell 2007). However, qualitative research approaches are limited to studying small numbers of individuals in depth, which means the results cannot be generalised or used for quantitative

predictions (Sim and Wright 2000). Furthermore, qualitative research is time-consuming and more labour-intensive than quantitative research (Sim and Wright 2000).

3.2 Research design

Given the nature of the phenomena of interest in this study, a sequential exploratory mixed-methods research study (QUAL → QUAN) was designed to develop a better understanding of the context of treatment intentions of IDUs in metropolitan Perth, Western Australia. The study involved collection and analysis of qualitative data in the form of personal interviews and focus groups, followed by quantitative data collected using a questionnaire-based survey. In this study, the qualitative component was dominant. It was conducted first to obtain richly detailed descriptions of participants' opinions regarding the factors that influenced their intentions to undertake treatment. The qualitative phase informed the quantitative phase and was designed to examine the associations between the HCV treatment intention and socio-demographic characteristics, drug-history characteristics and health-care-seeking characteristics, support, treatment factors and stigma among HCV-infected IDUs.

There were three benefits to this sequential mixed-methods process (Greene, Caracelli, and Graham 1989). Firstly, it allowed the researcher to create a novel data collection instrument for assessment of the intentions of IDUs in regards to uptake of HCV treatment. Secondly, using this design enabled the researcher to quantitatively study specific themes that arose from the qualitative data and better determine associations between the dependent and independent variables. Third, although the design of this study emphasised qualitative aspects, it included a quantitative component to add understanding about predictors of intention to undertake HCV treatment.

3.3 Study population

The target population comprised male and female HCV-infected IDUs aged 18 years and older living in the Perth metropolitan area.

3.4 Study Site

Participants were recruited through organisations that provide NSP services to IDUs. The West Australian Substance Users Association (WASUA) and WA AIDS Council (WAAC) are Perth's primary NSP service providers that offer needle and syringe exchange program (NESP) and provides outreach van services. HepatitisWA is a non-profit community organisation which provide free services to the community and is a secondary NSP service provider. It provides care and support for individuals affected by viral hepatitis and works to increase community awareness of hepatitis.

3.5 Study duration

Data collection occurred over 26 months from September 2012 to November 2014. Semi-structured interviews were conducted between September 2012 and March 2013, focus groups from June 2013 to August 2013, and quantitative data collection from December 2013 until November 2014.

3.6 Qualitative study

As noted earlier, the qualitative phase of this study was designed to explore factors influencing intentions of HCV-infected IDUs with respect to HCV treatment through collection and analysis of rich descriptions of the perceptions of IDUs who had and had not experienced treatment. Data was collected using semi-structured interviews and focus groups. The focus groups were used to follow up the themes identified from the semi-structured interviews and to explore HCV-infected IDUs' perceptions about triple treatment. The information obtained in the qualitative phase supported

development of the survey questionnaire for the quantitative phase of the study.

3.6.1 Sampling

The study adopted a non-probability sampling approach using purposive sampling and 'snowball sampling'. In purposive sampling, participants are chosen based on their knowledge of phenomena and their characteristics (Bryman 2015). Participants in this study were purposively selected using certain criteria to ensure the sample covered an appropriate group of IDUs who had experienced HCV treatment (the treatment group) and who had not (the non-treatment group and focus groups). Purposive sampling was utilised to recruit the desired number of participants for each group. In snowball sampling, potential participants are nominated or suggested by existing participants. The snowball technique is the most common form of purposive sampling and is useful when participants are not easily accessible (Suri 2011), enabling the researcher to approach potential participants who were familiar about a given research topic.

3.6. 2 Data collection

3.6.2.1 Semi-structured interviews

The first phase of data collection for this research project involved semi-structured interviews. A semi-structured interview format provided a uniform set of topics to discuss with each participant, as well as the flexibility to probe and draw rich descriptive statements from the participants, explore the phrasing of questions, and identify new ways of understanding the phenomenon under study (Patton 2002). Semi-structured interviews were used to explore the factors influencing the intentions of HCV-infected IDUs in regards to treatment uptake, experiences of HCV-related stigma and beliefs about HCV treatment. The researcher developed an interview guide through a series of informal discussions with the primary supervisor and reviews of past research in the field. The interview questions began with socio-demographic and drug-history questions (see Appendix 1) which were

adopted from a 1995 study (Loxley, Carruthers, and Bevan 1995), and then the questions asked in the interviews with the treatment group (see Appendix 2) were slightly different from those asked of the non-treatment group (see Appendix 3). This was necessary to identify the perceptions of IDUs who had experienced treatment regarding the factors that influenced their commencement and discontinuation of treatment, as well as the perceptions of IDUs who had not experienced treatment regarding the factors that stopped them from undergoing treatment. Interviews took approximately 30–45 minutes and this timing meets the recommended guidelines for this method (Gill et al. 2008).

3.6.2.2 Focus groups

Focus groups were the second data collection tool. They allowed the researcher to capture rich and detailed descriptions of HCV-infected IDUs with no treatment experience regarding triple therapy as requiring further explanation. The researcher developed the focus group questions (see Appendix 4) through consultations with HCV experts (primary supervisor and HCV nurse consultant at WASUA). The interview guide consisted of 5 open-ended questions. Demographic and drug-history questions were similar to those of the semi-structured interviews (see Appendix 1). The initial focus group question was an 'icebreaker' to get the participants warmed up and comfortable with the group, and to build confidence and willingness to participate. More sensitive questions were asked later, once trust had been established with the participants. Focus group discussions took 60–80 minutes.

3.6.3 Recruitment

The researcher gave verbal presentations about the study to the managers of WASUA and HepatitisWA, after which they consented to support the research. Participants were recruited from these settings using posters (see Appendices 5, 6 and 7) and information sheets (see Appendices 8 and 9) which placed where IDUs could see them during routine visits in the selected settings. Inclusion and exclusion criteria are documented in Table 3.1. IDUs

who self-reported as having received an HCV diagnosis from a health care professional (confirmatory tests were not carried out) and were interested were asked to contact the researcher directly. Potential participants contacted the researcher by telephone to ask further questions and arrange an appointment for the interview. Interviews occurred in a suitable room on the premises of the organisations involved in recruitment, or at local cafes, on dates and times convenient to the participants. All focus group discussions took place at WASUA.

Information and consent forms (see Appendix 10) were presented to participants prior to the semi-structured interviews. After the consent form had been signed, the researcher asked permission to digitally record the interview. Focus groups were held in spacious rooms that offered comfort, privacy and good ventilation and lighting. Light refreshments were provided at all sessions before the start of the discussion. These discussions were facilitated by the researcher. The participants and the researcher sat in a circle to create a friendly and non-threatening environment and to allow all participants to see and hear each other clearly. Each focus group discussion commenced with a welcome followed by a brief description of the intentions and procedures for the discussion, including expectations, discussion, duration and ethical considerations. Participants were provided with identification numbers to protect their identities.

3.6.4 Sample Size

The sample size for semi- structured interviews is suggested to be around 20-25, but a topic with two groups should be doubled up (Trotter 2012) and for focus groups should range from 5–10 (Onwuegbuzie et al. 2009). Eventually, the researcher interviewed 46 IDUs – 21 with treatment experience (treatment group) and 25 without (non-treatment group). Five focus groups were conducted, with five participants in each. The researcher expected that these numbers would provide rich data. All participants were reimbursed for their time and effort with an AU$35 supermarket voucher. Providing reimbursement for people who use illicit drugs and who give up their time

and their expertise to contribute in research is an acceptable method within the research framework (UN 2004). Table 3.1 summarises the inclusion and exclusion criteria for the qualitative phase. The main reason for choosing only genotype 1 for focus groups was because triple therapy was only used for genotype 1.

Table 3.1 Inclusion and exclusion criteria for the qualitative phase

	Semi-structured interviews		
	Treatment-group	Non-treatment-group	Focus group
Inclusion criteria	1. Current IDU who is actively injecting 2. Currently being treated or have recently been treated for chronic HCV (within the past 2 years) 3. Living in Perth 4. 18 years or older 5. Fluent in and could read and write in English	1. Current IDU who is actively injecting 2. Received an HCV diagnosis more than 6 months earlier by a health care professional 3. Did not take up HCV treatment 4. Living in Perth 5.18 years or older 6. Fluent in and could read and write in English	1. Current IDU who is actively injecting 2. Received an HCV diagnosis Genotype 1 more than 6 months earlier by health care professional 3. Aware of new treatment as triple therapy (pegylated interferon and ribavirin in combination with either boceprevir and telaprevir) for chronic HCV 4. Did not take up HCV treatment 5. Living in Perth 5. 18 years or older 7. Fluent in and could read and write in English
Exclusion criteria	1. Past IDUs 2. Did not read or speak English	1. Past IDUs 2. Did not read or speak English	1. Past IDUs 2. Did not read or speak English

3.6.5 Validity and reliability -qualitative study

In qualitative research, the validity of interview data depends on how the researcher designs the interview questions and collects the data. In this study, interviews were digitally recorded then transcribed by the researcher, increasing the researcher's familiarity with the data. NVivo analysis software (QSR, Melbourne) was used to prevent coding and transcription errors (Gerard et al. 2009). In order to maximise the validity of the data collected from the study participants, the researcher pilot-tested the semi-structured interview schedule with 10 IDUs and the manager at WASUA in September

2012. The focus group interview guide was pretested with one group of four IDUs in June 2013. They were reimbursed with $30 supermarket vouchers. No pilot-test participants had difficulty in understanding the questions and it was recommended that there was no need for changing or editing the final version of the interview guide.

In terms of the reliability of data collected from interviews, it has been suggested that IDUs are less likely to be reliable in their responses than other populations because of intoxication *"or because of a need to dissemble in order to facilitate a stigmatized and illegal lifestyle in a largely hostile environment"* (Ross et al. 1995, 2). However, many researchers disagree with this view. It is indicated that interview data from drug users is reliable and their responses show (unexpected) veracity (Dowling-Guyer et al. 1994, Napper et al. 2010, Hagan et al. 2006a). Likewise, other scholars have suggested that unreliability is principally *"associated with poorly worded questions and respondent characteristics"* (Needle et al. 1995, 242). These scholars argued that if drug users are well informed about the purpose of the study, the interview questions and the reimbursement for their research time, their responses can be reliable.

3.6.6 Data analysis

The qualitative data collected from the semi-structured interviews and focus groups were managed using ©QSR NVivo 10 software in order to organise and prepare the qualitative data for analysis. Sequential thematic analysis of interviews and focus groups data took place separately, which allowed the researcher to compare emerging codes from both individual interview data and focus groups data. This analysis was used to clarify relevant data and classified into themes, using several steps which are described below. The steps involved in the analysis were similar for both sets of data.

1. Familiarisation prior to commencing any coding of data. The researcher transcribed each interview and focus group in a sequential order to become more familiar with the data. Reading and re-reading of transcriptions was

performed to identify meaningful ideas and create an initial list relating to treatment intention of HCV-positive IDUs about the uptake of HCV treatment.

2. Creating initial codes by coding items through the whole data set and then gathering data relevant to each code. Codes refer to "*the most basic segment, or element, of the raw data or information that can be assessed in a meaningful way regarding the phenomenon*" (Boyatzis 1998 ,88). Transcripts were re-read several times to achieve a general sense of the data. Themes and patterns were then identified and documented across questions and participants (Braun and Clarke 2006). These first two steps aimed to explore the main themes emerging from the interviews and discussions, and to commence organising them.

3. After identifying an extensive list of the various codes from the interviews and discussions, the researcher searched for themes by gathering these codes into potential themes and collating all relevant data to each potential theme. Hence, ideas were categorized into themes and entered into the NVivo software.

4. The researcher checked that the themes applied worked in relation to the coded extracts. Also, the researcher regularly referred to the research questions (see Chapter 1) in order to ensure that the analysis remained focused. In the following qualitative results chapter, these themes are illustrated with quotes (stripped of identifying information). Findings were organised in relation to the main domain of data collection: the factors influencing the intention of HCV-infected IDUs to undertake treatment in Perth.

5. The common themes were used to design and develop the survey questionnaire in phase two.

3.7 Quantitative study

A cross-sectional survey was conducted to measure the prevalence rate of intention of HCV-infected IDUs to undertake HCV treatment in the Perth metropolitan area and to examine the associations between intention to undertake HCV treatment and socio-demographic characteristics, drug-history characteristics and health-care-seeking characteristics, treatment side effects, treatment efficacy, treatment duration and stigma. The quantitative phase was designed to identify the predictors of intention to undertake HCV treatment. This phase was guided by the themes arising from the qualitative interviews. (As mentioned previously, the qualitative interviews provided data which helped the researcher to construct an instrument to assess the factors influencing the intentions of IDUs towards HCV treatment uptake.) Activities in this phase of the research consisted of developing and conducting a questionnaire-based survey.

3.7.1 Sampling

The study planned to recruit 336 IDUs from the Perth community setting, using the formula given below. Existing data on intention to undertake HCV treatment was used to determine the sample size. An exploratory Australian study found that almost 70% of participants intended to have HCV treatment (Doab, Treloar, and Dore 2005), while another found that 67% of HCV-positive IDUs intended to have HCV treatment (Alavi et al. 2015). This study used the higher proportion of 70%, that is, it was assumed that 70% of the sample would intend to undertake treatment and 30% would not intend to undertake treatment. By an acceptable sampling error of 5% at a 95% level of confidence (Vaus 1991) and employing the following formula (Kirkwood 2000), confirmed by a statistician at Curtin University (Y.Zhao, personal communication Jaunary10, 2013), the sample size was calculated as shown in Figure 3.1.

Figure 3.1 Sample size formula

$$\frac{n\,(1\text{-}n)}{e^2} = \frac{70(100\text{-}70)}{2.5^2} = 336$$

Where: n is the proportion

e= the required size of standard error

Sampling error is two standard errors.

The eligibility criteria for study participants were: 18 or more years of age; current IDUs who were actively injecting drugs; self-reported as having received an HCV diagnosis by a health care professional more than 6 months (confirmatory tests were not carried out) prior to interview; no experience of HCV treatment; living in the Perth metropolitan area; able to read and speak English; and able to provide informed consent.

3.7.2 Data collection

The survey questionnaire was used to collect information from the targeted 336 participants on demographic characteristics, drug-use history, health-care- seeking characteristics, aspects of treatment, stigma, support and their intention to undertake treatment (see Appendix 11). A questionnaire was attached with a brief description of HCV standard combination treatment and triple therapy in order to give participants basic knowledge of HCV treatment before commencing the survey.

The socio-demographic and drug-history sections were adopted from a national study conducted in Australia in 1995 (Loxley, Carruthers, and Bevan 1995). Questions about health-care-seeking characteristics were added after receiving comments from participants in the pilot study (see Section 3.7.3); these questions were also adopted from the previous Australian study (McNally, Sievert, and Pitts 2006). Questions about the characteristics of treatment were developed by the researcher through consultations with key experts in the area of HCV. Questions relating to attitudes around social

support were adopted from validated surveys of perceived social support conducted in 1988 by Zimet, Dahlem, Zimet and Farley (Zimet et al. 1988). Questions about stigma were adopted from validated surveys, including the HIV stigma scale developed in the late 1990s (Berger, Ferrans, and Lashley 2001, Sowell et al. 1997). Questions resulting in an assessment of intention to undertake HCV treatment were informed by a review of a previous study (Treloar et al. 2012).

The questionnaire consisted of five sections. The first section (socio-demographics and drug history) contained questions about the participant's age, ethnicity, gender, level of education, employment and marital status, accommodation, living status, nationality, sources of income, drugs used in the past six months, frequency of injection in the last month, drug preference, duration of injection and drinking of alcohol over the last year.

The second section on health-care-seeking characteristics asked the participants the length of time since their HCV diagnosis, knowledge of their own HCV genotype, awareness of HCV treatment before commencing the survey and whether they had discussed their liver health with a GP.

The third section on treatment characteristics examined the participants' perceptions of treatment effectiveness, duration and side effects, and whether they had support if they chose to undertake HCV treatment.

Section four assessed participants' concern about stigma. In the fifth section, participants were asked whether they intended to undertake treatment, on four levels: in the next 12 months; in the next 1–2 years; in the next 2–5 years; not for at least another 5 years. Each questionnaire took approximately 15–20 minutes to complete.

Variables

Socio-demographic characteristics, drug-history characteristics, health-care-seeking characteristics and characteristics of treatment, support and stigma were the independent variables. Intention to uptake HCV treatment was the only dependent variable in this study.

3.7.3 Recruitment

Between December 2013 and November 2014, HCV-infected IDUs were recruited from multiple venues in the Perth metropolitan area including: WASUA; HepatitisWA; and the WAAC NSEP fixed site; and WAAC NSEP mobile van services, which operate in eight locations in the metropolitan area (Rockingham, Mirrabooka, Joondalup, Midland, Forrestfield, Armadale, Fremantle and Gosnells). NESP outreach workers introduced the researcher to NSEP clients in order to give them information about the study. Recruitment was undertaken through the distribution of study posters (see Appendix 12) and information sheets (see Appendix 13) at the venues described above, and potential participants contacted the researcher directly by phone for additional information about the study, to determine eligibility and to arrange a time to complete the questionnaire. The researcher gave each potential participant an informed consent form (see Appendix 10); once signed, the participant was given a paper questionnaire to complete in a private room at the recruitment site or in the WAAC mobile van, or next to the mobile van wherever they felt comfortable and safe reading and responding to the questions. After completing the questionnaire, each participant was asked to wait for five minutes to ensure that all questions had been answered. A supermarket voucher valued at AU $20 was given to participants who completed the questionnaire. Recruitment continued until the target sample size was obtained (in November 2014).

3.7.4 Validity and reliability quantitative study

The validity of the questionnaire, defined as "*the degree to which the content of a test is congruent with testing purposes*" (Sireci and Faulkner-Bond 2014 101), was established in pilot testing. A pilot test is a small case study designed to test the validity of a questionnaire (Saunders, Thornhill, and Lewis 2009), conducted to improve procedures before commencing a larger study. Twenty draft questionnaires were distributed to IDUs at WASUA and Hepatitis WA and the manager at WASUA to determine the likelihood of participants being unable to understand the questions, and to ensure salience.

Prior to this, a brief description of the purpose of the study and information about HCV treatment were provided in plain and clear language. The pilot test participants were reimbursed with an AU$20 supermarket voucher. The pilot study enabled the survey questionnaire to be tested in terms of *"length, flow, and salience, ease of administration and response and acceptability to respondents"* (Burns et al. 2008 , 248) and to ensure its reliability. Participants were asked to provide feedback on the format and clarity of questions at the conclusion of the survey. The feedback from these participants led to the addition of a health-care-seeking characteristics section to the questionnaire. The pilot-study participants made the following comments:

- Giving a brief description about HCV treatment at the beginning of the questionnaire was a good idea, but it would be better to find out how many IDUs were aware of HCV treatment and know about their HCV genotype.

- The content of the questionnaire is relevant to the issues of current HCV treatment, but knowing about how long IDUs have been diagnosed with HCV would be helpful.

- Because of the stigma attached to HCV, it would be good to ask whether IDUs have discussed their liver health status with GPs.

- All questions were clear and easy to understand. The questionnaire was not boring or time-consuming.

The results of the pilot study illustrated that the questionnaire was clear and acceptable to the target population, and revealed the time needed for completion.

The reliability of the questionnaire was also assessed for internal consistency. Internal consistency correlates the answers to each question in the questionnaire with answers to other questions in the same questionnaire (Saunders, 2003). The responses to treatment effectiveness, treatment duration, treatment side effects, stigma, support and intention were statistically tested for internal consistency. Cronbach's alpha for five domains were produced and values ranged from 0.71 to 0.87. Therefore, Cronbach's

alpha surpassed the acceptable limit of 0.6, representing that the items within each domain were consistent (see Table 3.2)

Table 3.2 Instrument reliability

Variables	Number of items	Cronbach's alpha
Treatment effectiveness	2	0.878
Treatment duration	2	0.926
Treatment side effects	4	0.975
Stigma	3	0.990
Support	2	0.978
Treatment intention	3	0.716

3.7.5 Coding quantitative data

Intention to undertake HCV treatment, characteristics of the treatment, stigma and support were measured on a 5-point Likert scale: "strongly disagree"; "disagree"; "neutral"; "agree"; and "strongly agree". Analysis of Likert scale involves estimating the median score of all items to combine the responses from the items, thus generating a new variable (Sullivan and Artino 2013). This method was also confirmed by a statistician at Curtin University (Y.Zhao, personal communication November 10, 2015). Answers were transformed into dichotomous variables: "disagree" (grouping together the first three responses) and "agree" (the last two answers); the response "neutral" was included in the first group as it indicated that the subject did not necessarily agree (Alavi et al. 2015, Treloar et al. 2012). This scoring system was also adopted for the following variables characteristics of treatment, stigma and support.

Age in years was converted into a binary variable using the median score as the cut off (Tolmie, Muijs, and McAteer 2011, Singh 2007): < 40 years old and $\geq$ 40.

Ethnicity was re-categorised into "Aboriginal" and "non-Aboriginal", as they were the only two responses from participants.

The accommodation variable was re-categorised into "non-homeless" (living in either own house/flat or parent's house, rented house/flat, shared house) and "homeless".

Education was re-categorised into "Year 11 or less" and "Year 12 or University/TAFE"; employment was re-categorised into "employed" and "unemployed"; sources of income was re-categorised into "government benefits" and "employment" (fulltime, part-time, casual).

Marital status was re-categorised into "single" and "married or lived with sexual partner". Living was re-categorised into "alone" and "sharing with others or partners".

Drug preference and drugs used in the last six months were re-categorised into "heroin" and "methamphetamine", because all participants selected heroin or methamphetamine as their preferred drug and the drug that they had injected in the last six months.

All participants reported injecting drugs for "8–10" years or "more than 11 years", therefore the duration of injecting was re-categorised accordingly.

Participants reported injecting drugs either "once a day" or "more than once a day", so frequency of injection was re-categorised accordingly.

Time since HCV diagnosis was re-categorised into "5-10 years" and "more than 10 years", as these were the only two responses from participants.

3.7.6 Data analysis

The following data analysis was confirmed by a statistician at Curtin University (Y.Zhao, personal communication November 10, 2015). Data from the questionnaires was coded and entered into SPSS (version 22; IBM, Chicago, USA) and cleaned prior to data analysis. Descriptive analysis was conducted to describe the background characteristics on all variables (predictors and outcomes) in the study and percentage distributions for all variables were calculated to describe the full sample of participants. The Chi-Square test and odds ratio were used to test for the statistical significance of

any observed association between the independent variables and the dependent variable. In this study, the association between intention to take up HCV treatment and a set of demographic, drug history health-care-seeking characteristics, characteristics of treatment, support and stigma were investigated.

Then multivariate analysis was conducted by entering all variables associated with intention to undertake HCV treatment at p was equal to or less than 0.1 in the univariate analysis were entered into a multivariate logistic regression model, using odd ratios to examine the strength and direction of the observed associations. In the multivariate analysis p<0.05 was considered for the retention of variables. Logistic regression models were used to determine the predictors of the intention to undertake treatment adjusting for potential confounding. The probability level of 95% was applied in all statistical tests. The multivariate analysis consisted of two parts in separate models according to the type of predictors variables. The first part of the multivariate analysis focused on the full sample of IDUs and examined the socio-demographic, drug-history and health-care-seeking characteristics associated with intention to undertake HCV treatment. A separate logistic regression analysis was conducted on the full sample of IDUs and examined the characteristics of treatment, stigma and support associated with intention to undertake HCV treatment.

3.8 Ethics

Ethical approval for the study was granted by the Curtin University and Fremantle Hospital Human Research Ethics Committee (Reference Number: 12/198 and HR 77/2012) (see Appendix 9). As noted previously, to ensure that participants were able to give informed consent, the objectives, procedures and implications of the study were explained clearly to interested potential participants. IDUs were allowed to reach a rational, autonomous decision and were not coerced to join the study. An information sheet and consent form were offered, and participants were informed that they were free to withdraw at any time.

All data were de-identified and referred to only by a subject number that could not be linked to participants. The interview recordings were transcribed as soon as possible after interviews and transcriptions of the data were de-identified, with participants free to use pseudonyms. The transcripts were stored separately from the signed statements of informed consent to ensure data could not be linked to individual participants by name.

No information about individuals was accessible to other study participants or health workers. All paper records were kept in a secure filing cabinet in the researcher's office in the Health Sciences Graduate Research Hub, Curtin University (Bentley, WA). The Hub has the same level of security as the rest of the University, including being accessible only with a valid student identification/building access card, password-protected computers, and lockable filing cabinets. All electronic data were stored on a computer without identifiers and were only accessible to the researcher. This data will be stored for a minimum of seven years following publication, after which it can be destroyed.

Risks to which the participants might be exposed (although minimal) were considered warranted because of the possible benefits of the study in terms of the development of culturally and context specific interventions based on the participants' perspectives. The Australian National Health and Medical Research Council's (2007) ethical guidelines identify particularly vulnerable groups, including persons involved in illicit activities – a category relevant to all of the participants in this study. The high prevalence of HCV among IDUs is a public health issue, rendering this group's inclusion in this project of genuine importance. However, psychological harm was possible because the study involved an examination of individual's attitudes, beliefs and behaviour relating to a sensitive issue, and could have uncovered feelings of guilt due to postponing of antiviral therapies and minimising the likelihood of liver damage. The researcher was very much aware of the study's potential for psychological harm, so ensured that the questions posed and the manner in which they were posed were sensitive in order to limit the possibility of harm.

Chapter 4: Qualitative Results

This chapter presents the findings of the qualitative phase of the research. Individual face-to-face semi-structured interviews were conducted with 46 IDUs who self-disclosed that they were infected with HCV. In order to capture rich and detailed descriptions of IDUs' perceptions regarding triple therapy, focus group discussions were also conducted with HCV-infected IDUs who had not experienced HCV treatment. This section presents the themes drawn from the analysis, illustrated with direct quotations from participants.

4.1 Semi-structured interviews

Face-to-face interviews were conducted with participants both with and without experience of HCV treatment. This section contains the findings of analysis of this data.

4.1.1 Sample characteristics of treatment group

Twenty-one HCV-infected IDUs who had experienced HCV treatment participated in the qualitative phase of this study. Table 4 provides an overview of the treatment group characteristics. In summary, the numbers of male and female participants were almost equal (47.6% male). Participants' age range was 28–56 years with a median of 47. More than half of the participants lived alone. Most participants had completed Year 12 and were employed, deriving their main income from paid employment. Most participants described themselves as non-Indigenous (see Table 4.1).

Most of these participants reported heroin as their drug of choice and the drug that they had injected most frequently in the last six months; only a few nominated methamphetamine. Most participants reported injecting once a day and a minority more than once a day (Table 4.1). A large majority reported injecting drug-use histories of more than 10 years. None of the participants reported drinking alcohol in the past year.

Sixteen of participants (71.4%) had genotype 1 and they had not cleared the virus during treatment. Two participants with genotype 2 reported eradicating the virus through treatment. The remainder, who had genotype 3, had relapsed; one male participant who had discontinued treatment a week before being interviewed did not know whether he had cleared the virus.

4.1.2 Sample characteristics of non-treatment group

The non-treatment group consisted of 25 individuals who were current IDUs living with HCV and with no experience of HCV treatment. As illustrated in Table 4.1, almost half of these participants were men. Participants ranged in age from 30 to 47, with a median age of 38 years. Over half of the participants reported stable accommodation; with most living alone; the remainder either with their parents or family. Over half of the participants had completed Year 12. A small proportion of this group identified as Aboriginal; more than two thirds were single; a large minority was unemployed and derived income from welfare payments.

Most of the non-treatment group nominated methamphetamine as their preferred drug and the most common drug injected in the last six months; the remainder preferred heroin (Table 4.1). Most participants reported injecting once a day. Most reported injecting for more than 10 years. A majority of participants had not consumed alcohol in the past year.

Table 4.1 Characteristics of treatment and non-treatment groups

Socio-demographic and drug characteristics	Treatment Group n=21	Non-treatment n=25
Gender		
Male	11(52.4)	12 (48)
Female	10 (47.6)	13 (52)
Median age (range)	47 (28-56)	38 (30 - 47)
Accommodation		
Homeless	0	10 (40)
Non-homeless	21 (100)	15 (60)
Live with		
Alone	12 (57)	12 (57)

Partner/family	9 (43)	9 (43)
Education		
≤Year 11	2 (9.5)	6 (24)
Year 12	13 (62)	14 (56)
TAFE/Uni	6 (28.6)	5 (20)
Ethnicity		
Aboriginal	1 (4.8)	4 (16)
Non-Aboriginal	20 (95.2)	21 (84)
Marital status		
Single	12 (57)	19 (76)
Married/lived with sexual partner	9 (43)	6 (24)
Employment status and source of income		
Non-Employed and Government benefits	6 (28.6)	10 (40)
Employed and job	15 (71.4)	15 (60)
Preferred drug and drug used in the last 6 months		
Methamphetamine	3 (14.3)	17 (68)
Heroin	18 (85.7)	8 (32)
Frequency of injection		
>Once a day	6(28.6)	10(40)
Once a day	15(71.4)	15(60)
Drug use duration	8-10 years 3 (14.3)	8-10 years 5 (20)
	>10 years 18 (85.7)	>10 years 20 (80)
Consumed alcohol in the past year		
Yes	0	8 (32)
No	21(100)	17 (68)

4.1.3 Themes from treatment and non-treatment groups

The themes associated with the factors that influenced treatment intention emerged through the steps of analysis detailed in Chapter 3. These themes describe the factors that contributed to the perceptions of the treatment group and the factors that contributed to the perceptions of the non-treatment group of HCV treatment. The themes provide a better understanding of the factors that influence the intention of HCV-infected IDUs in regards to treatment uptake. Several themes emerged from the interview data. These themes were: treatment side effects; treatment effectiveness; treatment duration; stigma associated with IDU and HCV; and lack of support. In addition to these

factors, protecting family, increasing quality of life and maintaining careers were concerns also reported by the treatment group, and unstable housing was reported by the non-treatment group, as important factors that influenced their treatment intention in relation to treatment uptake. Both groups reported that peers' experience of treatment, both positive and negative, was also an important influence on their intention in relation to treatment uptake.

4.1.3.1 Treatment side effects

Treatment group

Most (71%) participants in the treatment group had not completed a full course of treatment. All participants reported feeling physically and mentally ill due to unpleasant side effects of HCV treatment and feeling better when they stopped. The most frequently reported side effects were physical, neuropsychiatric and dermatological problems. Physical side effects included weight loss, anorexia, dry mouth, nausea and vomiting. One participant commented:

"Interferon killed my appetite, I wasn't hungry, I had no food inside me, I had no appetite to eat. I had to force myself to eat something, but I couldn't. Plus I had constant vomiting; I had to carry a vomit bag all the time, particularly on public transport and I thought I was going to die because of the constant vomiting" (female, 39 years).

Some participants experienced physical side effects such as body, bone, joint and muscle aches, fever, chills, fatigue and loss of energy (similar to flu symptoms) for most of the time while they were on treatment. These were particularly felt in the days following the injection of pegylated interferon and affected their daily activities, work and family life. One participant commented:

"I had constant aches all over my body. My exercise level dropped off over time, I didn't have energy, I was lethargic due to lack of sleeep, and I had to lie on the couch and rest for long periods. I was too tired to do anything, but I was so exhausted from doing nothing. I had to push myself hard, but then I

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became so sick easily. I experienced chest pain, meaning I wasn't able to walk for fifteen minutes. The worst thing is that after stopping treatment, even now after six months, I still experience very hot flushes with sweating, which I didn't have before at all and I really don't know if it is because of after treatment or I am going through menopause. In general, I would say coping with such a situation was very hard" (female, 39 years).

Those participants who were employed complained of constant vomiting, nausea, headaches and dizziness interfering with their work. Some participants took anti-nausea medications, which were not effective. The majority described severe, migraine-like headaches. One stated:

"I had constant headaches every day; I've had this issue for quite a while. When I first went to the hospital, I thought it was gonna go away, but it didn't. The medication wasn't making me well. It was really horrible. It affected my job; I wasn't well enough to work. I ended up having three weeks off work. You know, there was something you needed to change to get better. I couldn't deal with it and then I found it easier to go off the treatment" (female, 37 years).

Psychiatric side effects of HCV treatment included depression, mood swings, anxiety, insomnia and suicidal thoughts. All participants experienced depression, mood swings and anxiety, and complained that their sleep patterns were considerably disturbed despite using methods to assist sleep, such as reading books, having baths and watching TV. One commented that:

"Through the period while I was on treatment I felt worthless, I didn't feel I was part of society. All afternoon when I was emotionally down and cried at random times, I felt that I couldn't take it anymore ... so I ended up going to bed, but I couldn't sleep at night most of the time. I couldn't give my full attention to my disabled partner, I couldn't do anything for my disabled partner, who is reliant on me, so this made it difficult for me to continue treatment" (male, 47 years).

Another described her experience as follows.

"I didn't know how bad the depression could be; it was so intense. I felt low and I didn't have hope because I was so grumpy and moody with anxiety. I was up most nights. I was also so aggressive. I couldn't stand anything or anyone. Sometimes I lost my control, so I hurt my partner. I made uncomfortable situations for my partner at home. I hated myself so ... and I ended up trying to commit suicide. That's why I stopped treatment straight away" (female, 40 years).

A few participants experienced cognitive symptoms including forgetfulness or difficulty in remembering, and attention and concentration difficulties. These symptoms impacted on daily activities and occupational functioning, resulting in work absences and declines in productivity and job performance. Two participants provided the following comments:

"The medication wasn't letting me think straight, stopping me from functioning and processing information about my duties and responsibilities. I lost my short-term memory and it was very hard for me to track my bills. I couldn't remember what day it was, how much the bill was, as well as the due date to pay the bills. In my workplace, I sent the stock to the wrong company, then the company called me back and I said to them I am so sorry, 'I am on chemotherapy', which is why I stopped treatment" (female, 47 years).

"I usually park my car in a certain car park, but I couldn't remember where it was. I usually call my husband during the day while I was working, but one day I forgot to take my phone with me and I couldn't remember the phone number, which was very frustrating for me, and I got to the point where I couldn't remembe. It threw me off the treatment" (male, 50 years).

Some participants in the treatment group experienced dermatological side effects that persisted post-treatment. A participant who was on treatment for eight weeks remarked:

"I had such a bad skin rash, it was itchy and burning I used lotion and cream, they didn't work. Due to constant itching and burning on my skin, I couldn't

stay longer on treatment. Also, I couldn't sleep and it was so annoying. Even after stopping treatment I still have this issue, even though it has been nearly more than one year. I can't do anything with my hands, I can't touch any chemical products with my hands, and I can't touch metal, such as on a tap. For everything I have to use gloves, even for taking a shower, as whenever I touch metal I get an electrical shock" (female, 40 years).

Another participant described the dermatological side effects:

"I had such a bad skin rash on my face and legs, it was embarrassing. I tried topical cream and lotion and they were not helpful. I couldn't shave my legs at all. I didn't use any soap or body wash. I took showers with warm water. It was so challenging for me not to use soap or body wash. The rash was so itchy. I couldn't go out in public, which meant I had to stay at home. I couldn't wear comfortable clothes; if I did go out, I had to wear something that covered my entire body. The worst part was I couldn't sleep because of skin soreness and itchiness. It was a very uncomfortable situation, I couldn't handle it anymore, ending with stopping. I think I was unlucky that I received treatment in spring and summer" (female, 39 years).

Non-treatment group

Participants in the non-treatment group were concerned about the possible side effects of treatment, and this deterred some from enrolling in treatment. Concerns about the psychiatric side effects were particularly prominent. One participant, who had no history of psychiatric problems, said that the reason she did not take up treatment was because of her concerns about depression, anxiety, mood swings and panic attacks:

"I haven't had any history of mental health issues. I just can't, you know. I don't wanna face things like feeling hopeless, feeling low, feeling useless, mood swings and suicidal thoughts, as they really scare me. At the moment, I've got too many other things on my plate, so I can't struggle to cope with such side effects too. Particularly, I am scared of the mood swings the most, as I am a babysitter. I mean, if I get grumpy with the kids, and can't

understand them and handle them, then I might go off my head and hit them"
(female, 32 years).

Some participants had pre-existing depression and described how they had been sick for much of their recent lives, dealing with both their drug addiction and depression. This precluded some from taking up treatment. One participant had the following to say:

"I have been on anti-depressant medications for four years, and I am not happy and bright. Sometimes suicidal thoughts were going through my mind, you know, I hated myself. My depression can get worse during treatment with interferon. I am not strong enough to cope with such depression" (male, 34 years).

Some participants in the non-treatment group expressed fear of the physical side effects of HCV treatment; they did not want to risk becoming sick from HCV treatment.

"I have been sick too much in my life because of my multiple sclerosis. I have already got pain and aches in my legs. I am tired of being sick, I can't take it no more, I don't wanna get worse than my current situation. I don't want to get tired and fatigued, as I already am because of my multiple sclerosis. I don't want to lose more energy, I want to be able to do my daily routine. That's why I don't want to go on HCV treatment, unless something different comes up that won't make me sick" (male, 40 years).

In particular, employed participants were worried about losing their employment due to the physical side effects of HCV treatment. These side effects could stop them from working and fulfilling other daily commitments. Their jobs were considered a significant part of their life and they were afraid of becoming unemployed. These participants believed that finding employment is very difficult, especially for drug users. They did not want to lose their jobs because of HCV treatment. One of the employed participants who put more importance on her job than undertaking HCV treatment said:

"I have been thinking about HCV treatment since I was diagnosed with HCV, but having fear of losing my current job, I couldn't convince myself to go for it. Because my job is the foundation of my life, and my family life and if I go for HCV treatment I will lose my job, definitely. You know, especially in my case, as a drug user, getting a job is very difficult. I am so very lucky that I have this job and, seriously, I don't want to lose it because of bloody HCV treatment" (female, 41 years).

Other participants mentioned that the physical side effects of HCV treatment made them frightened of becoming unemployed, influencing their intention regarding HCV treatment.

"I am scared of taking up HCV treatment because of losing my job. I worked hard to build to get here where I am, so I don't want to lose it because of physical side effects which make me so sick and fatigued" (female, 34 years).

Many participants believed that their job was essential, giving them direction in their life, and feared that physical side effects of HCV treatment would interrupt this. One participant who had recently gained stable employment said:

"You know, I am not silly to go onto HCV treatment. I had been waiting for this job for ages, so I'm not going to take the risk of losing this job by facing physical side effects. I know the side effects of treatment could disrupt my life and pull me somewhere, where I have to lose my job" (male, 40 years).

Some participants who were single parents noted that their work was financially vital. They did not want to lose their income due to physical side effects:

"I am a single mum and have two children. I have to work full time to earn money. I want to keep my job, which means I don't want to lose my job because of physical side effects" (female, 45 years).

In addition to physical and psychiatric side effects, most participants discussed dermatological side effects such as hair loss and skin rashes/

irritation and itchiness. In particular, female participants believed that these factors stopped them from undergoing on HCV treatment. One participant said:

"I'm worried about a bad skin reaction on my face and legs. If the spots stay on my face and my body, this will be embarrassing. How can I go to work with these rashes? Also, I can't go to a public place or work. I know a friend of mine who had skin problems even one year after completing treatment" *(female, 30 years).*

4.1.3.2 Treatment duration

Treatment group

The second theme was lengthy treatment duration. Many participants in the treatment group found having treatment for a long time very tiring and a heavy burden. They described devoting six months to one year to HCV treatment as very difficult, resulting in stopping treatment early. One individual who was on treatment for 11 weeks said:

"One year is a long commitment. I was so tired and sick of being on the treatment. So I reached the point where it was not worth it, then I pulled up earlier than was expected. It takes a really long time. I believe no one can handle such a long time on HCV treatment" *(female, 47 years).*

Most participants in the treatment group considered "burnout" one of the negative effects of long-term HCV treatment. One participant explained that her treatment was scheduled to last 12 months, but after 6 months she felt she was about to burn out of the treatment and discontinued:

"That's the thing, being on treatment for such a long period was very hard. After six months, I realised I just couldn't, I reached the point where I was emotionally and physically drained over the six months. I felt I was going to burn out" *(female, 42 years).*

Some participants in the treatment group suggested that the long duration of treatment resulted in their failure to complete the full course, even though

they understood that the chance of clearing the virus was much higher when the full course was completed.

"You know we can't deny that people don't like taking medication over the long term. And you know, I've learned that if I go off the medication earlier than I was supposed to take, I'm not gonna get rid of the virus" (male, 45 years).

However, the lengthy treatment duration had a positive impact for one participant in the treatment group who described the long duration of HCV treatment as acting a reminder of the danger associated with sharing needles.

"In the past I used to share needles, especially when I was desperate to take drugs. And I didn't care. But now that I went through treatment and cleared the virus; there is no way to share stuff" (male, 49 years).

In summary, excluding the three treatment group participants with genotype 2, the participants were unanimous that lengthy treatment duration dissuaded them from continuing their regimens.

Non-treatment group

The importance of treatment duration with respect to course completion was clearly acknowledged by most participants in the non-treatment group. One participant, who had genotype 1, remarked:

"I believe being on treatment for one year makes people lose their patience and energy, making them so exhausted. I think I'm the type that gets exhausted after a couple of weeks being on treatment; seriously, it is too long" (female, 42 years).

Participants in the non-treatment group believed that the lengthy duration of HCV treatment was not compatible with their busy work schedules which appeared to overshadow all other aspects of their lives, including activities, family relationships, work life and social activity:

"I couldn't go for HCV treatment for one year. I really don't know how I would look after my three children properly. How could I manage my full-time job? I could have done treatment if it was shorter, like three months, because I could have taken three months' leave from my job and my sister could look after my kids" (female, 41 years).

Participants knew that not completing the course would make HCV treatment less effective and decrease the chances of success. Fear of not completing the full course of HCV treatment, reported by the majority of participants and deterred them from undergoing HCV treatment.

"It was fear of not finishing the treatment which made me pull out form taking treatment. I believe if I don't finish the whole treatment I wouldn't clear the virus, because I can't dedicate myself for such a long period. So I just think that when you can't finish the treatment process, it is not worth it to being the treatment, because you won't clear the virus" (male, 39 years).

4.1.3.3 Treatment effectiveness

Treatment group

The treatment group included 18 participants who did not clear the virus (genotype 1); two participants with genotype 2 who cleared the virus; and one participant with genotype 1 who did not know whether he had cleared the virus. This participant was part of a clinical trial of triple therapy (pegylated interferon, ribavirin and telaprevir) when interviewed. He had experienced HCV treatment three times: monotherapy interferon; combination therapy interferon and ribavirin; and combined pegylated interferon and ribavirin. He referred to the low efficacy of HCV treatment:

"Having a guarantee to clear the virus is very important, because it didn't work well for me; I failed three times in HCV treatment. I started my fourth round about two months ago and I couldn't handle it, so I stopped it a week ago. I have to suspend my hope; whether it's going to work or not, I really hope it's my last time going through treatment. Do you think so? I don't think

so. If the nature of the treatment was effective, it would've worked for me in the previous rounds" (male, 49 years).

Most participants who had not responded well described how their doctors had stopped their HCV treatment at week 12 or 24. Despite having been informed by their doctors that their response to the treatment might be poor, they were frustrated and unsatisfied about not clearing the virus. Two participants explained:

"Going through HCV treatment was a very hard thing to do, and the most awful thing was, after twelve weeks, my doctor told me the treatment didn't work for me, saying it's better to stop you now, rather than letting you continue with treatment until forty-eight weeks. I just wanted to try my chance and in this case I would say how unlucky I was" (male, 46 years).

"I went through treatment , took all my medications plus injections for twenty-four weeks, and how annoying it was when I found out that it didn't work and I had to stop the treatment after twenty-four weeks of being on HCV treatment. I was so fed up although my doctor had told me I might not get rid of it. You know, going through all that and I still have the virus" (male, 49 years).

Three participants who had genotype 3 completed the full course of six months treatment and successfully cleared the virus, but had virological relapses after both completing HCV treatment courses and eradicating the virus. One participant had a recurrence of HCV after one month and the other after two months. They also believed that the treatment effectiveness should not last for only short period short period during therapy. Once the treatment stopped, the efficacy of treatment stopped as well. One participant who had a viral relapse stated:

"I never wanted to experience treatment with no guarantee of success. My test result showed that I didn't have the virus, but the virus came back just a month after I finished the treatment. This was because of the low effectiveness of treatment, if it was effective; there was no way the virus would have

returned after finishing, I used all the time fresh fits which I always get from WASUA, so I didn't share with anyone because I knew if I shared, the treatment wouldn't work" (female 48 years).

Non-responder participants commented that the next generation of HCV treatment should be offered to individuals with a guaranteed cure. One participant who had genotype 3 and relapsed after treatment stated:

"I wouldn't go through treatment again until the next one comes with a guarantee and a high chance of getting rid of the virus. Hopefully, I'll get better treatment later" (female 38 years).

Non-treatment group

Participants in the non-treatment group repeatedly mentioned treatment effectiveness as an issue. None of these participants intended to undergo HCV treatment. Participants in the non-treatment group who had been diagnosed with HCV more than 10 years previously stated that low efficacy of treatment was the main factor that dissuaded them from undergoing treatment.

"I guess failing and not having a positive successful result is another thing that also makes me not take HCV treatment. I have got type 1; it is already twelve months' treatment, so if I do twelve months I completely stuff myself, plus if I fail to clear the virus, which means going to hell for two years of your life" (female, 39 years).

Many participants believed that the foundation of any treatment is cure and commented that the efficacy of HCV treatment was not high enough to encourage them to undertake it. They described HCV treatment as gambling, where individuals take a risk to become winners or losers. They did not want go through a painful process that did not guarantee a cure for the virus.

"Why should I be bothered to go for such a treatment? It doesn't give me any motivation when there is a lack of efficacy. HCV treatment to me is gambling, which means you have a fifty-fifty chance to become a winner or loser. I'm not a good gambler. I don't think it's worth putting myself in a risky situation

when there is no guarantee to clear; as long as there is no guarantee I'm not into it" (male 37 years).

Participants in the non-treatment group described HCV treatment as a battle in which HCV is the enemy they wanted to kill. They acknowledged that it is in the nature of human beings to want to win a battle; however, the low efficacy of HCV treatment meant they were not optimistic about clearing the virus – they saw little chance of winning. The "guarantee" idea surfaced repeatedly:

"Going on HCV treatment is like fighting the enemy, in this case the enemy is the virus. As human beings, we always want to be winners, not losers. So I'm not willing to take treatment as there is a low chance to kill the virus. This means I will fail to kill the virus and I can't fight with the virus, the virus will be the winner, not me. Therefore, as long as I can't be assured that I can eradicate it, I won't go for the treatment"(female, 39 years).

"In my view, the only thing I care about is getting positive outcome from doing everything. Getting a positive outcome from taking HCV treatment reinforces our intentions and determination. But I have got type one of HCV, which is less likely to get a positive outcome, so why should I take it?" (male, 34 years).

Most of the non-treatment group believed that with no guarantee, there was little point in having treatment with such a low probability of eradicating the virus.

"I believe that taking fragile people who caused drama in their life, they are not going to survive and it's a cruel things to do at the moment with a treatment which has a low success rate and there is no guarantee to be cured, so what's the point? I believe it's not a wise thing to do" (female, 32 years).

4.1.3.4 Stigma

Treatment group

All participants in the treatment group described stigma as a very old notion derived from individuals' attitudes, behaviour and actions towards the drug-user community, particularly those who were infected with HCV. The participants would pretend to be non-drug users, because they did not want to be denigrated and suffer emotionally and psychologically. They described being very cautious about whom they opened up to about their addictions and infections. They did not want to disclose their illicit drug use to HCV care providers due to lack of trust in the patient–provider relationship, and they feared being judged. They experienced and perceived stigma attached to IDU and HCV treatment. The following quotes illustrate the IDUs' attitudes towards stigma:

"Stigma and discrimination is an old concept which is coming from people's attitude, behaviour and action towards us. I didn't tell the clinical nurse and my specialist that I'm a drug user because I didn't want them to show negative reactions towards me and to treat me differently ,which could affect my self-esteem and especially losing myself. I am happy that I hide my drug addiction" (female, 48 years).

"Stigma and discrimination complete each other and there is no difference between them. When I was on HCV treatment I didn't mention that I'm a drug user. Also, I told my doctor and my nurse in the liver clinic that I got HCV through a blood transfusion. As soon as I mention that I'm a drug user, I get labelled as a junkie person on the forehead forever. I've learned not to disclose my status to the point where I am judged. Once I'm a drug user, I can't be trusted. Even before going on treatment I prefer not to discuss about my addiction and my HCV to my GPs unless it's relevant, for example, if they wanted to do a relevant procedure (male, 52 years)."

These participants reflected on feeling that there is always a difference between drug users and non-drug users; they believed they were second-class citizens who were not good enough to receive health care services without stigmatisation or discrimination. They perceived insensitivity and ignorance among health care providers, which led them to hide their IDU status when

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they commenced HCV treatment. They felt that being a drug addict is like any other disease and, as an individual, they had the right to be treated the same as others without discrimination. The following statement is indicative of how stigma was manifested:

"Basically, as a person who is [an] injecting drug user over the last twelve years, I have seen a big gap between non-drug users and drug users. Let me give an example. Once I had to go to the emergency department as I had a car accident. I was in such bad pain and I asked for sedation; the nurse told me 'nothing works for you or will reduce your pain because you're a drug user, your body doesn't respond to our medication'. I'm a person like other people, why should I be discriminated against? I have a right to receive health care without stigma. I came to a point where I wouldn't be honest about my drug addiction, I always have to lie that I'm not a drug user" (female, 50 years).

Unfortunately, drug-user-related stigma exists in the health care setting; some health practitioners knowingly or unknowingly stigmatise and discriminate against IDUs. All the participants agreed that GPs at health care facilities are more likely to practise stigmatisation than professional staff or HCV specialists. This was expressed by the majority of participants in the treatment group, which influenced their decision to hide their drug-using status when undergoing HCV treatment, as they did not want to feel uncomfortable during the HCV treatment course, specifically when they wanted to discuss any issue related to HCV treatment with their health care providers. One participant said:

"I had some GPs who were so judgemental. They never discussed with me anything about HCV treatment. They think that I'm trying to get more drugs from them; this assumption had a negative impact on me emotionally. Many GPs believe we are junkies. Personally, I prefer not to visit a GP. I changed my GP three times to see any difference, but nothing changed at all. My GPs, they were all the same, they would criticise me in a negative way, so I learned

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from past experience not to mention to any health care providers that I'm a drug addict" (female, 38 years).

Two participants in the treatment group reported being treated differently by their families on discovery of their drug addiction. Consequently they were fearful of telling their family about their HCV treatment. They did not disclose their treatment status to family members or in their workplaces due to fear of being judged by their families and encountering poor reactions from their colleagues. They did not wish to lose their dignity and confidence, which would have negatively affected their mental wellbeing.

"I come from a well-educated family and I live with my parents and sibling. Nobody knows about my HCV in my family. I didn't even tell my parents about my HCV, because I didn't want to lose my pride and dignity in front of them, particularly my sibling. They already label me as dirty or a junkie, and they reproach me and discriminate against me, they behave towards me differently, and they don't ask me to join them for lunch or dinner because of my drug addiction. So I didn't want to make the situation worse by telling them about my HCV status. If they knew, I have no idea how much worse the scenario could get, maybe I would have become homeless while I was on treatment, which I didn't want. That's why I didn't tell, there wasn't any point to tell them. Can we get rid of stigma attached to drug users or HCV? I don't think so!" (female, 28 years).

Non-treatment group

All participants in the non-treatment group perceived HCV stigma as disrespectful and dehumanising, through interaction with both drug users' and non-drug users' community where they might be labelled as untrustworthy or irresponsible. They felt high levels of stigma and discrimination related to their HCV status, which caused them to exclude themselves from their former social networks. Being HCV-positive made it harder for them to project and reconfigure their identities; as a result, they became isolated from their social networks.

"You know, as a drug user and HCV-positive person, I haven't seen anyone respect me and take me into account as a human being. People, even drug users with no HCV, look at me as useless, reckless and unreliable. I'm shamed because of my HCV and I don't have a good reputation in my community and other communities, they don't trust me, they see me as a junkie. Let me give you an example. One of my friends who used to put their kids with me for half-days babysitting, since they found out about my HCV, they never put their daughter and son with me. For them I was a different person who needed to reshape and reform my personality and my character because of HCV. Eventually my friends found out about my HCV, so they distanced themselves from me, so I had to put myself away from them with no social activity because they didn't want me to be included in their social activities. They used to invite me for their birthday or other social events; they just stopped communicating with me. So I didn't see any point in keeping in touch or catching up with them. I always feel rejected and not accepted by others. We can't ignore the fact that as long as a stigma is attached to HCV and inseparable, less people including myself will be willing to go on HCV treatment" (female, 40 years).

Most participants in the non-treatment group who did not disclose their HCV status linked their low intention to enter HCV treatment to fear of exclusion from the community, their family, workplace and even the IDU community. One participant described his apprehension about HCV treatment as follows:

I'm too scared to go on HCV treatment, as I did not tell anyone that I'm HCV-positive, especially my parents, my manager, my colleagues and especially my friends. I don't want to reveal my HCV by going on HCV treatment. It would be so embarrassing. I didn't want to be left out them and not feel attached to them. I believe it is a very common reason that has stopped people going on HCV treatment" (male, 37 years).

Some of the participants in the non-treatment group did not want to disclose their status to their families and those who lived with them because of fear of exposing themselves to judgement from those individuals. However, hiding their HCV-positive status made the situation harder, as they felt loss or self-

loathing. Moreover, they feared negative reactions from their families due to seeing friends rejected and disavowed by their families when they disclosed their HCV status. They associated this issue with refusal to undertake HCV treatment. Two participants expressed their opinions about HCV stigma as follows:

"You know it's very hard for me that I haven't told anyone that I have HCV, it's not me but because of HCV, I have to hide my HCV. I didn't tell my partner, but thinking every day that I have hidden my HCV status from my partner annoyed me all the time and I hate myself to death" (male, 38 years).

"I didn't tell my family and my partner because I know them very well, they can't cope with this, they would start telling me off, especially my partner, who is very cautious not to share any injecting equipment with others. I hate myself that I'm not honest with my parents. They would be very negative towards me, so I was worried they would reject me and not want me to be a part of their family. I couldn't handle this. That's why I didn't tell them I have HCV" (female, 41 years).

Another dimension of the impact of stigma among non-treatment group participants was that their interactions with health care providers did not involve with the ethical stance they expected. They felt they were judged and discriminated against when they did approach health care services. They believed that, as most HCV infections are derived from IDU, health care providers linked HCV and the act of injecting, leading to discriminatory behaviour. The following quote demonstrates how some GPs avoid physical contact with HCV-infected people:

You know better than me that HCV is a blood-to-blood contact and is not transmitted by touching or doing physical examination, but all my GPs never ever did check my breast lumps. I wasn't comfortable with them at all, because all the time she just wanted to get rid of me quickly, she wouldn't let me to ask her anything and what do I need. We had distance between her and me. I never ever got what I wanted. I assume that because I am HCV-positive and most of the infected people with HCV are drug users, the doctor jumped

to the conclusion that they should be discriminated from others. I believe as a doctor and educated person they should see all people as a normal person regardless of drug use, HCV or even HIV status. We have a right to receive the same and equal health care. I have to tell you, it took me ages to find a friendly dentist who doesn't discriminate" (female, 39 years).

Participants believed that stigma remains central in the experiences of IDUs and HCV, so enduring a whole year of treatment with this stigma would expose them to emotional distress.

"Stigma is attached to HCV for a long time and going on HCV treatment with this stigma attached to it for six months or twelve months is very difficult and it hurts you emotionally and it could have an impact on your mental health" (female, 30 years).

4.1.3.5 Lack of Support

Treatment group

As mentioned above, while participants in the treatment group discontinued treatment due to not coping with the side effects, lack of family support was also a factor for many. Most participants in the treatment group reported receiving low levels of family support while they were on treatment. They stated that this lack of support made managing treatment much harder, reducing their motivation to continue. It was very difficult for them to tolerate the treatment and its side effects without a supportive family.

You know, I believe having a supportive family is very effective in managing HCV treatment, addressing treatment side effects and to stay motivated to complete the treatment. I didn't have such support from my partner, he is suffering from MS and he is really sick, so at this point I couldn't expect him to be supportive and help me while I was dealing and coping with side effects on my own. I did try a lot to stay on treatment, but after a couple of months I couldn't handle it, then I stopped it. You know, I think if I'd had someone who could have supported me, I wouldn't have stopped, so by now I would have cleared the virus" (female, 42 years).

Participants who discontinued treatment and did not clear the virus reported that their partners were not supportive during the treatment and had constant arguments, reported that their partners did not understand their situation and did not help them, or they had sustained significant emotional hurt from their partners which resulted in them feeling isolated, lonely and depressed. When family support – sympathy, love and attention – was missing, participants were more likely to experience an increased burden, which magnified the side effects of treatment, slowed down remission and led them to discontinue treatment and consequently not clear the virus. They claimed their families did not support them when they attended the liver clinic for follow-up appointments or when they experienced side effects. Two female participants who split from their partners during HCV treatment reported an extreme lack of support and that they had absolutely no motivation to remain on treatment:

"My partner had an awful temper and blamed me for every single fault that happened in the house. I had to argue with him for everything from household items to looking after the kids. He couldn't understand what I had been through; he had no clue whatsoever about my treatment side effects. Day by day I was getting down to the point where I was limiting myself to my bedroom. I felt so depressed that I couldn't even see my kids and deal with them. I felt sorry for myself because I had to manage the treatment on my own without my bloody partner, who could see only himself, not others around him. He didn't even make me a cup of tea while I was on treatment. He didn't give me any motivation to keep going on treatment. I remember one day when I was suffering from the side effects, he told me 'hey babe, just quit the treatment, I can't stand you anymore" (female, 40 years).

"You know, when I was on treatment I was miserable because my partner tried to pick on me all the time, because I was so depressed and down. I had to argue with him all the time because of his stupid actions and his behaviour. He didn't have any physical or emotional relationship with me. He didn't help me, he couldn't stand me, and he made me choose between him and quitting treatment. I chose treatment, and then he left me. I felt so lonely and depressed, as my close family lives in NSW, and my depression got worse,

which also affected my physical activity as well. I didn't have anyone here except my partner. I couldn't believe he did this to me. I was in hell, my situation got worse day by day because of the horrible side effects, so I came to the conclusion that I had to stop the treatment after seven months and I did not end up clearing the virus" (female, 42 years).

On the other hand, those participants in the treatment group who had completed the treatment course and cleared the virus described family support that provided a comfortable and peaceful environment for them to cope with treatment. They reported that their families were engaged in the treatment process, particularly when they administered pegylated interferon injection and took ribavirin, and their family members made sure they took their medication properly and on time. Family support encouraged these participants to complete treatment and clear the virus; the participants felt that without this support, they were not capable of completing treatment and eradicating the virus. In this regard, one participant stated that:

"You know, HCV treatment was a time of remarkable change where you need someone to be with you during the treatment journey. In my case I was very lucky because I had a very supportive family, especially my partner, who provided me with the most comfortable situation. He did not let me do anything he constantly stood by my side and didn't leave me alone, not even for one minute, mainly when I was about to get my injection. He hugged me, he kept telling me 'you are very close to getting rid of the virus, you can do it, please don't give up. I'm with you no matter what and we can have a better life together'. Then after my injection he put light music on and made me herbal tea which made me very calm; without him I wouldn't have got through it" (female, 50 years).

Having family support reduced participants' stress levels and prevented them feeling isolated during treatment. They affirmed that their families created pleasant social interactions and provided relief, both emotionally and physically. The constant support provided by their families was highly valued by participants, who were initially concerned about how treatment side effects

would affect them physically and emotionally. They believed that their family sacrificed themselves by providing care for the participant.

"When I just started treatment, I was so worried how I could manage the treatment with the nasty side effects, but ... my wonderful partner ... quit his job because of my treatment. While I was on treatment, he kept me busy by watching movies, inviting friends for dinner, taking me out sometimes in order to not feel lonely and down. He didn't let me think about any negative things, we did some meditation together to release the stress and took positive energy from the outside. Trust me, without him I couldn't have make it" (female, 48 years).

All participants in the treatment group concluded that family support was the strongest determining factor for staying on and completing HCV treatment by helping them cope with side effects.

Non-treatment group

Most participants in the non-treatment group reported not having family support. They felt helpless and had no confidence to undertake HCV treatment without a supportive family. Constantly thinking about who would look after them during the HCV treatment course discouraged them from undertaking treatment; they feared emotional distress and poor mental health. They affirmed that lack of support led them to quit HCV treatment due to loss of self-esteem, hope and self-efficacy.

"I have family here, but they are not helpful. I have to manage everything on my own if I go on HCV treatment, and keep thinking about who is gonna take care if me if I go on HCV treatment. How can I go without having support from my family?. When you don't have support, it means you don't have confidence and any hope to take the treatment, it also stresses me out. Again, if I go on treatment on my own, I'll be in hell mentally and emotionally" (female, 43 years).

They spoke of family support providing kindness, sympathy unconditional love which could simplify and smooth the treatment journey for them. They

believed family support could reinforce their personal strength and make them feel attached, connected and accepted.

"I would say having a supportive family for the HCV treatment is a key item which gives you everything, such as love, caring, value, sympathy and respect. These items can make the treatment journey easy for you, especially when you are trying to adjust yourself with the treatment life. Having family around you when you are on treatment gives you more power by hanging out with your family all the time, feeling connected to their family, which is the best way to overcome the challenges during the treatment journey" (female, 48 years).

Some participants believed that lack of a supportive family stopped them from undergoing HCV treatment. They believed that living with their family would mean receiving better care, and greater comfort and support, and help them cope with the side effects. Several non-treatment group participants did not live with parents or partners:

"I live on my own. All my family is not here, they are in the eastern states. Living with family gives you luxury to feel relaxed and comfortable. It's also helpful when you face nasty side effects. Living away from my family makes me not to think about going on HCV treatment" (male, 37 years).

Similar feelings were conveyed by other two participants:

"I don't live with my family. My family are in Queensland. I don't have a silver spoon and I don't have privilege. I live on my own. I have to manage my life on my own" (female, 34 years).

"I live alone and I'm getting old and I believe it would be challenging for me to go on treatment on my own. My family lives overseas. If I experience several side effects, who will look after me?" (male, 42years).

Participants felt that in the absence of family support, there was no motivation for them to undertake HCV treatment. They predicted exhaustion, fear and

isolation and, as a result, felt that they could not overcome treatment side effects and difficult times during the treatment journey.

"You know, when you don't have support from your family, you don't have motivation to go on HCV treatment. Going on treatment on your own means stress, tiredness, isolation and not being able to cope with treatment side effects with no positive results. When you can't communicate with your family, which means there is no help and empathy, it makes you unwilling to take HCV treatment. You know the chance of exposing yourself to side effects increases when the support decreases, as family support can act as a buffer against the challenges and the side effects" (female, 39 years).

4.1.3.6 Peer experience of treatment

Treatment group

Hearing positive and negative treatment experiences from their peers were influential in determining participants' intention to commence HCV treatment. Some participants in the treatment group felt that they were at the same level as other IDUs who did take up treatment. In other words, feeling behind or equal to their peers persuaded them to undertake HCV treatment. Hearing positive stories improved their confidence and reinforced their strength to manage the HCV treatment course. Participants learned from the success stories of their peers, particularly their strategies for coping with treatment side effects. Participants in the treatment group reported increased self-efficacy through hearing positive experiences and that they had changed their negative beliefs, especially when they observed their peers successfully undergoing HCV treatment. The following quotes from two participants are illustrative:

"In my opinion hearing or listening to other people who have done treatment really helps to figure out your way through HCV treatment. When I saw my next-door neighbour, who did complete a treatment course and did clear the virus, then I felt that I am behind and I thought 'why shouldn't I?' Feeling behind pushed me and encouraged me to go for treatment. It gave

me confidence to believe in myself, that I can do it. Since I met her I've changed my mind about treatment. She gave me hints about how to cope which helped me a lot while I faced the nasty side effects" (female, 48 years).

"I am happy that I met one of my friends who did HCV treatment at a friend's birthday. I felt that she is the same as me and both of us are on the same page and are equal. If she could do it, I can do it. She was very helpful for me; constantly telling me I can handle the treatment, building my confidence by providing me with some effective guidance on how to deal with treatment side effects and how to adjust myself with the treatment course. I followed whatever she said. All her tips were so helpful and helped me to handle the treatment. If I hadn't heard her story, I would've had a tougher time than what I experienced. I would recommend to anyone who wants to go on treatment that they listen to the stories of others who have done treatment" (male, 49 years).

Several participants in the treatment group said that their intention to undertake treatment was based on hearing about positive experiences and they considered it treatment persuasion. They stated that such stories made them realise that by undertaking HCV treatment and being without the virus, their health and wellbeing would improve and their lives would be prolonged.

"I was always scared of treatment. After meeting my cousin who did treatment and lived in Sydney, I decided to go for the treatment. She was one of the treatment motivators for me and she convinced me HCV treatment is not a big deal and anyone can do it, otherwise I wouldn't have gone for treatment. Hearing positive stories simplified the treatment journey. Being free of HCV means living longer and having a healthy life" (female, 50 years).

Non-treatment group

Many participants in the non-treatment group highlighted that HCV treatment was one of the most tragic things that had happened to their friends. They indicated that hearing about negative experiences of HCV treatment from

other IDUs strongly influenced their own treatment intention. Several IDUs reported friends discontinuing treatment due to the long duration of the treatment and the side effects.

"My friend has been on HCV treatment for six months. When she started HCV treatment, she was working part-time. She experienced very nasty side effects, she became very depressed, very isolated, having constant headaches and vomiting all the time; she even tried to kill herself. She was meant to finish the treatment within forty-eight weeks, but because of experiencing horrible side effects, she couldn't handle it and she stopped after six months. That's why I don't want to go for it" (female, 40 years).

"A friend of mine who had to quit his job because of bloody treatment, he couldn't cope with treatment side effects while he was working. Seriously, who can afford to be on HCV treatment for one year? One year is a long time. You can't devote yourself for one year to be on treatment" (male, 42 years).

"I thought after finishing HCV treatment, people can feel free, live without HCV and have a better quality of life. However, my friend did complete the treatment and did not clear the virus. So that's why I don't want to go on treatment, it is extremely terrible and after being on treatment for one year, you can still carry the virus" (male, 38 years).

One participant in the non-treatment group described the tragic effect of the long duration of treatment which, along with the side effects, was suffered by a friend of his:

"If HCV treatment was shorter than one year, my friend's tragedy wouldn't have occurred. He just ended up committing suicide when there was only one month left to finish out of forty-eight weeks' treatment. I believe being on treatment for one year makes people lose their patience and energy, making them so exhausted. Why should it take such a long time? One year is a very long time and I think only the minority of people can deal with it" (male, 38 years).

Participants in the non-treatment group believed that a mentor who had experienced HCV treatment could be helpful to individuals contemplating treatment. They acknowledged that hearing about negative experiences caused them to imagine similar experiences and influenced their intention not to undertake HCV treatment. They suggested that exposure to others' experiences opened their minds and gave them a comprehensive picture of HCV treatment.

"I believe sharing other people's treatment stories is useful for others who haven't experienced treatment yet. I've HCV for a long while; I have a negative attitude towards HCV treatment. My negative attitude got worse when I met one of my mates who went through treatment and had a horrible time during treatment. When he was telling me his treatment stories, I did see myself in his shoes. Since I met him I did visualise myself in his position, then I thought it's not time to go on it. My friend's experience definitely influenced me not to go for the treatment" (female, 39 years).

Hearing negative experiences led participants in the non-treatment group to become emotional and anxious in anticipation of what would happen if they were to undertake HCV treatment. They refused treatment because of negative stories from peers who failed to clear HCV. They stated that it was hard to trust the treatment. As noted previously, treatment efficacy was a major concern:

"... thinking about what's gonna happen to me if I go for the treatment is killing me. I couldn't make up my mind to go for it, since my dad had been through the treatment and he had to stop in the middle of the treatment because he did not respond to treatment. I jumped to the conclusion, what's the point of going on treatment when there is no chance of clearing the virus? It's useless thing to do. To start something you should have hope to get through it; when you already know you could fail to clear the virus, of course I don't take it" (female, 41 years).

"Um, certainly since I've heard from my friend who still has the virus after twelve months of being on treatment and tolerating treatment. You know, I

couldn't believe that. I thought once you on treatment you can get rid of the virus. When I saw my friends who were disappointed with the treatment, I decided not to go. I'm glad that I met him, otherwise I would be pissed off and become mad if that had happened to me"(female, 38 years).

Hearing about negative experiences of side effects made the participants in the non-treatment group worried and anxious about whether they could manage them. That is why most participants in the non-treatment group had decided not to undertake HCV treatment.

"I don't want to go for the treatment, because I have seen my housemate, who has been through treatment, and she couldn't handle the side effects because they were out of her control. If I face the same side effects that my housemate faced, I wouldn't be able to manage them and they could be out of my control. So I don't want to go for it" (male, 35 years).

4.1.3.7 Protecting family, health and wellbeing and career goals

Some of the participants in the treatment group said that the "benefit of being treated" acted as a motivator to undertake HCV treatment. They were at a stage in their lives where they wanted to eliminate their concerns about their future. They were taking steps toward healthy lives.

Protecting family

Concerns related to the transmission of HCV to family members were important in deciding to undergo HCV treatment. Protecting partners, children and family from HCV transmission was repeatedly mentioned. For example:

"Protecting my kids and my partner against the virus pushed me towards treatment. I have two little kids, so I just wanted to keep them safe. I didn't want to pass the virus to them because they're just kids. We have only one toilet and one bathroom in the house they might go and use my toothbrush or razor, then catch the virus, so I wouldn't forgive myself for the rest of my life.

To me it is the most horrible thing someone can do to their kids or their family" (male, 37years).

Prior to undergoing treatment, some participants physically isolated themselves from the other members of their family, causing emotional stress:

"I couldn't handle my situation, living every day in hell where I limited myself to my bedroom and my own TV. I separated myself physically and emotionally from my family. It was very hard for me. I wanted to be with my kids but, because of HCV, I couldn't. I always gave excuses to my kids in order to avoid playing with them, even though if I didn't think about my HCV it was always in the back of head of my mind that I'm HCV-positive and my kids and partner were not safe around me and I always worried that I could give it to them somehow" (male, 37 years).

Some wanted to maintain strong connections with their grandchildren; they considered HCV a barrier to this goal. This perception was very common among participants whose children (the parents of their grandchildren) found it hard to deal with their parents' HCV. They felt embarrassed about their HCV status.

"My daughter never trusted me to look after her kid, she always preferred to put her kid in day care and pay a fortune rather than letting me look after her kid. Even for any social activity she put her kid away from me, she didn't even let me feed her, all because of my HCV. She always worried that something would happen and her kid would get HCV. That's why I did treatment and I fortunately cleared the virus. Now I can look after my gorgeous grand kid!" (female, 48 years).

On the other hand, two participants in the treatment group looked after their grandchildren despite their HCV and believing they were not healthy enough. One participant stated:

"I take care of my grandchildren three days per week. I just want them to be safe when they're with me. I remember when my son was four years old and

he put my razor in his mouth. I'd hate something like this happen to my grandchildren. So I just wanted to be a healthy person and not carrying the virus when I'm with my grandkids" (female, 50 years).

Another participant described feeling anxious as a grandmother:

"I had an anxiety attack when I was with my grandkids, it made me feel awful and I felt guilty as an HCV-infected person looking after my grandkids"(female 50 years).

Health and wellbeing

Participants in the treatment group who did not have children or family undertook treatment to become healthier and live longer. They perceived HCV treatment as a second chance in life which assisted them to return to their pre-HCV lifestyle and extended their life expectancy. Being HCV-free improved their confidence; they typically described this as giving them a new lease on life. The vast majority of treatment-experienced participants spoke about becoming HCV-free changing their lives for the better.

"I'm not old enough to die, I still have life to live. I want to have a better life with a better health status and live longer. I can start a new life without HCV, so HCV treatment is extremely important for me because it can save my life and give me more time to be alive"(male, 49 years).

"I still have plenty of time to live young. I can have a better quality of life and live longer and even have a new life free of HCV, why not? When I can extend my life expectancy and have a healthy life by clearing the HCV, why not? I would be stupid if I didn't take HCV treatment" (male, 37 years).

The majority of participants in the treatment group felt unwell and related their health problems to having had HCV for a while. Feeling fatigued all the time, brain fog, dry eyes and depression were the most common HCV symptoms experienced by participants in the treatment group. They acknowledged that HCV can have a long-term negative impact on individuals' health and wellbeing, both physically and emotionally, which

might stop them from participating in their normal daily routine. Participants wanted the energy levels they had before being infected and to have a normal life. They spoke about HCV increasing the chance of liver disease such as fibrosis, cirrhosis and liver cancer, which could lead to an early death.

"I want my energy back. I couldn't get up in the morning even when I had enough sleep at night, about nine to ten hours, then when I woke up in the morning I felt so tired and slept again. Most of the time I had to sleep again in the morning or lie down for a while to get my energy back, but I still didn't have enough energy. I used to go sailing a lot, but because of being fatigued and lack of energy I wasn't able to do it. I wasn't able even to do my daily routine. HCV can cause early death as well, as one of my friends died because of HCV" (male, 47 years).

Other participants in the treatment group expressed fear and uncertainty about their health status in the near future. They had constant fear of becoming sick and being admitted to hospital and requiring high- dependency care. They did not want to experience ill health and be hospitalised with debilitating HCV-related disease in the near future.

"I always have a fear of ending up in hospital because of my HCV. I don't want to be hooked to a machine and the machine keeps you alive. When I think rationally about having a choice whether or not to undergo HCV treatment, my common sense told me I should go for it in order to save my health and not end up in hospital" (male, 49 years).

Some participants in the treatment group averred that HCV treatment had brought positive and healthy changes in their lives. Their intention to undertake HCV treatment had increased since they were diagnosed with HCV. They added that they were fortunate in having an option to undertake HCV treatment to clear the virus and live healthier lives. Living HCV-free gave them a greater sense of value, as well as tranquillity and pleasure.

"HCV treatment is a free gift for infected people, and it brings a positive and healthy change into people's lives. I always wanted to go on HCV treatment

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over the past years since I was diagnosed. I also believed that infected people could improve their lives without suffering with HCV every day in their life by going on HCV treatment. Once the virus is cleared, joy and happiness comes into your life" (female, 50 years).

Career

A desire to become healthy was not the only reason that encouraged IDUs to take up treatment. Those participants in the treatment group who were employed stated that their careers were a major motivation for HCV treatment uptake. They were satisfied with their current jobs, and did not want to become unemployed due to HCV. One female IDU who worked as a nurse said that her job motivated her to commence HCV treatment.

"The main motivation for me to go on HCV treatment was keeping my current job. I really love my job, I don't want to lose it because of HCV. I just wanted to be free from the HCV while I am working as a nurse and dealing with patients. In a psychiatric ward two years ago, one of my patients bit me and I had bleeding. His mouth was full of blood. I felt awful and dirty. After that, I decided to go on HCV treatment, because I was worried that I could pass it to my patients, particularly during some procedures" (female, 48 years).

The participants who worked in settings where there was a high chance of transmitting HCV to others did not disclose their HCV. They just wanted to clear the virus to put themselves at peace and without worry while they worked. One participant who worked as a chef in a city restaurant pointed out:

"You know, over the top of everything, my job was a key motivator to push me into the treatment. You know, working as a chef is really hard and stressful, especially with HCV; I was so under stress and pressure while I was working due to HCV. One day when I was working, I cut my hand very badly and blood was all over the place and my colleague wanted to help me, then I told him, 'please don't help me'. He insisted on helping me, then I had to tell

him I had HCV. It was so hard for me; I couldn't handle it anymore, so I decided to go on HCV treatment" (male, 37 years).

HCV symptoms were an extra burden for the employed participants in the treatment group, and this interfered with their working responsibilities. They perceived it as potentially jeopardising their lives, as all of them were the primary breadwinners in their families. As their HCV symptoms worsened and became unpredictable, the increasing hindrance to their work performance influenced their intention to undergo HCV treatment.

"I believe for me, my motivation or encouragement to go on HCV treatment is my job. My job is physical work and in the middle of the day I didn't have the energy to continue my job and I was so lethargic, with no energy. I wasn't able to manage my work while dealing with HCV symptoms at the same time. So I lost my job. It was a big loss for me because I am the only income source to my family. Then I thought it was now time to kill the virus, so I could get back to work. I am happier than ever now that I am with no HCV. I can work properly and earn good money" (male, 37 years).

Other participants were constantly exhausted due to experiencing HCV symptoms:

"Let me tell you that my job was the key to inspire me towards treatment. I worked as an assistant manager, full-time, and I tried a lot to keep my job. But because of having HCV for ages, I started showing symptoms such as constant fatigue and nausea every day, and the worst one was when I became forgetful with low focus" (female, 38 years).

4.1.3.8 Unstable housing

Participants in the non-treatment group who were homeless at interview described homelessness as increasing the likelihood of them engaging in risky behaviours such as sharing injecting equipment, exchanging sex for drugs and unprotected sex, which could expose them to other blood-borne viruses. They expressed their frustration with their lack of healthy food, sleep, showers, washing machines and particularly refrigerators for keeping HCV

medications. They did not have the resources to undertake HCV treatment and it did not make sense for them to do so while they lived in this unstable environment. They perceived the ongoing struggle of being homeless as a demotivating factor with respect to HCV treatment.

"You know, I'm homeless over the last two years. How can I go on HCV treatment while I am homeless, how can I keep my medication? As a homeless person, I do everything to earn money for my expenses, such as sleeping with any drug dealer at any time without using a condom. When I am desperate for the drugs and I don't have a clean needle, I use other users' needles. I don't eat, sleep and shower properly. At the moment, without a house, I just want to live and spend my life. HCV treatment doesn't mean anything to me. What sort of motivation is left for me to go on HCV treatment? Because of these reasons that I told you earlier, I can't go on HCV treatment" (female, 40 years).

Living on the street without permanent shelter caused depression and suicidal tendencies. Participants' mental illnesses eroded their ability to maintain a positive mindset towards HCV treatment, but in any case, they knew treatment with pegylated interferon could make their situation even worse. They stated that without shelter, they felt unable to look after themselves or care about their HCV.

"I am homeless over the last two years. How do you expect me to take HCV treatment? I'm struggling with living on the street where my depression got intense and worse. Often, I visit a GP for a prescription; without my depression medicine I wouldn't be alive. But sometimes I tried to kill myself because I'm tired of living on the street, so with the attitude of killing myself and my depression, I don't have a hope to kill the virus, especially with interferon treatment, which makes my depression worse and worse. I can't deal with my current situation, how I can deal with treatment while I am homeless? You know, based on my experience for nearly two and half years on the street, I would say all homeless are depressed, regardless of HIV and

HCV. The only disease you could generalise for the homeless is depression"
(male, 37 years).

Homeless participants noted that they could not register themselves with health care providers (clinical nurses, support services and doctors) in order to commence HCV treatment without a stable address and contact number.

"I have been living on the streets for the past three years. As you know, I need stable accommodation with a stable address and contact number to be able to enrol in HCV treatment. So if I want to take HCV treatment, I need to go through a registration process. At this stage, it is not possible. Having a stable address is one of the key parts to go on HCV treatment. As long as I'm homeless, I can't be registered for HCV treatment" (male, 34 years).

Some participants claimed that health care providers' negative perceptions of homeless clients resulted in homeless IDUs going without HCV treatment, which could lead to an increased risk of developing liver damage or liver failure. Feelings of mistreatment contributed to their low intention to undertake HCV treatment.

"I don't have shelter over my head since three years ago. I've had HCV for about eighteen years. I tried to go on HCV treatment; when I asked my GP about going on HCV, he didn't give me a referral for HCV treatment because of my depression. He already knew my liver is not good, I don't know what the problem is with my liver, but I know my liver is not okay. Without giving me a treatment choice, I will die soon from liver disease. I try my best to stay alive without having any proper health care" (male, 42 years).

Fear of unpleasant side effects was expressed by some homeless participants. Thoughts of encountering psychological and physical side effects of treatment while living on the streets were powerful disincentives. They expressed serious concerns about their capacity to cope with treatment side effects, especially while struggling with drug addiction.

"As a homeless person, I don't have a bed to sleep in, I don't bathe or shower. I love a shower because it makes me calm, it's the only place that I don't think about anything. It may sound silly to you, but I love it. I don't have a stove to cook on and I don't have my own peace. How can I deal with the HCV treatment side effects or how can I manage the side effects while I live on the street? Without a peaceful place and peaceful mind, I can't deal with interferon side effects which can affect my mental and physical health as well" (male, 36 years).

Two homeless participants described drinking large amounts of alcohol and injecting drugs in particularly risky ways. They confirmed that without shelter they did not have control of their lives, so they did not intend to undertake HCV treatment as their homelessness could jeopardise the outcome.

"I didn't have a stable place to live. I was homeless for seven months until a friend of my brother-in-law offered me a place to live without paying. This place is not good, because all the housemates are encouraging me to drink alcohol, try different drugs, injecting more than I used to, we even shared needles, especially on the weekend when we run out of needles, also using homebake as well. I would be stupid if I went on HCV treatment" (male, 42 years).

4.2 Focus groups

Focus groups were held to follow up and confirm the themes identified in individual interviews, as well as to explore HCV-positive current IDUs' perceptions about triple treatment. The results allowed the researcher to develop an instrument for assessing the factors that influence intention of HCV-infected IDUs to undertake HCV treatment. This section describes the focus group participants and the findings from the focus group discussions. The themes emerging from the focus groups were treatment side effects; treatment duration; treatment effectiveness; stigma; and lack of support.

4.2.1 Sample characteristics of focus groups

The five focus groups brought together 25 individuals (five in each group) who were current IDUs living with HCV and with no experience of HCV treatment. Table 4.2 provides the socio-demographic and drug-use history of participants. In summary, just over half of the participants were female; participants were aged from 33 to 47 with a median age of 39 years. Most had stable accommodation and just over half (52%) had completed Year 12 or TAFE/university (Table 4.2). A small percentage identified as Aboriginal. Most participants lived alone. More than half of the participants were unemployed and derived their income from government benefits (Table 4.2).

As indicated in Table 4.2, methamphetamine was the drug of choice and the most commonly drug injected in the last six months for just over half of the focus group participants, while the remainder nominated heroin. A large majority of participants reported injecting once a day. Injecting drug use histories were largely of more than 10 years. Most participants had not consumed alcohol in the past year.

Table 4.2 Characteristics of focus groups

Socio-demographic and drug characteristics	n	%
Gender		
Male	12	48
Female	13	52
Accommodation		
Homeless	8	32
Non-homeless	17	68
Live with		
Alone	16	64
partners /Family	9	36
Education		
≤ Year11	12	48
Year 12	11	44
TAFE/Uni	2	8
Ethnicity		
Aboriginal	2	8
Non-Aboriginal	23	92
Marital status		

Single	9	36
Married/lived with sexual partner	16	64
Employment status		
Non-Employed	11	44
Employed	14	56
Source of income		
Employed	11	44
Government benefits	14	56
Preferred drug and drug used most often in the last 6 months		
methamphetamine	13	52
Heroin	12	48
Frequency of injection		
More than daily	2	8
once a day	23	92
Drug use duration		
8-10 years	5	20
>10 years	20	80
Consumed alcohol in the past year		
Yes	6	24
No	19	76

4.2.1 Themes from focus groups

This section presents the results of thematic analysis of the transcripts of the focus group discussions involving HCV-infected current IDUs. Participants' verbatim quotations are included in the text to illustrate the primary themes. The themes presented describe the factors that contributed to these non-treatment-experienced participants' perceptions of HCV triple treatment. The findings from the focus group discussions are only from IDUs infected with HCV genotype 1.

Analysis revealed new insights into IDUs' perceptions of triple therapy. Focus group discussions revealed that efficacy, duration and side effects were mentioned as influences on intention to undertake HCV treatment. In most focus groups, participants were unanimous about the importance of these factors.

4.2.1. Treatment side effects

Most of the focus group participants asserted that the new triple therapy added a third drug and so added more side effects to the pegylated interferon and ribavirin. They cited dermatological side effects of the new drug as a factor which discouraged them from undertaking treatment. Most female participants were concerned about these side effects and their appearance. They mentioned skin rashes, irritation and itchiness that could damage their skin and that their skin might be affected for a long time, even after the completion of treatment. They believed the dermatological damage would be embarrassing in public, particularly in the workplace.

"I tried to look after my face and my body very well, because as a drug user I don't want people to judge me because of my appearance. So why should I go through a treatment that will affect my skin badly? The rashes might be itchy, which is so annoying. If the rashes stay on my skin for a while, I can't feel comfortable to go out in public" (female, 36 years).

Most focus group participants asserted that changes in physical appearance because of skin side effects, along with other physical side effects of pegylated interferon, could affect their functioning and particularly their working lives.

"I'm so scared to go through new treatment. How am I to face the new side effects? New meds mean more side effects, plus the interferon side effects, can affect my daily activities or limit my life in general. I know how the interferon affects you badly, plus the new side effects make us so sick for about one year. I really don't want to become sick" (female, 39 years).

The employed participants claimed that it was hard for IDUs to maintain permanent employment. They were worried that undertaking triple therapy might jeopardise their employment due to their inability to cope with harsh side effects while working full time. This led them to reject treatment. They believed that treatment side effects such as becoming anaemic, constant

headaches, vomiting and other side effects would be very difficult to tolerate while they were working.

"I can't lose my job because of the treatment side effects, as I have a permanent job. We are drug users; you should know that these days getting a job is very difficult especially for us drug users. We are not silly to put ourselves in a position where we have to think every day about losing our jobs because of not coping with the treatment side effects very well. Coping with the side effects such as headache, vomiting and et cetera is not easy to handle while working" (male, 38 years).

Participants received a powerful sense of personal satisfaction from their current jobs. It was very important for them to maintain their employment and keep their positions. They did not want to struggle to meet their work responsibilities while coping with HCV treatment.

"I've been working for a while, and as long as I'm very happy with it I can't see any point to lose my job because of HCV treatment. When I already know the physical side effects could debilitate my physical health, why should I lose my job because of HCV treatment? Why should I put myself in a situation where I have to struggle to do my work because of these side effects? Also, I can earn money which puts me away from financial pressure. To me, HCV treatment makes people lose their job, so why should I do it?" (male, 47 years).

Those participants who had a history of depression asserted that as long as interferon is involved in the HCV treatment course, they would encounter psychiatric side effects which could worsen their condition. One participant commented:

"I think as long as the interferon is attached to the HCV treatment, we are at risk of facing psychiatric side effects, so what's the point? To me it's not worth it; I've been dealing with my depression over the last six years. By going on HCV treatment, my depression can get worse" (male , 40 years).

However, those who reported no mental health problems similarly did not want to experience psychiatric side effects of treatment, which could disrupt their daily lives. They were also worried that psychiatric side effects might persist long after the treatment was completed. They perceived their drug addiction as a mental health issue which they were already struggling with; they did not have the capacity to deal with another psychiatric issue which might exacerbate their addiction.

"I never had any mental health issues except my drug issue. I believe if you don't face a mental health issue, you have it for a long time. It also can interrupt your daily life as well. You can't get rid of it easily. Already I have to deal with my drug addiction, so I don't want to deal with any other mental or psychiatric issue, which could intensify my addiction and I don't have the capability to handle it" (male, 42 years).

4.2.2 Treatment duration

A long treatment period was another hurdle identified by most of the focus group participants. They knew it may take 44 or 48 weeks because of their genotypes. They had no desire to make the commitment to undergo the triple therapy and in turn had a low level of intention to undertake this treatment.

"I believe the new triple treatment is still time-consuming and it is one of the main barriers which stops people from taking HCV treatment. This triple HCV treatment takes a long time and I think because of our genotype, which is type one, we have to be on treatment for nearly one year even with this new treatment of interferon, ribavirin with either telaprevir or boceprevir. This means we have to give commitment for a certain period to be on treatment. So at this stage we would not consider to go on HCV treatment until something comes up with a shorter duration" (female, 43 years).

Most of the focus group participants agreed that a commitment to 44 or 48 weeks of triple HCV treatment risked consequences such as loss of jobs, and hence income. They asserted that they would not be able to manage their HCV treatment while they were working. They spoke negatively of the time

required to attend clinics and undergo blood tests, which would interfere with their working lives.

"...Um everybody knows you can't handle treatment while you're working, especially those who have permanent jobs. There's a possible chance of losing your income, which drains you economically. As everybody disclosed their status at the beginning of this group discussion that we have a permanent job so for all of us taking HCV treatment with a permanent job is very hard. We can't give commitment to two things at the same time. Because HCV treatment is a long commitment, of forty-eight weeks, which we have to attend clinic appointments, blood tests and see the doctor or nurse on a regular basis which is not manageable while working on a full time basis and it can interrupt our work" (male, 40 years).

Some participants talked about the possibility of having to reduce their working hours during treatment, which might put them in a difficult financial position.

"It's hard to get through treatment while we're working. We have to be working at least on a part-time basis to be able to go on HCV treatment, and otherwise we have to deduct working hours. We don't want to earn less because of HCV treatment. This treatment needs a long commitment, which can have a negative impact on our work" (female, 42 years).

Problems related to duration of treatment were reported by other participants as influencing their intention to undertake HCV treatment. They affirmed that to be on treatment for 48 weeks or 44 weeks made them vulnerable to exhaustion, which would make them lose faith that they would be able to clear the virus. One participant stated:

"To be on HCV treatment for such a long time make us so exhausted and tired mentally and emotionally, also it make us negative about the result of treatment, thinking we won't get rid of the virus. It can get to the stage where we're sick of being on the treatment and we can't handle treatment, then we

have to pull out of treatment earlier than what is expected to finish" (male, 41 years).

Few thought they could stay on HCV treatment for 44 or 48 weeks; some said they would probably withdraw after a couple of weeks or in the middle of the course. Lengthy treatment duration is clearly one of the main reasons why so few HCV-positive IDUs undertake triple HCV treatment.

4.2.3 Treatment effectiveness

Another important theme common in the focus group discussions was the low efficacy of treatment. Lack of treatment efficacy led participants to feel uncertain and apprehensive about the uptake of HCV treatment, and the majority of the participants were hesitant about treatment and their chances of clearing the virus. They noted that there was a possibility that their HCV infection would rebound after treatment; this was because all focus group participants had genotype 1, and they believed that it is very hard to attain SVR through treating this genotype with interferon. Ultimately, they stated that they were unlikely to undertake triple therapy due to concerns about the efficacy of treatment.

"You know, I didn't know there is a new treatment for HCV until you informed us at the beginning of this group discussion. As you mentioned, the chances of success rate has increased with this new triple treatment compared to the old treatment, but it still doesn't guarantee 100% to get rid of the virus. So I don't see a specific point to go through such a journey while feeling insecure and unsure about the results. I believe as long as the treatment is not enough effective, the chances of clearing the virus is low, especially with our genotype. To me the most efficient treatment is a therapy which gives me a 100% guarantee to kill the virus, otherwise it is useless" (male, 37 years).

Participants in the non-treatment- group described HCV treatment as gambling. Likewise, the vast majority of focus group participants considered HCV treatment as gambling and as a risk that could result in emotional trauma

if they failed to clear the virus or pay off big if they succeeded in attaining SVR. In other words, it placed individuals in the stressful position of not knowing whether they would be a winner or loser. This is illustrated in the following quote:

"HCV treatment is like gambling, taking a risk. What I mean is you're taking a risk on whether or not you're going to be able to remove the virus from the body. Why should we put ourselves under pressure for something that we don't know if we will become a loser or a winner? If you think rationally, is it the right thing to do at this stage?" (female, 39 years).

They perceived HCV treatment as an investment and believed that this investment should produce a return, but were pessimistic about investing in it due to the low probability of eliminating HCV from their bodies. None was willing to pursue triple therapy. As another participant said:

"For me, if I go on HCV treatment, it is like investing my money on something. For any investment you put input and expect output. But if you look at the HCV treatment you just input, putting more effort and hard work for something that you don't know that you'll get something out of it. As my mate said, we can't do anything now about it. Of course nobody wants to waste their money and energy for something that there is no guarantee to clear it" (female, 42 years).

The vast majority of participants were not motivated to undertake HCV treatment due to having no guarantee of success. They claimed that they would undergo HCV treatment when a guarantee of eliminating the virus was given.

"Do you know why there are still lots of HCV cases? Users are still reluctant to undergo HCV treatment, because of fear of not clearing the virus. We don't want to experience HCV treatment and then at the end of treatment face a null response. This is so annoying, especially for us as active drug users, without an assurance to clear the virus, it is disappointing. That's why we are

still hesitant to go for HCV treatment; even the new treatment still doesn't have 100%" (male, 43 years).

"The issue with HCV treatment, even with the new treatment, is it is not medically developed enough to eradicate the virus. Also, we don't trust HCV treatment in general, even with the new triple treatment, so we don't have confidence in the treatment to actually get rid of the virus" (female, 40 years).

4.2.4 Stigma

All focus group participants acknowledged that they were susceptible to stigma because of HCV. They stated that there is a stigma associated with any HCV treatment. They described stigma as inseparable from HCV, which was a powerful barrier to undertaking HCV treatment. One participant had the following to say about stigma and treatment:

"Stigma is an important issue for people who are infected with HCV. We are at risk to be stigmatised and discriminated against. Stigma is always with HCV, old or new treatment doesn't make any difference and doesn't reduce the level of stigma. Stigma is still with HCV, as long as HCV exists, stigma is linked to it. Stigma can challenge us, when we have to perceive ourselves as new persons infected with HCV. This challenge may reduce our ability and intention to join with our social networks as well as disturbing our social activity. In order not to avoid this stigma and discrimination, we do not undergo treatment, even this new treatment" (female, 42 years).

Experience and fear of HCV-associated stigma were widely acknowledged in the focus groups. Most participants, who perceived stigma as a significant issue in their communities, brought up fears of being isolated from friends and family. They hid their HCV status, as they did not want to become socially isolated and suffer prejudice and stigmatisation.

"I don't want to tell anyone I'm HCV positive because I fear it will be revealed to my family and friends. I prefer not to tell anyone about my HCV status, because I can't handle the isolation and not being able to interact with my community, family and friends. This is hard and painful for me I don't feel

comfortable, because this is not who I am. I have to hide my status for avoiding stigma and discrimination" (male, 35 years).

In particular, employed participants resisted disclosing their status, as they believed that revealing their HCV status in the workplace would risk them being labelled and judged by their colleagues. Hence, they attempted to interact normally with their colleagues in order to avoid negative reactions associated with the HCV stigma.

"I am employed and it is not rational to reveal that we're HCV-positive so we are not stupid to disclose our status in the workplace, where others judge and label us. We attempt to have normal communication with our colleagues so we don't have to face a negative reaction in the workplace" (female, 38 years).

Concern about HCV-associated stigma was especially emphasised by those who had been discriminated against and stigmatised by their families and friends. They experienced social isolation and negative behaviour and reactions once they disclosed their HCV status. They experienced feelings of sadness, shame and particularly loneliness, and reduced self-esteem. They had lack of interaction with their family and their social network and so they felt like unvalued members of their community. This rejection by family and friends damaged their social functioning and their mental health; as one participant commented:

"I did the big mistake in my life that I told my family and my friend I have HCV. Since then I'm so sad, embarrassed and I felt so lonely because I'm judged all the time. Day by day the distance between me and my family gets bigger and I don't feel close to them anymore. I don't have confidence anymore to hang out with my friends or family. My family doesn't want me anymore, they never asked me for any social events such as birthdays and even New Year I always have to be on my own. I can't see myself as a valuable person within my family. When I see my family avoid me, what should I expect from others? It really hurts me mentally" (male, 37 years).

4.2.5 Lack of support

All of the focus group participants highlighted family as the most important source of support for enrolling in and completing HCV treatment. Without family support during HCV treatment, they felt they were likely to become exhausted and lose capacity for self-care and develop a sense of hopelessness, feelings of loneliness, isolation and depression. In other words, they believed that without a supportive family, they were more at risk of the psychological side effects of the treatment and the intensification of their mental health issues. They claimed that they do not wish to undertake HCV treatment if they did not have support from their family.

"The important thing is to have family support if we want to go on HCV treatment. I didn't tell my family I'm HCV positive, so I can't tell them if I go on treatment and I don't have a partner. With no family support, I can become so exhausted because I have to do everything on my own and this end up at the stage where I won't be able to take care of myself. Also I'll feel lonely, depressed, isolated and hopeless, plus the psychiatric side effect of interferon, which could amplify the effects. But if I had my family they could support me to cope with the treatment side effects, help me to adjust to the treatment and help me not to suffer from the emotional burden" (male, 38 years).

"How can I go on treatment when I don't have anyone to support me? I'm already depressed and isolated, so my mental health issue can get worse by undergoing HCV treatment. I don't have the capacity to handle everything on my own, so I'll be drained with no energy, become tired and not be able to care for myself. However, with family support you don't feel hopeless, depressed, and you don't suffer from emotional pain" (male, 43 years).

Participants placed great emphasis on family support as providing a strong and sustainable environment which can diminish the stress of HCV treatment and provide long-term emotional support, making it easier for them to cope with treatment side effects and other challenges.

"I believe that family support can provide a resilient, solid and defensible environment where they help to remove the stress and pressure from the treatment and make a peaceful environment for us. Family support is a reliable source of support which can help us to adjust with treatment" (male, 42 years).

The most important element of having a supportive family is the enhancement of self-esteem and hope for achieving SVR. Family support can also reinforce incentive to undertake HCV treatment.

"When people want to go on treatment they should make sure they have support from their family, have a close relationship and high interaction with their family. Because this boosts their self-esteem and their confidence to go for the treatment and give them hope to obtain a good outcome by strengthening their mental health, motivating and encouraging them to go for the treatment" (female, 34 years).

Besides emotional support, the participants agreed that family could play an important role in assisting them with daily activities.

"Having a supportive family gives a peaceful place where they are next to you, side by side, especially in daily activity. This is very important during HCV treatment, that you don't need worry about your daily tasks" (female, 38 years).

Finally, focus group participants concluded that a supportive family would enable them to express their frustration with HCV treatment and its side effects, talk about problems coping with side effects during treatment, and discuss anxiety and concern about clearing the virus during the treatment. Having a supportive family physically and emotionally during the treatment journey can help them to accomplish the full treatment course.

4.3 Summary

The results of the qualitative phase of the study were reported in this chapter. Analysis of the data collected through semi-structured interviews and focus group discussions found that HCV-infected IDUs who had experienced HCV treatment and those who had not experienced treatment maintained similar perceptions the treatment. While IDUs in the treatment group spoke about the factors that motivated them to undertake treatment, the entire qualitative sample reported common factors leading to treatment discontinuation and treatment refusal. There were no further themes that emerged from the focus groups, even though the efficacy of treatment was enhanced by triple therapy. The characteristics of the treatment, lack of support and stigma were the most common factors identified by these groups. The primary motivations for treatment uptake reported by the treatment group were to protect family, to increase personal quality of life and to preserve their careers. Hearing positive peers' experience of treatment or encountering peers who had cleared the virus motivated participants in the treatment group, while hearing negative stories from peers discouraged participants in the non-treatment group. In addition, some participants in the non-treatment group reported unstable housing as the most decisive factor determining their intention not to undertake HCV treatment. The results of the qualitative study contributed to the quantitative survey development to examine the factors that influence the intentions of IDUs infected with HCV to undertake treatment

Chapter 5: Quantitative Results

This chapter presents the findings of the quantitative phase of the research: a cross-sectional survey of HCV-infected IDUs who had not experienced HCV treatment. The quantitative phase assessed the prevalence rate of intention to undertake HCV treatment and determined the association between the independent variables and intention to undertake HCV treatment (the dependent variable). This chapter has three sections. The first section describes the socio-demographic characteristics of the quantitative sample and the responses from participants to the characteristics of treatment, stigma and support. The second section provides the results of univariate analysis of the associations between socio-demographic characteristics, drug-use history, health-care-seeking characteristics, characteristics of treatment, stigma and support and intention to undertake HCV treatment. Finally, multivariate logistic regression analysis identifies the independent predictors of intention to undertake HCV treatment.

No questionnaires had missing data or invalid responses. A total of 336 HCV-infected IDUs participated in the cross-sectional survey. Of these, 125 participants (37%) indicated that they had no intention to undertake HCV treatment and the remainder (n=211; 63%) indicated that they intended to undertake HCV treatment in the future.

5.1. Descriptive results

5.1.1 Socio-demographic characteristics

As indicated in Table 5.1, the sample contained almost equivalent numbers of males and females and the median age of participants was 40 years (range 24–60 years). Most participants had a stable home and lived with their partner or shared with others. A large minority (40%) of participants had left school at or prior to completing Year 11. A small proportion described themselves as Aboriginal. Just over half of all participants were married or in a

relationship. Most participants described themselves as unemployed and derived their main source of income from government benefits (Table 5.1).

Table 5.1 Socio-demographic data of survey participants

Socio-demo characteristics	n	%
Gender		
Male	162	48
Female	174	52
Median age (range)	40 (24-60)	
Accommodation		
Homeless	67	20
Not homeless	269	80
Live with		
Alone	34	10
Living with others or partners	235	70
Education		
≤Year11	134	40
Year 12 / TAFE/Uni	202	60
Ethnicity		
Aboriginal	41	12
Not Aboriginal	295	88
Marital status		
Single	150	44.6
Married/lived with sexual partner	186	61.3
Employment status and source of income		
Employed and employment	130	38.7
Not employed and government benefits	206	61.3

5.1.2 Drug -history characteristics

Participants identified heroin or methamphetamine as their preferred drug and these were the only commonly injected drugs in the six months prior to interview. A majority of participants reported methamphetamine as their preferred drug and the drug they had injected most often in the last six months. Most participants reported injecting once a day (Table 5.2).

The duration of injecting drug use for the participants ranged from 8 to more than 11 years. None of the participants reported injecting for less than 8 years. More than half of participants reported injecting for 8-10 years. About a third of participants indicated that they drank alcohol in the past year (Table 5.2).

Table 5.2 Drug-history characteristics of survey participants

Drug history	n	%
Preferred drug		
Heroin	139	41.4
methamphetamine	197	58.6
Drug most often used in the last 6 months		
Heroin	139	41.4
methamphetamine	197	58.6
Frequency of injection		
Once a day	135	40.2
> than once a day	201	59.8
Drug duration		
8-10 years	182	54.2
≥11 years	154	45.8
Alcohol		
Yes	119	35.4
No	217	64.6

5.1.3 Health-care- seeking characteristics

Of the 336 participants, nearly two thirds did not know their HCV genotype (Table 5.3). Just over half of all participants had been diagnosed with active HCV between 5–10 years before the survey, the remainder being diagnosed more than 10 years previously. A large minority of participants were unaware of HCV standard treatment and triple therapy before commencing the survey. Over half of participants reported that they had had a discussion about their liver health with their GP (Table 5.3).

Table 5.3 Health-care-seeking characteristics of survey participants

Healthcare-seeking characteristic	n	%

Knows HCV genotype,			
No		214	63.7
Yes		122	36.3
Years ago diagnosed HCV positive,			
5-10 years		188	56
>10 years		148	44
Being aware of HCV treatment before commencing the survey			
No		140	41.7
Yes		196	58.3
Had a discussion with GP about liver health status,			
No		148	44
Yes		188	56

5.1.4 Participants' perceptions of characteristics of treatment, stigma and support

As detailed in Chapter 3, an overall measure (combined median score) of perceptions of the characteristics of treatment, stigma and support in relation to the uptake of HCV treatment was computed and used in the analysis. A summary of participants' responses to these variables is presented in Table 5.4, which shows more than half of the participants (69.6%) agreed with the statement that they 'assumed that HCV treatment has a guaranteed cure' and 'once they clear the virus, the virus does not come back to them'. More than two-thirds (71%) stated that they assumed HCV treatment takes less than either 6 or 12 months, and does not involve harsh side effects. A similar proportion of the participants were concerned about the stigma associated with IDU and HCV. The vast majority of participants reported that they had a network of family and friends who could support them if they chose to undertake treatment.

Table 5.4 Proportions of IDUs' perceptions of characteristics of treatment, stigma and support

Statements	Strongly disagree	Disagree	neutral	Agree	Strongly agree

I assumed hepatitis C treatment has a guaranteed cure.	44(13)	50(15)	8(2.3)	89(26.4)	145(43.1)
I assumed once I clear hepatitis C virus, it does not come back.	44(13)	40(12)	18(5.3)	89(26.4)	145(43.1)
I assumed hepatitis C treatment takes less than 6 months.	35(10.4)	39(11.6)	22(6.5)	138(41)	102(30.3)
I assumed hepatitis C treatment takes less than 12 months.	45(13.4)	39(11.6)	12(3.5)	138(41)	102(30.3)
I assumed hepatitis C treatment does not involve harsh physical side effects.	20(6)	36(10.7)	40(12)	136(44.6)	104(30.9)
I assumed hepatitis C treatment does not involve harsh psychological side effects.	21(6.2)	35(10.4)	40(12)	130(38.6)	110(32.7)
I assumed hepatitis C treatment does not involve severe skin problems.	21(6.2)	30(9)	45(13.3)	120(35.7)	120(35.7)
I assumed hepatitis C treatment does not involve post-treatment side effects.	21(6.2)	35(10.4)	40(12)	130(38.6)	110(32.7)
I feel I need to hide the fact that I am a drug user and have hepatitis C.	48(14.3)	52(15.5)	0	130(38.6)	106(31.5)
I believe injecting drug users with hepatitis C are treated like outcasts.	48(14.3)	52(15.5)	0	130(38.6)	106(31.5)
I feel I wouldn't get as good health care if health care providers knew about my drug status.	47(14)	53(15.8)	0	131(39)	105(31.3)
I fear my family and my friend would reject me if they learned about my illness.	48(14.3)	52(15.5)	0	130(38.6)	106(31.5)
There is a special person who is around when I am in need with my daily chores.	40(12)	50(14.8)	50(14.8)	94(28)	102(30.3)
	40(12)	45(13.3)	55(16.3)	94(28)	102(30.3)

There is a special person with whom I can share my joys and sorrows.					
I have a special person who is a real source of comfort and help to me.	40(12)	50(14.8)	50(14.8)	94(28)	102(30.3)
I get the emotional help and support I need from either family or friends.	40(12)	50(14.8)	50(14.8)	94(28)	102(30.3)

5.2 Univariate analysis

5.2.1 Univariate analysis of socio-demographic characteristics by HCV treatment intention

Table 5.5 shows the characteristics of the study sample by intention to treat status. A large majority of women (84.5%) indicated an intention to undertake treatment, compared to men (39.5%) (p<0.001). Participants aged 40 or over (72%) were more likely to report an intention to undertake HCV treatment than those who were less than 40 years old (53.5%) (p<0.001). Seventy-six per cent of participants who had stable housing described an intention to undergo treatment compared to a small fraction of homeless participants (7.5%) (p<0.001). Most IDUs (78%) who lived with their partners or shared housing with others indicated an intention to undertake HCV treatment compared to those who lived alone (29%) (p<0.001). IDUs with a secondary school education or education beyond secondary school (91%) were more likely to report intention to undergo treatment than less educated participants (19%) (p<0.001) (Table 5.5).

Non-Aboriginal IDUs (70%) were more likely to indicate an intention to undergo HCV treatment than Aboriginal IDUs (12%) (p<0.001). Most IDUs (84%) who lived with their sexual partner or were married expressed their intention to undertake HCV treatment in contrast to (37%) of those who were either single or divorced (p<0.001). Non-employed IDUs who derived their major source of income from government benefits (67%) had higher levels of intention to undertake HCV treatment than employed IDUs who received their major source of income from their jobs (56%) (p=0.045) (Table 5.5).

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Table 5.5 Univariate analysis of socio-demographic characteristics by HCV treatment intention

Demographic characteristics	Overall 336(100%)	Intention to undertake HCV treatment 211(63%)	No intention to undertake HCV treatment 125(37%)	p-value &Chi-square	Odds Ratio& 95% CI
Gender					
Male	162 (48)	64 (39.5)	98 (60.5)	p<0.001	OR:8.33
Female	174 (52)	147 (84.5)	27 (15.5)	χ^2=72.64	CI:4.97,13.98
Age group					
< 40 years	170 (50.6)	91 (53.5)	79 (46.5)	p<0.001	OR:2.26
≥40 years	166 (49.5)	120 (72.3)	46 (27.7)	χ^2= 12.65	CI:1.42,3.56
Accommodation					
Homeless	67 (20)	5 (7.5)	62 (92.5)	p<0.001	OR:40.54
Not homeless	269 (80)	206 (76.6)	63 (23.4)	χ^2=109.68	CI:15.62,105.2
Living:					
Alone	34 (10)	10 (29.4)	20 (58.8)	p<0.001	OR:9.17
With others or partners	235 (70)	183 (78)	52 (22.1)	χ^2=76.04	CI:5.38,15.64
Education					
≤11	134 (40)	26 (19.4)	108 (80.6)	p<0.001	OR: 40.2
Year 12/ TAFE/Uni	202 (60)	185 (91.6)	17 (8.4)	χ^2=179.66	CI:23.46,87.0
Ethnicity					
Aboriginal	41 (12)	5 (12)	36 (88)	p<0.001	OR:52.17
Non-Aboriginal	295 (88)	206 (70)	89 (30)	χ^2= 51.18	CI:26.49,102
Marital status					
Single	150 (44.6)	55 (36.7)	95 (63.3)	p<0.001	OR: 8.98
Married/lived with sexual partner	186 (61.3)	156 (84)	30 (16.1)	χ^2=79.19	CI:5.37,14.9
Employment status					
Employed	130 (38.7)	73 (56.2)	57 (43.8)	p=0.045	OR:1.58
Not employed	206 (61.3)	138 (67)	68 (33)	χ^2=4.006	CI:1.0,2.49
Source of income					
Employment	130 (38.7)	73 (56.2)	57 (43.8)	p=0.045	OR:1.58
Government benefits	206 (61.3)	138 (67)	68 (33)	χ^2=4.006	CI:1.02,2.49

5.2.2 Univariate analysis of drug-history characteristics by HCV treatment intention

Table 5.6 provides an overview of the univariate analysis of drug-history and intention to treat. Methamphetamine users (those who nominated methamphetamine as their drug of choice and injected it most often in the last six months) were more likely to express an intention to undergo HCV (68%) treatment than heroin users (55.5%) (p=0.018). A significantly higher proportion of IDUs who had injected for between 8 and 10 years (77%) reported an intention to undergo HCV treatment than IDUs who had injected for more than 11 years (50.5%) (p<0.001). IDUs who did not drink alcohol in the past year (88%) were more likely to intend to undertake HCV treatment than IDUs who had consumed alcohol (17%) (p<0.001) (Table 5.6).

Table 5.6 Univariate analysis of drug-history characteristics by HCV treatment intention

Drug history	Overall 336(100%)	Intention to undertake HCV treatment 211(63%)	No intention to undertake HCV treatment 125(37%)	p-value &Chi-square	Odds Ratio& 95% CI
Preferred drug and drug most often used in the last 6 months					
Heroin	139(41.4)	77(55.4)	62(44.6)	p=0.018	OR:1.71
Methamphetamine	197(58.6)	134(68)	63(32)	χ^2=5.56	CI:1.09,2.68
Frequency of injection					
Once a day	135(40.2)	79(58.5)	56(41.5)	p=0.18	OR:1.35
> than once a day	201(59.8)	132(65.7)	69(34.3)	χ^2=1.76	CI:0.865,2.12
Drug duration					
8-10 years	182(54.2)	92(50.5)	90(49.5)	p<0.001	OR:3.32
>11 years	154 (45.8)	119(77.3)	35(22.7)	χ^2=25.49	CI:2.067,5.35
Alcohol					
Yes	119(35.4)	20(16.8)	99(83.2)	p<0.001	OR:36.36
No	217(64.6)	191(88)	26(12)	χ^2=166.82	CI:19.33,68.37

5.2.3 Univariate analysis of healthcare-seeking characteristics by HCV treatment intention

Table 5.7 provides an overview of the univariate analysis of health care seeking behaviour and intention to treat. IDUs who were aware of both HCV genotype (97%) and HCV treatment before commencing the survey (92%) were more likely to report an intention to undertake HCV treatment compared to those who were unaware of their genotype (43.5%) and HCV treatment (21.4%) (p<0.001). IDUs diagnosed with HCV infection more than 10 years before the survey (76.5%) were more likely to report an intention to undergo HCV treatment than those who were diagnosed from 5 to 10 years previously (52%) (p<0.001). A higher proportion of IDUs (97%) who had discussed their liver health status with their GPs had more intention to undertake treatment than IDUs who did not have discussion (19.6) (p<0.001) (Table 5.7).

Table 5.7 Univariate analysis of healthcare -seeking characteristics by HCV treatment intention

Health-care-seeking characteristic	Overall 336(100%)	Intention to undertake HCV treatment 211(63%)	No intention to undertake HCV treatment 125(37%)	p-value & chi-square	Odds Ratio & 95% CI
Knows HCV genotype					
No	214 (63.7)	93 (43.5)	121 (56.5)	p<0.001	OR:38.38
Yes	122 (36.3)	118 (96.7)	4 (3.3)	χ^2=94.35	CI:13.66,107.7
Years since diagnosed HCV positive					
5-10 years	188 (56)	98 (52.1)	90 (47.9)	p<0.001	OR:2.95
>10 years	148 (44)	113 (76.4)	35 (23.6)	χ^2=20.79	CI:1.84,4.76
Awareness of HCV treatment					
No	140 (41.7)	30 (21.4)	110 (78.6)	p<0.001	OR:44.24
Yes	196 (58.3)	181 (92.3)	15 (7.7)	χ^2=175.81	CI:22.78,85.9
Having had a discussion with GP about liver health					
No	148 (44)	29 (19.6)	119 (80.4)	p<0.001	OR:124
Yes	188 (56)	182 (96.8)	6 (3.2)	χ^2=211.3	CI:50.15,308.88

5.2.4 Univariate analysis of characteristics of treatment, stigma and support by HCV treatment intention

Table 5.8 shows the results of the univariate analysis using the combined explanatory variables and intention to undertake treatment. A majority of participants (87%) who assumed that the treatment provides a guaranteed cure with protection against relapse (treatment effectiveness) were more likely to intend being treated than those who did not assume these (p<0.001). Participants who assumed that HCV treatment takes less than either 6 or 12 months (treatment duration) (76 %) were more likely to report an intention to undertake HCV treatment than those who did not assume (29%) (p<0.001).

The same proportion of participants who assumed that treatment does not involve harsh side effects (76 %) reported an intention to undergo HCV treatment compared to 29% of those who did not make this assumption (p<0.001). IDUs who were concerned about stigma attached to IDUs and HCV (58.5%) were less likely to intend being treated than those who were not concerned (73%) (p=0.012). A higher proportion of participants who had social support for HCV treatment (92%) described an intention to undertake treatment, than those who did not have such support (12%) (p<0.001)

Table 5.8 Univariate analysis of characteristics of treatment, stigma and support by HCV treatment intention

Variables	Overall 336(100%)	Intention to uptake HCV treatment 211(63%)	No intention to uptake HCV treatment 125(37%)	P-value &chi-square	Odds Ratio & CI
(Treatment effectiveness) Assumption HCV treatment provides both a guaranteed cure and protection against relapse					
Disagree	102 (30.4%)	8 (7.8)	94 (92.2)	P<0.001	OR:76.9
Agree	234 (69.6%)	203 (86.8)	31 (24.8)	χ^2=189.32	CI:34, 173.7
(Treatment duration) Assumption HCV treatment duration takes less than either 6 or 12 months .					
Disagree	96 (28.6)	28 (29.2)	68 (70.8)	P<0.001	OR:7.7
Agree	240 (71.4)	183 (76.3)	57 (23.8)	χ^2=65.06	CI:4.5,13.2

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(Treatment side effects) Assumption HCV treatment does not involve harsh side effects					
Disagree	96 (71.4)	28 (29.2)	68 (70.8)	P<0.001	OR:7.7
Agree	240 (28.6)	183 (76.3)	57 (23.8)	χ^2=65.06	CI:4.5,13.2
Concern about Stigma					
Disagree	100 (29.8)	73 (73)	27 (27)	P<0.012	OR:0.521
Agree	236 (70.2)	138 (58.5)	98 (41.5)	χ^2=6.34	CI:0.31, 0.86
Having Support					
No	140 (41.7%)	30 (21.4%)	110 (78.6%)	P<0.001	OR:44.24
Yes	196 (58.3%)	181 (92.3%)	15 (7.7%)	χ^2=175.81	CI:22.78,.85.9

5.3. Multivariate analysis

5.3.1 Intention to undertake treatment and socio demographic, drug-history and health-care-seeking characteristics

The factors that were associated with intention to undertake treatment in the univariate analysis at a significance level of p<0.10 were included in a multivariate logistic regression model to determine the independent predictors of intention to undertake HCV treatment.

The variables included in the model were gender, age group, accommodation status, living arrangements, marital status, ethnicity, education, employment, source of income, methamphetamines and heroin users, drug duration, drinking alcohol in the past year, awareness of HCV treatment and genotypes, knowing about HCV status and having discussion about their liver health status with a GP. Interaction terms were examined by the following: drinking alcohol in the past year and having discussion about their liver health status with a GP; awareness of HCV genotypes and having discussion about their liver health status with a GP; and awareness about HCV treatment and having discussion about their liver health status with a GP, to eliminate potential multicollinearity effects (Aiken and West 1991). The level of significance for the retention of variables in the multivariate model was set at p<0.05.

The factors that remained significantly associated with intention to take up HCV treatment among HCV-infected IDUs included accommodation status, drinking alcohol in the past year and ethnicity (Table 5.9). The model was statistically significant, χ^2=310.741, indicating that it was able to distinguish between participants who intended and did not intend to undertake HCV treatment. The model as a whole explained between 60.3% (Cox and Snell R squared) and 82.3% (Nagelkerke R squared) of the variance in intention status and correctly classified 91.4% of cases. IDUs with intention to treat were more likely not to be Aboriginal (AOR: 8.07, 95% CI: 3.17, 20.54) and to have stable accommodation (AOR: 6.59, 95% CI: 2.302, 18.88). Also, those participants who intended to treat were more likely not to have drunk alcohol in the previous year (AOR: 6.32, 95% CI: 2.47, 16.15). The interaction terms described above were not significant and were not included in the final model.

Table 5.9 Multivariate analysis of socio-demographic, drug-history and HCV related characteristics associated with HCV treatment intention

Characteristics	n	p	AOR	95% CI
Ethnicity				
Aboriginal	37			
Not Aboriginal	301	<0.001	8.07	3.176,20.54
Accommodation				
Homeless	67			
Not homeless	269	<0.001	6.59	2.302,18.88
Drinking Alcohol				
Yes	119			
No	217	<0.001	6.32	2.476,16.15

5.3.2 Intention to undertake treatment and treatment effectiveness, treatment side effects, treatment duration, support and stigma

All the variables shown in Table 5.10 (treatment effectiveness, treatment side effects, treatment duration, support and stigma) were significant (p < 0.10) in the univariate analysis and were included in the multivariate analysis to

determine the independent predictors of intention to undertake HCV treatment adjusting for potential confounding.

In the multivariate analysis, variables were retained in the final model if p<0.05. All except treatment duration remained significantly associated with intention to undertake HCV treatment among HCV-infected IDUs (Table 5.10). The model was statistically significant, $\chi^2 = 297.649$ indicating that it reliably distinguished participants with and without intention to undertake HCV treatment. The model as a whole explained between 58.8% (Cox and Snell R square) and 80.2% (Nagelkerke R squared) of the variance in intention to undertake treatment and correctly classified 88.4% of cases. Significant predictors of intentions to undertake HCV treatment among IDUs were support, side effects, effectiveness, and stigma. IDUs with intention to treat were more likely to have social support (AOR: 51.75, CI: 12.47, 214.73), to assume no harsh side effects are involved in HCV treatment (AOR: 22.73, CI: 5.91, 87.47) and to assume treatment provides a guaranteed cure with protection against relapse (AOR: 10.675, CI: 3.889, 29.301). However, IDUs with intention to undergo treatment were less likely to express concern about stigma associated with HCV and IDU (AOR: 0.03, CI: 0.007, 0.19).

Table 5.10 Multivariate analysis of characteristics of treatment, stigma and support associated with HCV treatment intention

Characteristics	n	p	AOR	CI
Support				
No	140			
Yes	196	<0.001	51.75	12.472,214.73
Treatment side effects				
Disagree	96			
Agree	240	<0.001	22.73	5.910,87.474
Treatment Effectiveness				
Disagree	102			
Agree	234	<0.001	10.67	3.889,29.301
Stigma				
Disagree	100			
Agree	236	<0.001	0.36	0.007,0.198

5 .4 Summary

This chapter has demonstrated the results from the analysis of data collected from a survey of 336 participants recruited in the Perth metropolitan area. The quantitative analysis found a number of associations between intention to undertake HCV treatment and other variables. Several of these associations were statistically significant. After adjustment for confounding variables, the multivariate analysis of the factors associated with intention to undertake HCV treatment revealed several factors, including: the assumption that HCV treatment provides both a guaranteed cure and protection against relapse; the assumption that HCV treatment takes less than 6 or 12 months; the assumption that HCV treatment does not involve harsh side effect; concern about stigma; having social support; not drinking alcohol in the past year; non-Aboriginal ethnicity; and having stable housing status. Sixty-three percent of participants expressed their intention to undertake HCV treatment in the study sample. The next chapter of the thesis provides a discussion of these findings.

Chapter 6: Discussion

This chapter contains a discussion of the study findings of the factors influencing the intentions of HCV-positive IDUs in the Perth metropolitan area with respect to HCV treatment. The study was based on the standard combination treatment of pegylated interferon and ribavirin and triple treatment. The aim of the study was to gain a better understanding of what factors influence the intention of HCV-infected IDUs to undertake HCV treatment. The study involved both qualitative and quantitative methods: semi-structured interviews, focus groups and a cross-sectional survey. This mixed-methods approach enabled the researcher to gain a comprehensive understanding of the factors influencing the uptake of treatment. Although there were some inconsistencies between the qualitative and quantitative findings, there were also many complementary findings.

This chapter considers the empirical evidence produced in the current study in the context of other research in the area of HCV treatment. The chapter begins with a summary of the combined qualitative and quantitative findings in which the common factors (treatment side effects, treatment effectiveness, support, stigma and housing status) are discussed. Then, the remaining factors (treatment duration, peer experiences, the benefits of treatment, alcohol consumption and ethnicity are discussed separately because they were not common across all three data collection methods. Finally, the prevalence rate of intention to undertake treatment is discussed.

6.1 Summary of key findings in relation to research field

6.1.1 Treatment side effects

One the most important findings from the qualitative study was that the side effects of HCV treatment were the main reason for treatment discontinuation

and treatment refusal. The critical side effects reported by study participants in the treatment group were physical, psychological and dermatological. The physical side effects most frequently reported by participants in the treatment group were nausea with vomiting, anorexia, dry mouth, and flu-like symptoms (fatigue, body and muscle pain, and headaches). The psychiatric side effects most frequently reported were depression, mood swings, anxiety, insomnia and suicidal thoughts. Cognitive side effects were reported by several participants in the treatment group. These included forgetfulness, poor concentration, attention difficulties, and poor recall. Skin rashes, itching and skin dryness were also reported by some female participants in the treatment group. The importance of these physical and psychological side effects of treatment were confirmed by most participants in the non-treatment group and focus groups, who reported that fear of these side effects was one of the main reasons for not intending to undertake HCV treatment.

Physical side effects, particularly gastrointestinal disturbances (nausea, vomiting, decreased appetite) and flu-like symptoms, have been identified as key factors for treatment withdrawal and treatment refusal in similar studies (Fried et al. 2002, Hopwood and Treloar 2005), which noted between 43% (Fusfeld et al. 2013) and 69.5% (Manos et al. 2013) of patients reporting physical symptoms that resulted in early treatment discontinuation. Psychiatric side effects, particularly feelings of depression, decreased interest and pleasure, feelings of worthlessness, anxiety, insomnia and suicidal thoughts, have been identified as significant factors for treatment discontinuation and treatment refusal in other studies, occurring in 30% to 70% of patients (Schaefer et al. 2012 , Manos et al. 2013).

Scholars have reported the incidence of impaired concentration or "brain fog" ranging between 15% (Schaefer et al. 2012) and 53% (Manos et al. 2013). These and other cognitive side effects have resulted in early treatment discontinuation (Lotrich 2009, Janssen et al. 1994, Schaefer et al. 2012, Trask et al. 2000), as has experience of skin problems (Hopwood, Treloar, and Redsull 2006, Hopwood 2009, Sgorbini, O'Brien, and Jackson 2009, Veluru

et al. 2010), which were not physically painful but distressing to female participants in the treatment group in the current study.

Qualitative study highlights of the impact of physical and psychiatric side effects on treatment cessation and the fear of these side effects leading to treatment refusal. Several participants in the treatment group reported taking anti-nausea, antidepressants, pain relief and anti-inflammatory medications and resting thoroughly, but reported that these measures were ineffective and they were still unable to eat, experienced depressive symptoms and had fatigue and headaches. Impaired cognitive performance, such as difficulty in concentrating and forgetfulness, were very discouraging for several participants, leading to additional stress such as inability to remember job duties or recall required daily actions or tasks. The few participants who used moisturising lotions and topical steroid creams to relieve skin conditions reported that these were ineffective and they had still distressing skin problems. These treatment experiences reflected the expectations of non-treatment group and focus group participants' concerns about being unable to cope with treatment side effects.

The current study showed that physical and psychiatric side effects are associated with discontinued and refused treatment at least partly due to their negative impacts on ability to function, maintain a social life and maintain mental health and emotional stability. Several other studies have reported that HCV treatment can significantly decrease quality of life and affect lifestyle (Fusfeld et al. 2013, Doab, Treloar, and Dore 2005, Treloar and Hopwood 2008, Treloar, Newland, et al. 2010, Treloar et al. 2014), and that psychiatric side effects of HCV treatment can impair mental health and decrease patients' social engagement (Hopwood and Treloar 2005, Fraenkel et al. 2006, Russo and Frie 2003, Fried 2002, McNally, Sievert, and Pitts 2006, Fusfeld et al. 2013).

Participants in the treatment group reported that their reduced ability to function and to maintain social interactions, routine daily life and mental

health stability had an impact on work, home/family life and social life. Concern about the dermatological effects of treatment adversely affecting participants' appearance was also expressed by some. Participants in the non-treatment and focus groups reported a similar struggle and expectations of difficulties in fulfilling their day-to-day responsibilities due to the physical and psychiatric side effects of HCV treatment. Likewise, expected negative effects on family functioning, daily routines, work, finances and mental health were also reported by non-treatment and focus group participants. For example, several participants in the non-treatment group and focus groups who had pre-existing psychiatric illnesses such as depression expressed their concern about treatment exacerbating their mental health issues. Those with no history of mental health issues were concerned about becoming depressed or experiencing anxiety and mood swings and of the consequences of being prescribed and taking antidepressants for long periods.

Treatment group participants who were employed were often unable to maintain a balance between work, home life and treatment, finding it harder to plan their schedules, perform routine tasks and maintain their social contacts. This often resulted in isolation, lack of desire or interest to engage in social interaction, and poor work performance. Many reported a need to reduce their work hours, while others were forced to take sick leave. Employed participants in the non-treatment group and focus groups similarly reported that they did not want to jeopardise their employment status by undertaking HCV treatment. In particular, those who had re-entered the workforce in recent years were worried they might need to reduce or cease work due to the physical side effects of HCV treatment, and asserted that they had more pressing concerns and challenges in their lives.

Both univariate and multivariate analyses found that the expectation of not involving harsh side effects in HCV treatment increased intention to take up treatment. The qualitative analysis revealed that a significant proportion of non-treatment group and focus group participants had no or low levels of intention to undertake HCV treatment, either actively through refusal or

passively through deferring due to a very high incidence of unwanted side effects which were associated with poor quality of life. Therefore, it is clear that treatment side effects influenced intention to undertake HCV treatment. These results support the need for more refined treatment regimens that reduce treatment side effects.

Previous research has not determined treatment side effects as a potential predictor of intention to undertake HCV treatment. Nevertheless, further national study in this area is needed, particularly with the recent availability of new interferon-free treatments (DAAs) to confirm this predictor. As reported above, most of the treatment side effects were associated with interferon, so DAAs when given without interferon greatly reduce the occurrence and severity of adverse side effects. This greater tolerability makes HCV treatment more appealing and improves people's ability to comply with the prescribed regime, and is resulting in increased uptake and successful completion of treatment (Jensen and Holle 2016). It also reduces the need for lifestyle modifications, such as using adaptive or resilience techniques, and prescription medications. DAAs eliminate problems for patients with pre-existing psychiatric disorders, and employed individuals can undertake treatment without being concerned about their work performance.

Despite the vast improvements in tolerability associated with DAAs, a recent study showed that side effects such as fatigue, nausea, headache and anaemia still occurred in 19% of patients who were treated with sofosbuvir–velpatasvir for 12 weeks, 18% of those who were on sofosbuvir–velpatasvir for 24 weeks, and 16% of those who received 12 weeks of sofosbuvir–velpatasvir in combination with ribavirin (Curry et al. 2015). Treatment for genotype 4 still involves pegylated interferon in combination with the new HCV treatments (see Figure 2.1), which means some HCV patients will continue to suffer the harsh side effects of pegylated interferon.

6.1.1 Treatment effectiveness

Poor treatment effectiveness was one of the main reasons for treatment discontinuation and refusal by the qualitative study participants. Most treatment group participants reported at least one episode of treatment in which they had failed. Lack of treatment efficacy has been identified as a significant reason for withdrawal from treatment and treatment refusal in previous studies (Doab, Treloar, and Dore 2005, Treloar and Holt 2008, Treloar and Hopwood 2008, Treloar and Rhodes 2009, Treloar, Newland, et al. 2010, Treloar et al. 2012 , Treloar et al. 2014). Lower adherence to HCV treatment is seen among HCV-infected IDUs concerned about treatment efficacy (McNally, Sievert, and Pitts 2006, Treloar, Newland, et al. 2010, Khokhar and Lewis 2007, Parkes et al. 2006, Treloar and Holt 2008, Lally et al. 2008, Kinder 2009), ranging from 26% (Fusfeld et al. 2013) to 47% (Zeremski et al. 2014).

The results related to this finding provide additional insights into the lack of treatment effectiveness leading to treatment refusal and treatment cessation. For example, several treatment group participants were not satisfied with their treatment regime as they did not achieve SVR by the halfway mark, and some participants with genotype 3 relapsed after completion of treatment. Most treatment-naïve participants reported that lack of treatment effectiveness – as they saw it, too low a probability of clearing the virus – generated substantial uncertainty over whether to undertake treatment.

The qualitative findings highlight that fear of HCV relapse and having to undergo treatment again were the primary reasons that low treatment effectiveness led to treatment cessation or treatment refusal. In an Australian study, HCV-positive individuals under an opiate substitution treatment also questioned the efficacy of HCV treatment (Treloar, Newland, et al. 2010). Mehta et al. (2008) showed that 87% of participants who remained concerned about the efficacy of treatment refused to undertake HCV (Mehta et al. 2008). Studies have also reported that fear, scepticism and mistrust about treatment efficacy reduced adherence, while trust in drug efficacy and positive

expectations increased adherence (Mishra et al. 2011, Mohan et al. 2013). In this study's treatment group, participants with genotypes 1 and 3 reported that being unable to achieve SVR led to loss of hope about clearing the virus; in contrast, one male participant accepted the unpredictability of HCV treatment despite three failures.

Participants in the qualitative phase of the research agreed that they had to wait for another round of treatment to have a near-guarantee of achieving SVR. The necessity of a very high probability of cure was a strong theme across the qualitative phase of the study, and the lack of it caused much dissatisfaction and distrust with the HCV treatment process. The quantitative survey data fully supported this finding. Univariate and multivariate analyses found that the idea of a guaranteed cure with protection against relapse increased intention to undertake HCV treatment. Treatment effectiveness identified as a predictor of intention to undertake HCV treatment in this study. However, there is no published literature in the context of treatment efficacy as a potential predictor of intention to undertake HCV treatment.

Despite DAAs' huge improvement in treatment efficacy, a small proportion of HCV patients do not respond (Sarrazin 2016, Colpitts and Baumert 2016), particularly patients with advanced liver disease, HIV/HCV coinfection (Sarrazin 2016) or poor adherence, when the medications are not taken as prescribed and on schedule, and individuals miss doses (Smith, Chan, and Mohammad 2015). Factors influencing poor adherence to HCV treatment include unstable housing, forgetfulness, lack of priority, patients' lack of control in their lives, and pre-existing psychiatric illness (Weiss et al. 2009, Marcellin et al. 2011, Mishra et al. 2011), confirmed by the qualitative phase of the current study. These factors may create some restriction to full adherence to the prescribed new HCV treatment as instructed, and subsequently could increase the likelihood of developing drug resistance and treatment failure (Colpitts and Baumert 2016). Treatment adherence poses a similar challenge for DAAs as it did for interferon-based HCV medications;

further research needs to be undertaken to determine how to maximise adherence.

6.1.2 Support

Lack of support was another main reason for treatment discontinuation and treatment refusal specified by the qualitative phase participants. For example, several participants in the treatment group reported that their family did not respond to their negative thoughts and stressors, nor did they create a sympathetic environment. The absence of social support has been identified as a key factor for treatment withdrawal treatment and treatment refusal in similar studies (Evon et al. 2011, Phillips and Barnes 2016).

A lack of support increases the burden on the individual and can lead to treatment discontinuation, refusal or deferral of HCV treatment (Evon et al. 2011, Sgorbini, O'Brien, and Jackson 2009). Study participants lacking support reported reduced ability to cope with treatment side effects, to function and to maintain emotional stability. Other studies have reported that lack of social support can lead to increased depressive symptoms, decreased ability to cope with treatment side effects, and reduced motivation to undertake and complete treatment (Evon et al. 2011, Rifai et al. 2006). Studies have also reported that in the absence of support, maintaining stability, a normal lifestyle, daily routines and healthy behaviour is difficult (Blacklaws et al. 2009, Fraenkel et al. 2006, Evon et al. 2011). Due to a perceived lack of support, participants in the treatment group reported that they relied on their own efforts and ability during treatment, which imposed a burden of self-control, increased distress and depression, and lost confidence in their ability to complete treatment.

Qualitative phase participants reported their beliefs that lack of solid supportive networks (providing care, love, respect, understanding, hope, encouragement and physical support, such as help with household tasks and child care) would make the treatment journey even more challenging. However, the quantitative data indicated that 58% believed they would have

social support if they undertook HCV treatment. A possible reason for this discrepancy between the qualitative and quantitative outcomes is that more IDUs in the qualitative study lived alone and had experienced family breakdown, so lacked strong and intimate relationships with their families. Additionally, the family members of some of the qualitative phase participants suffered from drug addiction or chronic illness or were concerned about becoming infected with HCV, further reducing support. In the quantitative study, 70% of study participants lived with their families and placed great value on a supportive family in relation to the uptake of HCV treatment.

Similarly, the few participants in the treatment group who had cleared HCV reported that they obtained constant and full support from their family during treatment. They reported that their families sacrificed aspects of their own lives, resigning from their jobs and committing significant time and effort to keep them motivated to complete the treatment. HCV patients who perceived satisfying levels of social support experienced fewer adverse side effects during treatment, resulting in improved treatment outcomes due to reduced psychological distress (Evon et al. 2011, Sgorbini, O'Brien, and Jackson 2009). Support was identified as a predictor of intention to uptake HCV treatment in both univariate and multivariate analyses. This is line with other studies, which found that family support was independently associated with HCV treatment (Alavi et al. 2013 , Alavi et al. 2015, Wilson et al. 2010)

The quantitative study suggested that IDUs who intended to undergo HCV treatment in the future were many times more likely to have social support. This is congruent with previous studies which have reported that individuals with greater social support from family and/or friends are more willing and better equipped to manage HCV treatment and hence more likely to be assessed for treatment and to commence therapy (Grebely, Bryant, et al. 2011, Alavi et al. 2013 , Alavi et al. 2015). The role of family is important even with the new interferon-free treatments; for while the side effects of the new DAA treatment are less severe than with interferon-based treatments, they do

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still occur, adherence is crucial. Family members can remind patients to take their medications on schedule, support them to remain engaged in treatment and provide positive energy and emotional closeness. The availability of a safe and supportive network is associated with high adherence to HCV treatment, mainly because IDUs are cushioned against missing doses (Newman et al. 2013, Edlin 2002).

6.1.3 Stigma

Stigma was identified in the qualitative phase of this study as an important factor in relation to HCV treatment uptake. Almost all participants in the treatment group had hidden their current IDU status from their health care providers due to fear of being judged and labelled as dirty or second-class citizens and not being treated like other patients with HCV. Also, some participants in the treatment group were stigmatised by their own family for being IDUs and concealed their HCV status and treatment status due to fear of additional stigma. Similarly, most participants in the non-treatment group and focus groups reported fear of being judged by health care providers, their families and even friends, which made them reluctant to undertake HCV treatment. Stigma associated with IDU and/or HCV has been identified previously as a key reason to conceal IDU and/or HCV status, as well as for reduced intention to engage with HCV treatment. Family (Hopwood 2009, Wilson et al. 2010, Treloar, Rance, and Backmund 2013, Grebely et al. 2009) and health care settings can be significant sources of stigma for IDUs with HCV (Harris 2009, Tinda, Cook, and Foster 2010, Treloar, Rance, and Backmund 2013, Sgorbini, O'Brien, and Jackson 2009, Grebely et al. 2009).

In this study, most participants in the treatment group reported that they did not believe they could be honest about their IDU status and HCV status and therefore continued to interact normally with health care providers and their families. Many participants in the non-treatment group and focus groups reported that health care services treated them differently from people with other chronic diseases; they did not meet their needs and their expectations, and they inevitably assumed that the ineffective care they received was

because of being an IDU. Several other studies have reported that stigma reinforces perceptions of being poorly treated, isolates individuals and leads to unwillingness to seek HCV care and disclose HCV or drug status (Sgorbini, O'Brien, and Jackson 2009, Tinda, Cook, and Foster 2010, Harris and Rhodes 2013). Several participants in the treatment group reported that they did not obtain family and health care providers' support due to fear of rejection, verbal, physical and emotional abuse and disgrace. Some participants in the non-treatment and focus groups reported that they lost social interaction and social networks once they disclosed their HCV status.

Most qualitative participants reported that they perceived negative attitudes towards them in health care settings, particularly the GP setting, where they perceived both a lack of trust and unwillingness to treat IDUs with HCV. This finding is similar to several previous studies (Tinda, Cook, and Foster 2010, Marinho and Barreira 2013 , Treloar, Rance, and Backmund 2013). These results were confirmed in the analysis of the survey data. IDUs who were concerned about stigma were less likely to intend undertaking treatment. However, this is in contrast to a study by Wilson et al., the only quantitative study which assessed the association between stigma and undertaking HCV treatment (Wilson et al. 2010). Wilson and his colleagues showed that participants who were most concerned about the risks associated with disclosing their HCV status were more likely to consider treatment (Wilson et al. 2010). This discrepancy could be because only 44.5% of participants in that study were current IDUs, while the remainder were past IDUs and haemophiliacs. Unfortunately, further analysis was not conducted to identify which group of participants considered undertaking treatment, indicating greater concern with disclosing their HCV status.

Despite the significant impact of stigma on the uptake of HCV treatment, no previous research has examined stigma as a predictor of intention to undertake treatment. The current study identified that concern about stigma is a potential negative predictor of intention to undertake treatment. The results of this study show that stigma could remain a major factor influencing

the intention of IDUs to undertake treatment, particularly with respect to GPs' attitudes to IDUs, as new HCV medications can be prescribed by GPs. In addition, previous studies reported that stigma in health care settings leads to poor HCV treatment adherence and a lack of willingness to report missed doses, and was a common issue among IDU (Harris and Rhodes 2013, Marcellin et al. 2011). The new HCV treatments will not be immune from the effects of stigma. The new HCV treatments will not be immune from the effects of stigma. However, further quantitative studies need to be undertaken to verify the results of the present study, particularly with respect to the new DAAs. Moreover, further research should examine the impact of stigma on the disclosure of HCV status and the uptake of DAAs.

6.1.4 Unstable housing

Unstable housing was identified as an important reason for treatment refusal. Homeless participants stated that their highly precarious situation along with pre-existing mental health problems, made them anxious about meeting their basic survival needs, let alone considering HCV treatment. For many, lack of a safe place to live, clean clothing, healthy food, showers, toilets, clothes-washing machines and refrigerators to store medication made it impossible to undertake treatment. Many reported that depression and ongoing substance abuse issues, made them unable to deal with their health problems or engage with service providers for HCV treatment.

Other similar studies have noted housing instability as one of the key reasons for IDUs not undertaking HCV treatment due to having no sense of normalcy and no secure place to deal with or recover from side effects and facilitate access to better care (Treloar, Newland, et al. 2010, Harris, Rhodes, and Martin 2013). Moreover, research shows that homeless IDUs are more at risk of experiencing mental illnesses that can make treatment more challenging (Neal 2008, Cooper 2008). This is an important consideration, as strict adherence to the prescribed medication is essential with DAA treatment.

Homeless participants have diminished ability to maintain appointment schedules, consistent medical records and treatment regimens, and to connect with networks of support and care to cope with adverse effects of HCV treatment. Several studies have reported that lack of a permanent address and telephone number can prevent homeless IDUs from registering with a GP and other services in order to access treatment services and general health care (Cooper 2008, Jack et al. 2009, Harris and Rhodes 2013). The care requirements of the potentially severe side effects of HCV treatment are inconsistent with the lifestyle of homeless individuals (Treloar, Newland, et al. 2010, WHO 2012 , Harris, Rhodes, and Martin 2013, Gundlapalli et al. 2015).

Homeless participants in the non-treatment group and focus groups reported that they focused on the day-to-day problems of living on the street, including lack of regular sleep, physical exhaustion, daily anxiety and depression. Some homeless participants reported that they practised unsafe injecting, injected drugs very frequently and drank large amounts of alcohol. It was difficult for them to follow medical advice about coping with HCV treatment such as getting plenty of rest, eating nutritious food and following the strict schedule of daily medication and weekly injections. This is confirmed by the quantitative analysis, which found that stable accommodation was a significant predictor of high intention to undertake HCV treatment in the univariate analysis and multivariate analysis.

This is in line with other studies that reported unstable housing as associated with non-adherence to HCV treatment (Harris and Rhodes 2013, Mehta et al. 2008), and that high HCV treatment willingness and early treatment intent are associated with stable housing (Charlebois et al.2012, Gundlapalli et al 2015). As noted earlier, the new DAAs require strict adherence to be effective, hence unstable housing is likely to remain a significant factor deterring homeless IDUs from treatment uptake. Missing, forgetting or skipping doses are common issues among homeless IDUs, as are lack of a safe place to keep the

medications and constantly moving, all of which lead to failure to take medication as instructed (Weiss et al. 2009, Marcellin et al. 2011, Mishra et al. 2011). Additionally, physicians' lack of willingness to prescribe to homeless IDUs, often labelling them as non-adherent with poor appointment attendance (Mravčík et al. 2013 , Mathes, Antoine, and Pieper 2014), could lead to poor adherence to new interferon-free HCV treatments. It is important to examine the influence of unstable housing on DAAs uptake among the homeless population, and to consider homeless IDU's as a unique population with specific needs and issues that will need to be addressed for treatment availability and adherence.

6.1.5 Treatment duration

Study participants in the non-treatment group and focus groups reported difficulty in making a commitment to a lengthy antiviral therapy course, and treatment duration was one of the main reasons for treatment discontinuation and refusal. Extended treatment duration has been identified as a key factor for treatment withdrawal and treatment refusal in previous studies (Fusfeld et al. 2013, Berg et al. 2006). Prolonged treatment promotes higher rates of treatment interruption or default and patient non-adherence (Fusfeld et al. 2013, Berg et al. 2006). In one study, the rates of dropout among patients who were on a 48-week standard combination HCV treatment plan ranged from 24% to 41% within 12 and 24 weeks respectively (Berg et al. 2006).

Qualitative detail gathered in the treatment group, non-treatment group and focus groups provides additional insights as to the impact of treatment duration on cessation and refusal. For example, several treatment group participants reported that they eventually felt frustrated, fatigued and burnt out, and unable to find motivation to remain on treatment. Most participants in the non-treatment group and focus groups reported that prolonged treatment regimens, in the light of adverse medication effects, continuing household obligations and other responsibilities, discouraged them from undertaking treatment. Several studies have reported that duration of HCV treatment can decrease patience, stability and control and disturb family life,

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personal relationships and work obligations (Hopwood and Treloar 2005, Hopwood, Treloar, and Bryant 2006, Fusfeld et al. 2013). However, long treatment duration is necessary to maximise virological response (Marcellin et al. 2011).

Several participants engaged in paid work reported that they had no interest in reducing their number of shifts, earning less or losing their income to undergo prolonged HCV treatment. The survey participants confirmed this finding, reporting that coping with treatment in shorter-duration was associated with higher intention to undertake treatment. However, the multivariate analysis was unable to demonstrate that treatment duration was a significant independent predictor of intention to uptake treatment among HCV-infected IDUs. The advent of interferon-free treatment HCV with a shorter duration of treatment could attract many people (Zoulim et al. 2015) to undertake treatment and deter early discontinuation. Further study is needed to determine the association between shortened treatment duration and increased treatment uptake.

6.1.6 Peer experience of treatment

Treatment group participants reported that observing others going through HCV treatment or hearing positive stories from others who had been treated motivated them to undertake treatment. However, the non-treatment group and focus group participants reported that seeing or hearing peers who experienced harsh side effects and had unsuccessful treatment outcomes discouraged them from undertaking treatment. Peers' experiences of HCV treatment has been identified as a key factor for motivating and discouraging treatment in previous studies (Grebely and Tyndall 2011, Swan et al. 2010, Grebely et al. 2010, Munoz-Plaza et al. 2008).

Several treatment group participants reported that learning about peers' successful treatment led to the impression that they too could accomplish the treatment. Other participants reported that peers' experiences helped them to gain a full picture of HCV treatment and served as reference points. Studies

have shown that dissemination of positive HCV treatment stories can improve patients' coping strategies, reduce fears, boost confidence and develop control during treatment (Bova, Ogawa, and Sullivan-Bolyai 2010, Petraglia 2009). In contrast, having a friend or family member whose HCV treatment failed and/or who encountered harsh side effects was associated with negative attitudes towards the uptake of HCV treatment (Treloar et al. 2014, Swan et al. 2010).

Qualitative phase participants reported that they wanted to obtain information from peers about their experiences of HCV treatment. They wanted a deeper understanding of what was involved in treatment and especially the chances of encountering treatment side effects and of clearing the virus. Treatment group members reported that positive stories offered encouragement and inspiration, which resulted in more confidence and better treatment performance. In contrast, non-treatment group and focus group members reported that hearing negative stories increased their concerns, making them pessimistic about HCV treatment. Peer experiences are likely to be useful in the context of DAA treatment, due to positive reports of shorter duration, tolerable side effects, high effectiveness and simple management, attracting more IDUs to undertake treatment.

6.1.7 Protecting family, health and wellbeing and job goals

Study participants in the treatment group reported a fear of HCV transmission to their family and children, HCV symptoms, concerns about liver health and career worries as major influences on their treatment intention. These were strong motivators to undergo treatment. Previous studies have shown that concern about future liver damage and liver cancer (Swan et al. 2010, Strathdee et al. 2005, Grebely et al. 2008, Yap et al. 2014), and achieving career (Yap et al. 2014) and life goals (such as living a happy, healthy, and long life) are motivators for undertaking HCV treatment (Swan et al. 2010, Treloar et al. 2014).

This finding manifested two secondary reasons related to the primary impact of HCV and its symptoms leading to treatment uptake. These include the constant reminder that the participant was HCV carrier and the negative impact on functional ability. Treatment group participants reported that they were unable to restore themselves to normal levels of wellbeing and to fulfil both their family and occupational roles while experiencing HCV symptoms. Several other studies have also reported that the effects of HCV can significantly impair quality of life and subsequently create restrictions on lifestyle (Spiegel et al. 2005, Eriksson and Svedlund 2006, Fusfeld et al. 2013, Yap et al. 2014). Study participants who were the main breadwinners were often unable to maintain a balance between work and HCV symptoms, which led them to either lose their jobs or reduce working hours. These disruptions made them rethink their priorities about HCV treatment. They wanted HCV treatment to give them a better quality of life, a more productive working life, increase their life expectancy, reduce their concern over fibrosis, cirrhosis and liver cancer, and allow them to maintain their current job.

6.1.8 Alcohol

Quantitative analysis detected an association between not drinking alcohol in the past year and intention to undertake HCV treatment. Univariate and multivariate analyses showed that IDUs who intended to undergo HCV treatment were six times more likely not to drink alcohol in the previous year than IDUs with no such intention. More than half of participants reported not drinking alcohol in the past year. This could be related to their health-seeking behaviour, meaning a discussion with a GP convincing them that they needed to quit drinking. The implication of this is that IDUs with a desire to take care of their liver, who are more concerned about their health and more likely to follow their doctor's recommendations have higher intention to undertake HCV treatment. This finding was expected and is similar to that of Strathdee et al. (2005), who reported that intention to undertake treatment was higher in individuals who did not drink alcohol in the previous few years than in those who did (Strathdee et al. 2005). Studies also show that willingness to undergo HCV treatment decreases with increased alcohol use (Moirand et al.

2007, Gidding et al. 2011, Butt et al. 2007). However, this finding seems to be inconsistent with the recent figures from Western Australia which reported that 58% of IDUs who lived in Perth drank alcohol within the past year (Fetherston and Lenton 2015), along with alcohol which is perceived as the common way to facilitate communication among IDUs (NHMRC 2009). However, the current study did not explore the amount and type of alcohol consumed and the study samples may differ between the two studies. Further study about alcohol use among HCV-infected IDUs in Perth metropolitan is needed to provide accurate information and to confirm this result.

6.1.9 Ethnicity

In the univariate analysis, ethnicity was strongly associated with intention to undertake HCV treatment and it remained independently associated with HCV treatment intention in the multivariate analysis. These analyses found that IDUs who had intention to undergo HCV treatment were eight times more likely to be non-Aboriginal. This could be related to their health-seeking behaviour, where more than half of IDUs who were non-Aboriginal IDUs had a discussion with their GP about their liver health status. Australian studies indicated the significance role of a GP in supporting links to HCV treatment (Treloar, Newland, et al. 2010, Grebely, Bryant, et al. 2011). The finding of the current study was expected and is in agreement with those of previous studies. A recent study reported that 96% of non-Aboriginal people accessed HCV treatment compared to 4% of Aboriginal people (McDonald 2010). Alavi et al. suggest that non-Aboriginal Australian are more likely to undertake HCV treatment (Alavi et al. 2015) due to higher levels of health education and better access to health care services (Paquette, McEwan, and Bryant 2013).

Access to culturally appropriate health care services (AIHW 2011), coupled with higher socio-economic status (Grebely, Bryant, et al. 2011), is associated with higher willingness to undertake treatment among non-Indigenous than Indigenous people. This finding seem to be consistent with the view that non-Aboriginal people are more likely to have effective communication with

health care providers, stable lifestyles, higher health literacy and good comprehension of HCV treatment and the long-term effect of HCV on liver health compared to Aboriginal IDUs (Alavi et al. 2015, Treloar et al. 2016). However, the current study did not compare the factors associated with intention of treatment uptake between Aboriginal and non- Aboriginal people. Further comparison study needs to be undertaken to obtain better understanding of factors that might contribute to treatment uptake.

6.1.10 Intention to undertake HCV treatment

The quantitative analysis found a high level of expressed intention to undertake treatment among HCV-infected IDUs. Sixty-three per cent of the participants indicated an intention to undertake treatment in the future. The current study used measures of intention to uptake treatment similar to those used in two previous Australian studies, and the high level of intention among IDUs in this study is approximately in line with their results. Two recent studies were conducted in an opioid substitution treatment clinic in inner Sydney. Alavi et al. reported that 67% of IDUs were willing to be treated (Alavi et al. 2015). Similarly, Treloar et al reported that more than 53% of IDUs were interested in HCV treatment (Treloar et al. 2012). Other studies have reported even higher levels of HCV treatment intention among IDUs; 78% of IDUs recruited from a methadone clinic in inner Sydney (Doab, Treloar, and Dore 2005) and 77–86% in studies conducted in Canada and the United States (Fischer et al. 2005, Grebely et al. 2008, Strathdee et al. 2005, Zeremski et al. 2014). These higher rates could be explained by the use of different measures and less-stigmatising health care services that make HCV treatment easier and more convenient for clients.

The high level of HCV treatment intention found in the current study is surprising given low efficacy, lengthy duration and harsh side effects of HCV treatments based on standard combination treatment and triple therapy. However, as reported by participants in the qualitative phases of this study, if HCV treatment provides a guaranteed cure with protection against relapse, take less than either 6 or 12 months, and does not involve harsh side effects,

it is likely that this could increase IDUs' intention to undertake treatment. Additionally, the high rate of intention to be treated could be because participants were recruited from community settings, which provide opportunities for IDUs to engage with health care. Furthermore, the majority of participants were non-Indigenous (with all the disadvantage that status represents) and had stable housing, and this is consistent with a high rate of intention to undertake treatment. Further research using a cohort method with a large, nationally representative sample size would verify and enrich the results of the study. With the advent of new DAA HCV treatments, it is important to examine change in intention of IDUs towards HCV treatment and to precisely record and better understand the pattern of treatment uptake in Australia.

6.2 Summary

The qualitative research findings from treatment group, non-treatment group and focus groups revealed several common factors that influenced intention to undergo treatment, including: peer experience of treatment; the desire to protect family; health and wellbeing; and career. The quantitative findings largely confirmed the findings of the qualitative research which included significant associations between intention to undertake treatment, treatment side effects, treatment effectiveness, support, housing status and stigma. Not drinking alcohol in the past year and non-Aboriginal status were significantly associated with higher intention to undertake treatment in the quantitative findings.

Despite the advent of the new HCV treatments with reduced side effects, shorter duration of treatment and higher efficacy, some adverse effects still occur. These adverse effects are specific to HCV treatment and genotype 4, which is still based on pegylated interferon. Other factors including unstable housing, forgetfulness, lack of priority, patients' lack of control in their lives and pre-existing mental health issues could also lead to poor adherence to new HCV treatment, particularly among IDUs. Therefore, adherence to new HCV treatment brings challenges as it did for interferon-based HCV treatment.

Further research needs to be undertaken to enrich and verify the identified predictors in this study and to determine how to maximise adherence to the new treatment protocal.

Chapter 7: Limitations, Recommendations and Conclusions

This chapter describes the limitations of the study, provides some recommendations for further research and better clinical practice and health policies related to HCV treatment, and concludes the thesis.

7.1 Limitations of the study

This study had some limitations to consider when drawing conclusions from its findings.

Although this is the first mixed-methods study of HCV treatment intention that covered a sample of HCV-infected IDUs in the Perth metropolitan area, HCV status for all participants and HCV genotype 1 for participants in the focus group were self-reported. As a result, there may have been some recall bias. However, previous studies, particularly Australian studies indicated good levels of validity and reliability of self-reported data (Dowling-Guyer et al. 1994, Napper et al. 2010, Grebely, Matthews, et al. 2011b, Grebely et al. 2008). In order to minimise this bias, the researcher specified receiving an HCV diagnosis by a health care professional as an inclusion criterion for this study, which likely improved the self-reporting accuracy.

Self-reporting is also susceptible to social desirability bias. Sensitive issues such as housing status, education level and employment may involve social desirability bias, for example, an IDU with no job, a low level of education and unstable housing might feel embarrassed to disclose. They may also have indicated they had intention to undertake HCV treatment to avoid stigmatisation and remain socially acceptable, considering that most of them assumed HCV treatment provides a guaranteed cure with protection against relapse, takes less than either 6 or 12 months and does not involve side effects. However, giving a brief description of standard combination treatment and

triple therapy to the participants before commencing the survey may have reduced this form of bias.

Selection bias may have occurred in the study sample, as the sample was based on purposive sampling not random sampling. Recruiting from Perth community settings may have led to a potential bias towards participants who had easier and better access to health care services. To minimise this and to increase the geographical diversity in the sample, data were collected from HCV-infected IDUs at three different NSP sites and an NSP mobile service visiting eight suburbs. The study sample was not diverse particularly in terms of age and duration of injection, for example, a small minority of study participants (13%) were aged below 30 years and all study participants had injected for more than eight years, which is not representative of the entire population HCV-infected IDUs in Perth. Therefore the findings of this study may not be generalisable to other region in Australia. However, some adverse side effects still occur and other factors including unstable housing, forgetfulness, lack of priority, patients' lack of control in their lives and pre-existing mental health issues could also lead to poor adherence to new HCV treatment, particularly among IDUs.

Another limitation was the cross-sectional study design, which could only estimate intention to undertake treatment at one point in time, whereas participants' intention to undertake treatment may change over time. Finally, this study was conducted when pegylated interferon and ribavirin was the standard HCV treatment. New DAA HCV treatments with higher efficacious, shorter duration and more tolerable side effects became available in Australia in March 2016. The availability of these new treatments could significantly increase the intention of IDUs to undertake HCV treatment.

7.2 Recommendations for future research

Based on the findings of this mixed-methods study, this section presents suggestions for future research studies to increase understanding of the factors associated with treatment intention. These recommendations are designed to

increase access to and uptake of the new HCV treatments, and reduce the burden of HCV-associated disease in Australia.

- Further research on intention to undertake new treatments should adopt a prospective cohort design. Such a study could produce reliable information on treatment intention and data that could be used to develop appropriate interventions for populations that are both easier and harder to reach.

- The measures used in this study, such as treatment effectiveness, treatment side effects, and treatment duration have undergone checks for validity and reliability. However, the measures could benefit from further reliability and validity assessment, for example, systematic validation through factor analysis.

- Treatment effectiveness, treatment side effects, treatment duration support, stigma, housing status and peer experience of treatment need to be further examined in the context of new HCV treatments programs. This will provide understanding of any changes in the factors influencing IDUs' intention to undertake treatment, and subsequent policy and practice.

- Further qualitative study could explore IDUs' life changes after new HCV treatment, such as changes in their personal, family, social and work lives and general health status. This will add to current knowledge about improved overall health, physical and mental health–related quality of life and social function, and subsequently will increase understanding of IDUs' lives without HCV.

- The number of Aboriginal IDUs in the study was unexpected. As there is limited information about Aboriginal IDUs' intention to undertake HCV treatment, there is need for future research to measure their

treatment intention, as well as the factors associated with their either accepting or refusing treatment uptake within a cultural context.

- The amount and type of alcohol consumption and its relation to new HCV treatment uptake should be further examined in relation to HCV-infected IDUs and included in future studies.

7.3 Recommendations for clinical practices and health policies

The following recommendations are designed to increase access to and uptake of the new HCV treatments to reduce the burden of HCV-associated disease in Australia.

- Provide training on the new HCV treatments for all relevant health care providers, including GPs, clinical and practitioner nurses. The training should aim to raise awareness of the new HCV treatments and highlight the benefits of DAAs, so as to potentially increase treatment uptake. In particular, such training should be also provided for Aboriginal medical services in a culturally appropriate way.

- Provide grants or funds for clinical nurses who are interested in becoming nurse practitioners to increase delivery of the new HCV treatment in Western Australia.

- Set up HCV community clinics in NSPs (or near NSPs) to provide support, encourage IDUs to assess their liver health status and to undertake treatment and change their lifestyles. This treatment service should provide treatment in a non-judgmental environment. The benefits of such clinics need to be emphasised in an HCV treatment program. Setting up such clinics could also be recommended in Aboriginal health care settings.

7.4 Conclusion

This study was conducted when combination treatment with pegylated interferon and ribavirin and triple therapy were the only HCV treatment options available. The study used a mixed-methods approach that allowed for the collection of data rich in detail to gain better understanding of what factors can influence the intentions of HCV-infected IDUs to undertake HCV treatment. A qualitative study included semi-structured interviews and focus groups to explore the factors influencing the intention of HCV-infected IDUs in relation to the uptake of HCV treatment. A quantitative survey was used to measure the prevalence of intention to undertake treatment among HCV-infected IDUs and quantitatively assess the associations between treatment effectiveness, treatment side effects, treatment duration, stigma, support, demographic factors, drug-history and health characteristics, and intention to undertake HCV treatment. A unique element of this study was the incorporation of factors identified by study participants in the qualitative phase, in statistical predictor models.

Treatment effectiveness, treatment side effects, treatment duration, lack of support, and stigma were the most common factors identified in the qualitative study. Peers' experience of treatment, both positive and negative, were reported as an important influence on intention to undertake HCV treatment by both the treatment group and the non-treatment group in the semi-structured interviews. The motivating factors for treatment uptake reported by the treatment group were to protect family, to increase personal quality of life and to maintain their careers. Unstable housing was reported by the non-treatment group as a potential factor which influenced their intention not to undertake HCV treatment. Treatment effectiveness, treatment side effects, treatment duration, stigma, lack of support, drinking alcohol in the past year, ethnicity and housing status were all independently associated with intention to undertake treatment. Although there were some discrepancies between the qualitative and survey findings, the findings were largely consistent.

This study provided comprehensive information on HCV treatment intention and insight in regards to the factors influencing HCV-infected IDUs in Perth. The finding contribute to the international literature on intention to undergo HCV treatment in several ways. Identification of the prevalence of intention to undertake HCV treatment and the factors influencing this intention among HCV-infected IDUs who have not engaged in HCV treatment allows the early recognition of groups with special characteristics. These group that should be carefully supported along the antiviral treatment pathway, particularly in the context of new HCV treatments. Therefore there is a need to focus efforts on both development of HCV treatment programs and potential factors influencing treatment adherence, combined with non-judgemental environments and opportunities to enhance treatment uptake leading better health and well-being.

It is hoped that the recommendations resulting from this study will be of value to Australian policy makers in the development of interventions and policies aimed at highlighting the significance of interferon-free treatment in ways that encourage infected IDUs to undertake HCV treatment. Such an outcome would help to reduce steep rises in health care costs associated with HCV. The researcher believes that the results of this study will help to make the world a better place by scaling up HCV treatment for IDUs in the community setting.

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Note

Appendices

Appendix 1: Demographic and drug-history questions for semi-structured interviews and focus groups.

1. Are you:
1. Male
2. Female
3. Other (specify)………………………………………………

2. How old are you? yrs old……………..

3. What type accommodation do you have?
1. Own house/flat
2. Rented house/flat
3. Sharing house
4. Homeless

4. Are you currently?
1. Single / separated / divorced?
2. Married/ living with sexual partner?

5. Who do you live with? (Please tick all that apply)

1. Partner
2. Alone
3. Parents
4. Children
5. Share with others

6. Are you Aboriginal or Torres Strait Islander Origin?
1. No
2. Aboriginal
3. Torres Strait Islander

7. What is the highest level of education you have completed?
1. Primary School
2. Some high school education
3. Year 10
4. Year 12
5. TAFE/University

8. How are you employed at the moment?

1. Full time work

2. Part time/Casual work

3. Student full time

4. Student part- time

4. Unemployed

9. What is your MAIN source of income?

1. Unemployment benefits

2. Sickness benefits

3. Pension

4. Job

5. None

10. What country were you born in?

1. Australia

2. Other (specify)………………………………………………

11. What is your current residential postcode? ……….

12. What language was the main one spoken at the home you grew up in?

1. English

2. Other (specify)

The following questions are about your drug use history.

13. How long have you been injecting drugs?

1. Six months -one year

2. Two- four years

3. Three-six years

4. Six-eight years

5. Eight-ten years

6. More than ten years

14. What is your preferred drug?

1. Amphetamines

2. Heroin

3. XTC

4. LSD

5. Cannabis

15. Which of the following drugs have you used in the past 6 months?

1. Amphetamines

2. Heroin

3. XTC

4. LSD

5. Cannabis

6. Cocaine

7. Other opioids (for example oxycodone)

16. How many times have you injected any drugs in the last month?

1. Hasn't hit up

2.Once a week

3.More than once a week

(but less than once a day)

4. Once a day

5. 2-3 times a day

6. More than 3 times a day

17. Did you drink alcohol over the last year?

A. Yes

B. No

Appendix 2: Interview questions for treatment group

1. In general, what would you say about hepatitis C treatment?

2. What factors influenced your intention to have hepatitis C treatment? What was the main factor?

3. What are the challenges you have noticed while you are on treatment? How do you cope with them?

4. What is your opinion about hepatitis C treatment? What kind of problems do you see with the treatment as it is now?

5. Do you wish to add any other comments that may assist us with the research?

Appendix 3: Interview questions for non-treatment group

1. In general, what would you say about hepatitis C treatment?

4. What factors influenced your intention not to have hepatitis C treatment until now?

4. Do you have HCV symptoms? How do you cope with HCV symptoms?

5. Do you think HCV treatment is challenging? In what way do you think HCV treatment is challenging?

5. What is your opinion about hepatitis C treatment? What kind of problems do you see with the treatment as it is now?

6. Do you wish to add any other comments that may assist us with the research?

Appendix 4: Focus groups questions

1.Have you thought about HCV treatment? If you haven't can you tell what the main reasons are?

2.What factors influenced your intention not to uptake new HCV treatment (triple therapy?

3.How or in what way do you think new HCV treatment is challenging?

4.What would encourage you to go for HCV treatment?

5.For what other reasons do you think people who infected with HCV don't take treatment?

Appendix 5: poster treatment group

Hepatitis C Treatment Study

I am looking for people who are injecting drug users and are in hepatitis C treatment or have recently been treated for chronic HCV (within the past 2 years)

I am conducting an interview to find out your opinion about hepatitis C treatment. If you are happy to take part in an interview, you will be reimbursed $35 **Coles or Kmart Voucher** for any out of pocket expenses. It will take 45-60 minutes.

- To take part in this study you need to be:
- Currently injecting drug (actively injecting)
- Over 18 years of age, and
- **Currently being treated or have recently been treated for chronic HCV (within the past 2 years**
- Have English as your first language
- Living in Perth

Your involvement in this study will improve access to treatment for hepatitis C. For more information or an appointment Phone Amineh: 0405805614 and leave your name and contact details. Study Approved by Curtin University and South Metropolitan Area Health Service Human Research Ethics Committees. All information is strictly confidential.

Appendix 6: poster non-treatment group

Hepatitis C Treatment Study

Do you have hepatitis C?
I am conducting an interview to find out your opinion about hepatitis C treatment. If you are happy to take part in an interview, you will be reimbursed $35 **Coles or Kmart Voucher** for any out of pocket expenses. It will take 45-60 minutes.

To take part in this study you need to:

- Currently injecting drugs (actively injecting)
- **Received hepatitis C diagnosed by a health care professional more than 6 months earlier**
- **Have No Experience with HCV treatment.**

- Be over 18 years of age, and
- Be comfortable to speak English
- Living in Perth

Your involvement in this study will improve access to treatment for hepatitis C. For more information or an appointment Phone Amineh: 0405805614 and leave your name and contact details. Study Approved by Curtin University and South Metropolitan Area Health Service Human Research Ethics Committees. All information is strictly confidential.

Appendix 7: poster focus group

Hepatitis C Treatment Study

Do you have hepatitis C?
I am conducting focus groups to find out your opinion about hepatitis C treatment. If you are happy to take part in a focus group, you will be reimbursed $30 **Coles or Kmart Voucher** for any out of pocket expenses. It will take 60-80 minutes.

To take part in this study you need to:

- Currently injecting drugs (actively injecting)
- **Received hepatitis C diagnosed by a health care professional more than 6 months earlier with Genotype 1**
- **Being aware of new hepatitis C treatment known as triple therapy (pegylated interferon and ribavirin in combination either boceprevir and telaprevir)**
- **Have No Experience with HCV treatment.**
- Be over 18 years of age
- Be comfortable to speak English
- Living in Perth

Your involvement in this study will improve access to treatment for hepatitis C. For more information or an appointment Phone Amineh: 0405805614 and leave your name and contact details. Study Approved by Curtin University and South Metropolitan Area Health Service Human Research Ethics Committees. All information is strictly confidential.

Appendix 8: Information Sheet semi-structured interview

Name of Investigators: Amineh Rashidi

                          Dr Susan Carruthers (Supervisor)

This study is about hepatitis C treatment. I would like to understand what the intentions of injecting drug users are in regards to hepatitis C treatment and the best way to do this is to find out their thoughts directly from them. This study is being performed for my doctor's dissertation and has been approved by the Curtin University of Technology and the South Metropolitan Area Health Service Human Research Ethics Committees.

If you decide to take part in this research study, it is important that you understand the purpose of the study and the procedures you will be asked to undergo. Please read the following pages, which will provide you with information about the procedures involved, and also the potential benefits, discomforts and precautions of the study. If you are currently involved in a research study you will be ineligible to participate in this one.

Nature and Purpose of the Study

You are being invited to take part in the study as you are an injecting drug user and are either currently receiving hepatitis C treatment or have sought information about treatment. This study aims to provide evidence for developing appropriate interventions that can assist in increase intention to uptake treatment. It is hoped that this study will provide specific outcomes, from which I will develop an appropriate model for delivery of hepatitis C treatment programs to hepatitis C positive populations, particularly injecting drug users.

What the Study Will Involve

You are invited to take part in this study.

If you decide to participate, I will ask you questions about your background, and drug history. Then, I will ask you more detailed questions about factors which affect your intention to undertake hepatitis C treatment. The interview will take 45-60 minutes. With your permission, the interview/s will be taped-recorded.

Benefit

Research studies from overseas and within Australia have identified a number of common barriers to accessing hepatitis C treatment, especially for those people who may be current illicit drug users. There may no direct benefit to you participating in the study, however, the information obtained in connection with this study may be used to modify existing national guidelines for the management of hepatitis C treatment. The information may also be used to provide information and advice to current illicit drug users who may wish to access hepatitis C treatment.

Discomfort and Risks

Talking about illicit drug use or hepatitis C treatment may cause mild psychological discomfort to participants. If you feel any discomfort please inform the interviewer who can provide referral to appropriate support. Referral will be made to Hepatitis WA, a non-government community organisation, which provides a support service for people with hepatitis C, their carers and family members.

The risks associated with participating in this research are minimal. However, if you feel there are questions about your drug use which you do not wish to answer please tell the interviewer. If you have any concerns about any of the questions you may refuse to answer these questions without giving a reason.

Confidentiality

Any information that is obtained in connection with this study will remain confidential. The information you provide will not be communicated back to your treating clinician/counsellor, unless you specifically request that I do so. The information will not have any bearing on the care you receive at the service you are attending. The findings from this study will be published in my Master's dissertation and in journal articles for publication. You are free to use pseudonyms.

Tape recordings will be quickly transcribed, all identifying information will be removed, and the tape recordings immediately destroyed by means of bulk-erasure (shredder eraser) equipment. All computer data will be kept in password protected accessible only by the Student Researcher for five years then will be shredded and disposed into confidential document disposal bins.

Any information that is obtained in connection with this study will remain confidential. The consent forms will be stored separately to interview data obtained during the study; there will be no identifying link between the interview information and consent forms. The information from the research will still be published- just in an unidentifiable format, grouped with other responses.

You will be reimbursed up to $35 for out of pocket expenses involved in taking part in the including travel or any costs study.(you are required to provide a receipt of any expenses that you have incurred)

Voluntary Participation and Withdrawal from Study

You are free to decide whether or not you want to participate in this study. If you decide not to participate, this will have no consequences and you will be treated according to routine clinical guidelines, without any prejudice to present or future management of your condition. You don't have to sign anything to notify your withdrawal, and you don't have to say why you decided not to participate. You are also free to withdraw your participation at any time during the study for whatever reason. Such withdrawal will not in any way influence decisions regarding future standard or conventional medical treatment you may require.

If you would like any more information about this study, please do not hesitate to contact my supervisor Dr Susan Carruthers of the National Drug Research Institute, Curtin University of Technology (Telephone Number 9266 1604). She will be happy to answer your questions.

If you have any concerns or complaints regarding this study, you may contact the Chairman of the South Metropolitan Area Health Service Human Research Ethics Committee on (08) 9431 2929. Alternatively you may contact the Human Research Ethics Officer at Curtin University of Technology (telephone number (08) 9266 2784) on a confidential basis. Your concerns will be drawn to the attention of the Human Research Ethics Committee that is monitoring the study.

Appendix 9: Information Sheet focus groups

Name of Investigators: Amineh Rashidi

                                          Dr Susan Carruthers (Supervisor)

This study is about hepatitis C treatment. I would like to understand what the intentions of injecting drug users are in regards to new hepatitis C treatment known as triple therapy (pegylated interferon and ribavirin in combination either boceprevir and telaprevir) and the best way to do this is to find out their thoughts directly from them. This study is being performed for my doctos's

dissertation and has been approved by the Curtin University of Technology and the South Metropolitan Area Health Service Human Research Ethics Committees.

If you decide to take part in this research study, it is important that you understand the purpose of the study and the procedures you will be asked to undergo. Please read the following pages, which will provide you with information about the procedures involved, and also the potential benefits, discomforts and precautions of the study. If you are currently involved in a research study you will be ineligible to participate in this one.

Nature and Purpose of the Study

You are being invited to take part in the study as you are an injecting drug user and have sought information about new HCV treatment (triple therapy). This study aims to provide evidence for developing appropriate interventions that can assist in increase intention to uptake treatment.It is hoped that this study will provide specific outcomes, from which I will develop an appropriate model for delivery of hepatitis C treatment programs to hepatitis C positive populations, particularly injecting drug users.

What the Study Will Involve

You are invited to take part in focus group.

If you decide to participate, I will ask you questions about your opinion about hepatitis C treatment and it will take 60-90 minutes. With your permission, the conversation will be taped-recorded.

Benefit

Research studies from overseas and within Australia have identified a number of common barriers to accessing hepatitis C treatment, especially for those people who may be current illicit drug users. There may no direct benefit to you participating in the study; however, the information obtained in connection with this study may be used to modify existing national guidelines for the management of hepatitis C treatment. The information may also be used to provide information and advice to current illicit drug users who may wish to access hepatitis C treatment.

Discomfort and Risks

Talking about illicit drug use or hepatitis C treatment may cause mild psychological discomfort to participants. If you feel any discomfort please inform the interviewer who can provide referral to appropriate support. Referral will be made to Hepatitis WA, a non-government community organisation, which provides a support service for people with hepatitis C, their carers and family members.

The risks associated with participating in this research are minimal. However, if you feel there are questions about your drug use which you do not wish to answer please tell the interviewer. If you have any concerns about any of the questions you may refuse to answer these questions without giving a reason.

Confidentiality

Any information that is obtained in connection with this study will remain confidential. The information you provide will not be communicated back to your treating clinician/counsellor, unless you specifically request that I do so. The information will not have any bearing on the care you receive at the service you are attending. The findings from this study will be published in my Master's dissertation and in journal articles for publication.

All information from the study will be stored in a Curtin University approved secure location in locked storage for a period of 5 years and then destroyed. All computer and data analysis files will be password-protected.

You will be reimbursed up to $30 Coles or Kmart Voucher for out of pocket expenses involved in taking part in the including travel or any costs study

Voluntary Participation and Withdrawal from Study

You are free to decide whether or not you want to participate in this study. If you decide not to participate, this will have no consequences and you will be treated according to routine clinical guidelines, without any prejudice to present or future management of your condition. You don't have to sign anything to notify your withdrawal, and you don't have to say why you decided not to participate. You are also free to withdraw your participation at any time during the study for whatever reason. Such withdrawal will not in any way influence decisions regarding future standard or conventional medical treatment you may require.

If you would like any more information about this study, please do not hesitate to contact my supervisor Dr Susan Carruthers of the National Drug Research Institute, Curtin University of Technology (Telephone Number 9266 1604). She will be happy to answer your questions.

If you have any concerns or complaints regarding this study, you may contact the Chairman of the South Metropolitan Area Health Service Human Research Ethics Committee on (08) 9431 2929. Alternatively you may contact the Human Research Ethics Officer at Curtin University of Technology (telephone number (08) 9266 2784) on a confidential basis. Your concerns will be drawn to the attention of the Human Research Ethics Committee that is monitoring the study.

Appendix 10 Consent form qualitative and quantitative study

Consent from

TO BE USED IN CONJUNCTION WITH THE INFORMATION SHEET

PROJECT TITLE: Treatment of Hepatitis C (HCV) in Injecting Drug Users (IDUs) in Perth Metropolitan area

Participant's Name…………………………………

1. I agree entirely voluntarily to take part in the **Treatment of Hepatitis C in Injecting Drug Users in Perth Metropolitan area**. This study is being undertaken as part of the requirement for a Doctor's of Philosophy post-graduate degree at Curtin University in Perth, Western Australia. I am over 18 years of age.

2. I have been given a full explanation of the purpose of this study, of the procedures involved and of what will be expected of me. The researcher has explained the possible problems that might arise as a result of my participation in this study.

3. I understand that I am entirely free to withdraw from the study at any time and that this withdrawal will not in any way affect my future standard or conventional treatment or medical management.

4. I understand that I will not be referred to by name in any report concerning this study. In turn, I cannot restrict in any way the use of the results that arise from this study.

5. I have been given and read a copy of this Consent Form and Information Sheet.

If you would like any more information about this study, please do not hesitate to contact my supervisor Dr Susan Carruthers of the National Drug Research Institute, Curtin University of Technology (Telephone Number 9266 1604). She will be happy to answer your questions.

If you have any concerns or complaints regarding this study, you may contact the Chairman of the South Metropolitan Area Health Service Human Research Ethics Committee on (08) 9431 2929. Alternatively you may contact the Human Research Ethics Officer at Curtin University of

Technology (telephone number (08) 9266 2784) on a confidential basis. Your concerns will be drawn to the attention of the Human Research Ethics Committee that is monitoring the study.

Signature by participant Signature by Student Researcher

Signed…………………………………
Signed………………………………...

Date……………………………………..
Date………………………………...

Appendix 11 Survey questionnaire

HCV treatment for Genotype 2 and 3

HCV treatment (combination therapy) specifically for hepatitis C genotype **2** and **3** is a combination of two drugs interferon and ribavirin. Interferon is a drug taken by injection under the skin (subcutaneously) once a week and it can increase a person's immune response and stop the growth of hepatitis C virus in the body. Ribavirin is a drug taken orally twice a day which changes the body's immune response to hepatitis C virus. For HCV these drugs are given together to help the immune system and to stop or slowing down the diseases process.

The treatment is given over a 6 month period with a success rate of up to 80% (8 out of ten people will be cured).

Some people report no side effects while others may have flu-like symptoms, such as fever, chills, muscle aches and headaches. Other side effects may include becoming forgetful, short-tempered, tired or depressed. These are usually experienced in the first few months of treatment.

HCV treatment for Genotype 1

HCV treatment (triple therapy) specifically for hepatitis C genotype **1** is now available which still combines weekly interferon injections with daily ribavirin tablets, and a course of daily boceprevir or telaprevir tablets (they are oral medications which must be taken three times daily). The success rate for the treatment of hepatitis C genotype **1** has increased from 40 to 70%.

The side-effects of pegylated interferon and ribavirin side-effects still could occur in addition to any side effects of boceprevir or telaprevir tablets but for a shorter duration.

Boceprevir triple-therapy regimen : it should be taken with a light meal or snack. For the first 4 weeks of treatment only interferon plus ribavirin must be taken then Boceprevir is added at week 5. Therefore interferon, ribavirin and boceprevir must be taken for 24-44 weeks.

The most common side effects of boceprevir in combination with interferon/ribavirin include fatigue, anemia, nausea, headache, and a change in taste. In some patients, anemia may become severe. (Anaemia is a decrease in number of red blood cell or less than the normal quantity of haemoglobin in the blood).

Telaprevir triple-therapy regimen: it should be taken with food containing approximately 20 grams of fat. At the beginning of day 1 telaprevir, interferon and ribavirin must be taken for the first 12 weeks and then interferon and ribavirin is continued for an additional 12 to 36 week.
The most common side effects of telaprevir in combination with interferon/ribavirin include rash, with and without itchiness, and anemia. Although rash is usually mild, it can become severe.

However, it is important to remember that everyone is different and side-effects from treatments vary from person to person. If anemia and rashes become sever the treatment will be stopped.

Thank you for being part of my research. Your answers will allow me to provide an overview of the people who complete this questionnaire.

Part One
I. The first part of this questionnaire is about your background and includes some short questions about your drug use. Please answer the following questions.

1. Are you:
1. Male
2. Female
3. Other (specify)…………………………………………

2. How old are you? yrs old……………..

3. What type accommodation do you have?
1. Own house/flat
2. Rented house/flat
3. Sharing house

4. Homeless

4. Are you currently?
1. Single / separated / divorced?
2. Married/ living with sexual partner?

5. Who do you live with? (Please tick all that apply)

1. Partner
2. Alone
3. Parents
4. Children
5. Share with others

6. Are you Aboriginal or Torres Strait Islander Origin?
1. No
2. Aboriginal
3. Torres Strait Islander

7. What is the highest level of education you have completed?
1. Primary School
2. Some high school education
3. Year 10
4. Year 12
5. TAFE/University

8. How are you employed at the moment?
1. Full time work
2. Part time/Casual work
3. Student full time
4. Student part- time
4. Unemployed

9. What is your MAIN source of income?
 1. Unemployment benefits
 2. Sickness benefits
 3. Pension
 4. Job
 5. None

10. What country were you born in?

1. Australia

2. Other (specify)……………………………………………

11. What is your current residential postcode? ……….

12. What language was the main one spoken at the home you grew up in?

1. English

2. Other (specify)

The following questions are about your drug use history.

13. How long have you been injecting drugs?

1. Six months -one year

2. Two- four years

3. Three-six years

4. Six-eight years

5. Eight-ten years

6. More than ten years

14. What is your preferred drug?

1. Amphetamines

2. Heroin

3. XTC

4. LSD

5. Cannabis

15. Which of the following drugs have you used in the past 6 months?

1. Amphetamines

2. Heroin

3. XTC

4. LSD

5. Cannabis

6. Cocaine

7. Other opioids (for example oxycodone)

16. How many times have you injected any drugs in the last month?

1. Hasn't hit up

2.Once a week

3.More than once a week

(but less than once a day)

4. Once a day

5. 2-3 times a day

6. More than 3 times a day

17. Did you drink alcohol over the last year?

A. Yes

B. No

Part Two
The second part of this questionnaire health care seeking characteristics

1. How long have you been diagnosed with hepatitis C?

    A. Less than five year

    B. More than five years

    C. More than ten years

2. Do you know about your hepatitis C genotype?

A. Yes please specify your genotype

B. No

3. Were you aware of hepatitis C treatment before commencing to fill the survey ?

A. Yes

B. No

4. Have you discussed with your GP about your liver health status?

A. Yes

B. No

Part three

For each of the following statements, please indicate how much you agree or disagree by circling the number that most closely corresponds to your opinion. The number '1' indicates strong disagreement, whereas '5' indicates strong agreement

1. I assumed hepatitis C treatment has a guaranteed cure.

Strongly disagree disagree neutral agree strongly agree

1---------------2----------------3 ------------------4------------------5

2. I assumed once I clear hepatitis C virus, it does not come back.

Strongly disagree disagree neutral agree strongly agree
1---------------2----------------3 ------------------4------------------5

3. I assumed hepatitis C treatment takes less than 6 months.

Strongly disagree disagree neutral agree strongly agree
1---------------2----------------3 ------------------4------------------5

4. I assumed hepatitis C treatment takes less than12 months.

Strongly disagree disagree neutral agree strongly agree
1---------------2----------------3 ------------------4------------------5

6. I assumed hepatitis C treatment does not involve harsh physical side effects.

Strongly disagree disagree neutral agree strongly agree
1---------------2----------------3 ------------------4------------------5

7. I assumed hepatitis C treatment does not involve harsh psychological side effects.

Strongly disagree disagree neutral agree strongly agree
1---------------2----------------3 ------------------4------------------5

8. I assumed hepatitis C treatment does not involve sever kin problems.

Strongly disagree disagree neutral agree strongly agree

1----------------2----------------3 -----------------4-----------------5

9. I assumed hepatitis C treatment does not involve post treatment side effects.

Strongly disagree disagree neutral agree strongly agree

1----------------2----------------3 -----------------4-----------------5

10. I get the emotional help and support I need from either family or friends.

Strongly disagree disagree neutral agree strongly agree

1----------------2----------------3 -----------------4-----------------5

11. I have a special person who is a real source of comfort and help to me..

Strongly disagree disagree neutral agree strongly agree

1----------------2----------------3 -----------------4-----------------5

12. There is a special person with whom I can share my joys and sorrows.

Strongly disagree disagree neutral agree strongly agree

1----------------2----------------3 -----------------4-----------------5

13. There is a special person who is around when I am in need with my daily chore.

Strongly disagree disagree neutral agree strongly agree

1----------------2----------------3 -----------------4-----------------5

Part Four
This part of this questionnaire is about stigma .

1. I feel I need to hide the fact that I am a drug user and have hepatitis C.

Strongly disagree disagree neutral agree strongly agree

1----------------2----------------3 ------------------4------------------5

2. I believe injecting drug users with hepatitis C are treated like outcasts.

Strongly disagree disagree neutral agree strongly agree
 1----------------2----------------3 ------------------4------------------5

3. I felt I wouldn't get as good health care if health care providers knew about my drug status.

Strongly disagree disagree neutral agree strongly agree
 1----------------2----------------3 ------------------4------------------5

4. I feared my family and my friend would reject me if they learned about my illness

Strongly disagree disagree don't know agree strongly agree
 1----------------2----------------3 ------------------4------------------5

Part five
Please select the most appropriate response to each question below which is about the intention to go on hepatitis C treatment.

1. I am planning to undertake hepatitis C treatment within the next 12 months.

Strongly disagree disagree neutral agree strongly agree
 1----------------2----------------3 ------------------4------------------5

2. I am planning to undertake hepatitis C treatment within the next 1-2 years.

Strongly disagree disagree neutral agree strongly agree
 1----------------2----------------3 ------------------4------------------5

3. I am planning to undertake hepatitis C treatment in the next 2-5 years.

Strongly disagree disagree neutral agree strongly agree
 1----------------2----------------3 ------------------4------------------5

4. I am planning to undertake hepatitis C treatment BUT not at least for another 5 years.

Strongly disagree disagree neutral agree strongly agree

1----------------2----------------3-------------------4------------------5

Appendix 12 poster for questionnaire survey

Hepatitis C Treatment Study

Do you have hepatitis C?

I am conducting a survey questionnaire to find out your opinion about hepatitis C treatment. If you are happy to take part in a survey, you will be reimbursed $20 **Coles or Kmart Voucher** for any out of pocket expenses. It will take 10-15 mintues

To take part in this study you need to:

- Currently injecting drugs (actively injecting)
- **Received hepatitis C diagnosed by a health care professional more than 6 months earlier**
- **Have No Experience with HCV treatment.**
- Be over 18 years of age, and
- Be comfortable to speak English
- Living in Perth

Your involvement in this study will improve access to treatment for hepatitis C. For more information or an appointment Phone Amineh: 0405805614 and leave your name and contact details. Study Approved by Curtin University and South Metropolitan Area Health Service Human Research Ethics Committees. All information is strictly confidential.

Appendix 13 Information Sheet survey questionnaire

Name of Investigators: Amineh Rashidi

                          Dr Susan Carruthers (Supervisor)

This study is about hepatitis C treatment. I would like to understand what the intentions of injecting drug users are in regards to hepatitis C treatment and the best way to do this is to find out their thoughts directly from them. This study is being performed for my doctor's dissertation and has been approved by the Curtin University of Technology and the South Metropolitan Area Health Service Human Research Ethics Committees.

If you decide to take part in this research study, it is important that you understand the purpose of the study and the procedures you will be asked to undergo. Please read the following pages, which will provide you with information about the procedures involved, and also the potential benefits, discomforts and precautions of the study. If you are currently involved in a research study you will be ineligible to participate in this one.

Nature and Purpose of the Study

You are being invited to take part in the study as you are an injecting drug user and have sought information about treatment. This study aims to provide evidence for developing appropriate interventions that can assist in increase intention to uptake treatment. It is hoped that this study will provide specific outcomes, from which I will develop an appropriate model for delivery of hepatitis C treatment programs to hepatitis C positive populations, particularly injecting drug users.

What the Study Will Involve

You are invited to take part in a survey questionnaire.

If you decide to participate, I will ask you questions aboutbcakground, your drug use history, treatment intentions and beliefs about HCV treatment. It will take 15-20 minutes.

Benefit

Research studies from overseas and within Australia have identified a number of common barriers to accessing hepatitis C treatment, especially for those people who may be current illicit drug users. There may no direct benefit to you participating in the study; however, the information obtained in connection with this study may be used to modify existing national guidelines for the management of hepatitis C treatment. The information may also be used to provide information and advice to current illicit drug users who may wish to access hepatitis C treatment.

Discomfort and Risks

Talking about illicit drug use or hepatitis C treatment may cause mild psychological discomfort to participants. If you feel any discomfort please

inform the interviewer who can provide referral to appropriate support. Referral will be made to Hepatitis WA, a non-government community organisation, which provides a support service for people with hepatitis C, their carers and family members.

The risks associated with participating in this research are minimal. However, if you feel there are questions about your drug use which you do not wish to answer please tell the interviewer. If you have any concerns about any of the questions you may refuse to answer these questions without giving a reason.

Confidentiality

Any information that is obtained in connection with this study will remain confidential. The information you provide will not be communicated back to your treating clinician/counsellor, unless you specifically request that I do so. The information will not have any bearing on the care you receive at the service you are attending. The findings from this study will be published in my Master's dissertation and in journal articles for publication.

All information from the study will be stored in a Curtin University approved secure location in locked storage for a period of 5 years and then destroyed. All computer and data analysis files will be password-protected.

You will be reimbursed up to $20 Coles Voucher for out of pocket expenses involved in taking part in the including travel or any costs study

Voluntary Participation and Withdrawal from Study

You are free to decide whether or not you want to participate in this study. If you decide not to participate, this will have no consequences and you will be treated according to routine clinical guidelines, without any prejudice to present or future management of your condition. You don't have to sign anything to notify your withdrawal, and you don't have to say why you decided not to participate. You are also free to withdraw your participation at any time during the study for whatever reason. Such withdrawal will not in any way influence decisions regarding future standard or conventional medical treatment you may require.

If you would like any more information about this study, please do not hesitate to contact my supervisor Dr Susan Carruthers of the National Drug Research Institute, Curtin University of Technology (Telephone Number 9266 1604). She will be happy to answer your questions.

If you have any concerns or complaints regarding this study, you may contact the Chairman of the South Metropolitan Area Health Service Human Research Ethics Committee on (08) 9431 2929. Alternatively you may contact the Human Research Ethics Officer at Curtin University of Technology. "This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number HR**77/2012**). The Committee

is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing hrec@curtin.edu.au."

Appendix 14 Letter of ethics approval

Government of **Western Australia**
Department of **Health**
South Metropolitan Area Health Service

Human Research Ethics Committee

ab
Ref. 12/198
26 July 2012

Ms Amineh Rashidi
4A Roberts Road
Carlisle
6101 WA

Dear Amineh,

Re: Treatment of Hepatitis C (HCV) Injecting Drug Users (IDUs) in Rural and Urban Western Australia (THIRU Study).

Further to my correspondence dated 19 July 2012, I am writing to confirm that on 26 July 2012 the Chief Executive's delegate, under delegated authority from the Minister for Health incorporated as the Board of the Hospitals formerly comprised in the Metropolitan Health Service Board, endorsed the South Metropolitan Area Health Service (SMAHS) Human Research Ethics Committee's (HREC) recommendation to approve the above study.

Since writing previously, I have received your response addressing concerns raised by the HREC at the previous meeting and enclosing an amended Patient Information Sheet, Consent Forms, Patient Questionnaire, updated Research Application Form and Poster.

I have perused your response including the revised documents and I am satisfied that you have addressed the concerns raised by the HREC and that the protocol now conforms to the requirements of the NHMRC *National Statement on Ethical Conduct in Human Research (National Statement)*. As the conditions of approval have now been addressed, you may commence the study.

Please note that HREC approval is for a three year period from the date of final approval and the research should be commenced and completed within that period. If the study period is longer than three years, you are required to seek an extension to the approval before the end of this period. In the event that the study does not commence within 12 months from the date of final approval the study must be resubmitted to the HREC for approval.

The HREC is bound by NHMRC Guidelines to monitor the progress of all approved projects until completion, to ensure they continue to conform to approved ethical standards. In accordance with the *National Statement Chapter 5.5.3*, researchers also have a significant responsibility in monitoring their research activity and must submit the following to the HREC, in relation to this study:

- Annual reports on the progress (including compliance with any conditions of approval and maintenance and security of records).
- Final report on completion (including a copy of the results and any publications).
- Reports of adverse/serious adverse events, according to the Committee's SAE Reporting Guidelines and advise the Committee if the event has resulted in an amendment to the protocol and/or to the informed consent document.
- *Protocol amendments, or changes to informed consent documents.

281s.doc

DHEL121

Human Research Ethics Committee

Ms Amineh Rashidi
4A Roberts Road
Carlisle
6101 WA

Dear Amineh,

Re: Treatment of Hepatitis C (HCV) Injecting Drug Users (IDUs) in Rural and Urban Western Australia (THIRU Study).

Thank you for your correspondence enclosing, a Protocol Amendment and revised Patient Information Sheet and Consent Form, Questionnaire and Group Poster, for the above study. Your correspondence and attachments were reviewed by the SMHS Human Research Ethics Committee at its meeting on 4 June 2013.

At the meeting the Committee approved the Protocol Amendment and revised Patient Information Sheet and Consent Form, Questionnaire and Group Poster.

Please quote the following reference number on any future correspondence with the Committee regarding this protocol: **12/198**

Yours sincerely

MR RICHARD WOJNAR-HORTON
A/CHAIRMAN
HUMAN RESEARCH ETHICS COMMITTEE

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Government of **Western Australia**
Department of **Health**
South Metropolitan Health Service

Human Research Ethics Committee

Ms Amineh Rashidi
4A Roberts Road
Carlisle
6101 WA

Dear Amineh,

Re: Treatment of Hepatitis C (HCV) Injecting Drug Users (IDUs) in Rural and Urban Western Australia (THIRU Study).

Thank you for your correspondence enclosing, revised Research Plan, Patient Information Sheet and Consent Form and Survey Questionnaire, for the above study. Your correspondence and attachments were reviewed by the SMHS Human Research Ethics Committee at its meeting on 3 September 2013.

At the meeting the Committee approved the Research Plan, Patient Information Sheet and Consent Form and Survey Questionnaire.

Can you please ensure that all participants that are currently on the trial are provided with the updated Patient Information Sheet and are re-consented where appropriate.

Please quote the following reference number on any future correspondence with the Committee regarding this protocol: **12/198**

Yours sincerely

MR RICHARD WOJNAR-HORTON
A/CHAIRMAN
SOUTH METROPOLITAN HEALTH SERVICE
HUMAN RESEARCH ETHICS COMMITTEE

Memorandum

To	Dr Susan Carruthers, NDRI
From	Professor Stephan Millett, Chair, Human Research Ethics Committee
Subject	Protocol Approval **HR 77/2012**
Date	9 August 2012
Copy	Miss Amineh Rashidi, NDRI

Thank you for your application submitted to the Human Research Ethics Committee (HREC) for the project titled *"Treatment of Hepatitis C (HCV) injecting drug users (IDUs) in rural and urban Western Australia (THIRU Study)"*. The Committee notes the prior approval by South Metropolitan Area Health Service HREC (12/198) and has reviewed your application consistent with Chapter 5.3 of the *National Statement on Ethical Conduct in Human Research*.

- You have ethics clearance to undertake the research as stated in your proposal.
- The approval number for your project is **HR 77/2012**. *Please quote this number in any future correspondence.*
- Approval of this project is for a period of twelve months **08-08-2012** to **08-08-2013**. To renew this approval a completed Form B (attached) must be submitted before the expiry date **08-08-2013**.
- If you are a Higher Degree by Research student, data collection must not begin before your Application for Candidacy is approved by your Faculty Graduate Studies Committee.
- The following standard statement **must be** included in the information sheet to participants:

  This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number HR 77/2012). The Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing hrec@curtin.edu.au.

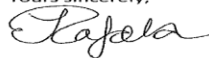Applicants should note the following:

It is the policy of the HREC to conduct random audits on a percentage of approved projects. These audits may be conducted at any time after the project starts. In cases where the HREC considers that there may be a risk of adverse events, or where participants may be especially vulnerable, the HREC may request the chief investigator to provide an outcomes report, including information on follow-up of participants.

The attached **FORM B** should be completed and returned to the Secretary, HREC, C/- Office of Research & Development:
When the project has finished, or
- If at any time during the twelve months changes/amendments occur, or
- If a serious or unexpected adverse event occurs, or
- 14 days prior to the expiry date if renewal is required.
- An application for renewal may be made with a Form B three years running, after which a new application form (Form A), providing comprehensive details, must be submitted.

Yours sincerely,

Professor Stephan Millett
Chair Human Research Ethics Committee

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Memorandum

To	Dr Susan Carruthers, NDRI
From	Professor Stephan Millett, Chair Human Research Ethics Committee
Subject	Protocol Amendment & Extension Approval **HR 77/2012**
Date	13 June 2013
Copy	Miss Amineh Rashidi, NDRI

Thank you for keeping us informed of the progress of your research. The Human Research Ethics Committee acknowledges receipt of your progress report and indication of modifications / changes for the project *"Treatment of Hepatitis C (HCV) injecting drug users (IDUs) in rural and urban Western Australia (THIRU Study)"*. Your application has been **approved**.

The Committee notes the following amendments have been approved:
1. Study has been extended and converted from Masters by Research to PhD.
2. The extended study will explore IDU perceptions of the new treatment regime and assess whether the new regime has a potential to attract and encourage IDU towards treatment along with considering how to provide access to the new regime and identifying and understating important processes to be in place for the IDU to enable them to access treatment.
3. The extended study will be divided in two parts. The target population of interest is IDU who self report being infected with HCV and have no experience with HCV treatment. Key in this regard will be to obtain data that will shed light on IDUs' decisions not to uptake HCV treatment. Respondents for both parts will be selected using purposive sampling. The main reason for selecting purposive sampling is that the researcher aims to recruit current IDU, diagnosed with chronic HCV, not in treatment. Participants will be recruited from clients in the West Australian Substance Users' Association (WASUA), a peer based community group representing drug users in WA, followed by advertising in Hepatitis WA and drug treatment clinic.
4. Part One: Five focus groups will be held with 20 participants in order to explore in-depth understanding of perceptions of IDU about the new treatment.
5. Part Two: A cross-sectional survey questionnaire, coupled with pilot testing of questionnaires will be conducted on 20-30 participants. A voucher valued at $ 20 will be given to participants who will complete and return the questionnaires

Approval for this project is extended to **30-06-2014**.

Your approval has the following conditions:
   (i)   Annual progress reports on the project must be submitted to the Ethics Office.

Your approval number remains **HR77/2012**. Please quote this number in any further correspondence regarding this project.

Yours sincerely

Professor Stephan Millett
Chair Human Research Ethics Comittee

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Memorandum

To	Dr Susan Carruthers, NDRI
From	Professor Stephan Millett, Chair Human Research Ethics Committee
Subject	**HR 77/2012 amendment approval**
Date	25 September 2013
Copy	Miss Amineh Rashidi, NDRI

Thank you for keeping us informed of the progress of your research, *"Treatment of Hepatitis C (HCV) injecting drug users (IDUs) in rural and urban Western Australia (THIRU Study)"*. The Committee affirms the approval granted by South Metropolitan Health Service Human Research Ethics Committee for the following amendments:

1) Amendment to the Research Plan, Patient Information Sheet and Consent Form and Survey Questionnaire.

Approval for this project has been extended until **08-08-2016**.

Your approval number remains **HR 77/2012,** please quote this number in any further correspondence regarding this project.

Your approval has the following conditions:

1) Annual progress reports on the project must be submitted to the Ethics Office.

Thank you.

Professor Stephan Millett
Chair Human Research Ethics Committee

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