DOCTOR OF PHILOSOPHY

Integrating Health Psychology into Hepatitis C treatment

a self-efficAcy intervention to reDuce injecting risk behAviour and hePatitis c reinfecTion rates (ADAPT)

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Integrating Health Psychology into Hepatitis C treatment: a self-efficAcy intervention to reDuce injecting risk behAviour and hePatitis c reinfecTion rates (ADAPT)

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List of Abbreviations

ADP – Alcohol and Drug Partnerships

BBV – Blood Borne Virus

BCT – Behaviour Change Technique

BIPQ – Brief Illness Perception Questionnaire

BMT – Buprenorphine Maintenance Therapy

CI – Confidence Intervals

CSM – Common Sense Model

DAA – Direct Acting Antivirals

DBS – Dry Blood Spot (testing)

DOT – Daily Observed Therapy

EMCDDA – European Monitoring Centre for Drugs and Drug Addiction

ESLD – End-Stage Liver Disease

GAD-7 – Generalised Anxiety Disorder

GIS- Group Identification Scale

HAPA – Health Action Process Approach

HBV – Hepatitis B Virus

HCC – Hepatocellular Carcinoma

HCV – Hepatitis C Virus

HIV – Human Immunodeficiency Virus

IEP – Injecting Equipment Provision

IFN – Interferon

II – Implementation intentions

IRAS – Integrated Research Application System

IRQ – Injecting Risk Questionnaire

ISD Information Services Division

LARC – Long-Acting Reversible Contraception

LOCF – Last Observation Carried Forward

LTFU – Lost To Follow-Up

mITT - modified Intention To Treat (analysis)

MMT – Methadone Maintenance Therapy

MSM – Men who have Sex with Men

NESI – Needle Exchange Surveillance Initiative

NHS - National Health Service

NICE – National Institute for Health and Care Excellence

NIHR – National Institute for Health Research

NRS National Record Scotland

OST – Opiate Substitution Therapy

PC-PTSD – Primary Care Post Traumatic Stress Disorder

PEG-INF – Pegylated Interferon

PHE – Public Health England

PHQ-9 – Patient Health Questionnaire

PI – Principal Investigator

PTSD – Post Traumatic Stress Disorder

PWID – People Who Inject Drugs

R&D – Research & Development

RCT – Randomised Controlled Trial

REC – Research Ethics Committee

SCS – Social Connectedness Scale

SDF – Scottish Drugs Forum

SDT – Self-Determination Theory

SES – Self-Efficacy Scale

SIGN – Scottish Intercollegiate Guidelines Network

SNS – Subjective Norms Scale

SOC – Stages of Change Model

SPICe - Scottish Parliament Information Centre

SVR – Sustained Virological Response

TASC – Tayside Medical Science Centre

TPB – Theory of Planned Behaviour

UNODC – United Nations Office for Drugs and Crime

VHS – Volitional Help Sheet

WHO – World Health Organisation

ZTPI – Zimbardo's Time Perspective Inventory

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Declaration

I declare that I, Amy Malaguti, am the author of this thesis, and that the work presented in this thesis was undertaken by me. This work has not been previously submitted or accepted for any other higher degree. All the references that I have cited have been consulted and appropriately acknowledged.

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Amy Malaguti

Thesis abstract

This thesis is divided into two main sections. The introductory section comprises studies one and two, while the pilot RCT section comprises studies three and four. The initial two studies were carried out to inform the latter two.

Injecting behaviour in people who inject drugs (PWID) is a significant risk factor for hepatitis C virus (HCV) infection. Self-efficacy has been shown to be associated with injecting risk behaviour. The risk of HCV re-infection in people who inject drugs (PWID) treated for HCV remains high when sharing of injecting equipment continues post-treatment.

The first study aimed to assess the effectiveness of forming implementation intentions to reduce substance use. Implementation intentions are self-regulatory processes which help achieve health-related behaviour change. A systematic search of published literature was conducted to gather evidence on the effectiveness of the use of implementation intentions for substance use behaviours from existing studies. The findings of studies selected from this search were collated to carry out a meta-analysis in order to produce evidence for the effectiveness of implementation intentions within substance use behaviours, informing study 3. Significant effects were found of implementation intentions on alcohol use and tobacco smoking. A small non-statistically significant result was reported for self-efficacy. No studies were found in the systematic search on the use of implementation intentions for the reduction of illicit drug use.

The second study aimed to investigate possible injecting behaviour changes associated with clinical treatment of HCV. The chapter reports the results from a data analysis exercise completed in January 2018 on participants of Eradicate-C, a clinical trial of HCV treatment in PWID. A significant reduction in weekly injecting frequency was reported by participants on treatment (n=84).

The third study, ADAPT, represents the main study of this thesis. ADAPT is a pilot randomised controlled trial testing the use of implementation intentions with people who inject drugs on treatment for hepatitis C to increase self-efficacy and reduce sharing of injecting equipment. It involved four visits over the course of participants' HCV treatment. The intervention was carried out during the second visit. Psychosocial

factors measured during visit 1 of ADAPT (n=50) were explored as predictors of the primary outcome, injecting risk behaviour. A regression analysis was performed with bootstrapping to test a predicting model of injecting risk behaviour as explained by injecting frequency, identification with family and identification with drug network. Identification with drug network was the only significant predictor of injecting risk behaviour. Correlation analyses showed strong correlations between self-efficacy, injecting risk behaviour, injecting frequency and group identification with drug network. No significant differences were found between control and intervention groups on self-efficacy and injecting risk behaviour (n=32).

The fourth study is a sub-study of ADAPT. This study was a qualitative investigation of the lived experience of PWID who are infected with HCV. Thematic analysis was used to analyse the findings of the study. It was run concurrently with ADAPT. Three overarching themes were identified in the interview transcripts: 1. “Changing illness perception”; 2. “Shifting agency”; 3. “Treatment adherence”.

The last chapter of the thesis aims to integrate the findings of study 3 and 4 into one final discussion. It also aims to provide a narrative reflection on the lessons learnt whilst planning and conducting the research with a hard-to-reach population, concluding with implications of the findings, the limitation of the studies and the suggestions for future research.

Chapter One: Introduction

This chapter presents a literature review exploring definitions and characteristics of the disease and the population under investigation. It will provide an introduction to hepatitis C virus, its progression, transmission, diagnosis, treatment and costs; it will explore injecting drug use risk behaviour and its psychosocial predictors. The numerous harm reduction strategies utilised in Scotland will then be briefly discussed. The current challenge of hepatitis C reinfection, facing health care systems around the world, will be presented, followed by the role health psychology can play in the context of substance use and hepatitis C care. Finally, an overview of the thesis will conclude the chapter.

1.1 The Hepatitis C Virus

1.1.1 Definition and epidemiology

Hepatitis C is a blood-borne infectious disease which primarily affects the liver. The Hepatitis C Virus (HCV) can cause both acute and chronic infections of the liver. An acute hepatitis C infection typically presents itself as a mild, usually asymptomatic infection lasting for a few weeks which is spontaneously cleared without any treatment. A chronic infection (lasting longer than six months) can become a very serious long-term and life-threatening condition (British Medical Journal - BMJ, 2017), yet still remain asymptomatic for years or decades. There are 6 major genotypes and more than 50 subtypes, with genotypes 1, 2 and 3 being predominant, yet prevalence of different genotypes varying extensively by continent (BMJ, 2017). In Scotland and the UK, the most prevalent genotypes are genotypes 1 and 3 (Public Health England - PHE, 2014).

The World Health Organization (WHO) estimates that, globally, 71 million people are chronically infected with HCV, accounting for 1% of the global population, with the Mediterranean and Eastern European regions showing the highest prevalence (WHO, 2017a). In the UK, it is estimated that rates of HCV positivity have fallen from 214,000 people (PHE, 2017a) to 143,000 people (PHE, 2019). Two-thirds remain undiagnosed, and around 1% of the Scottish population remains affected (Health Improvement

Scotland, 2017). As of the last day of December 2016, 40,154 cases of HCV antibody-positivity had been diagnosed in Scotland (Health Protection Scotland - HPS, 2017a).

1.1.2 Progression of the disease

Between 20 and 50% (in special populations) of people acutely infected with HCV, usually presenting an asymptomatic infection, will spontaneously clear the virus and will not require any treatment (Gerlach et al 2003; Pawlotsky, 2004). Up to 80% of the infected population, however, will develop a chronic infection (Figure 1), resulting in variable progression rates and levels of hepatic inflammation and fibrosis. The progression of fibrosis to cirrhosis will occur in about 20% of chronic infected patients in 20 years of infection (Figure 1). The prevalence of chronic infection in clients of needle exchanges in Scotland is estimated to be 31% (HPS, 2019).

Of those who develop cirrhosis, approximately half will die as a consequence of liver disease, with an annual 1 to 4% risk of developing hepatocellular carcinoma and a similar risk of developing end-stage liver disease (Figure 1) (Pawlotsky, 2004).

Figure 1.1: HCV disease progression

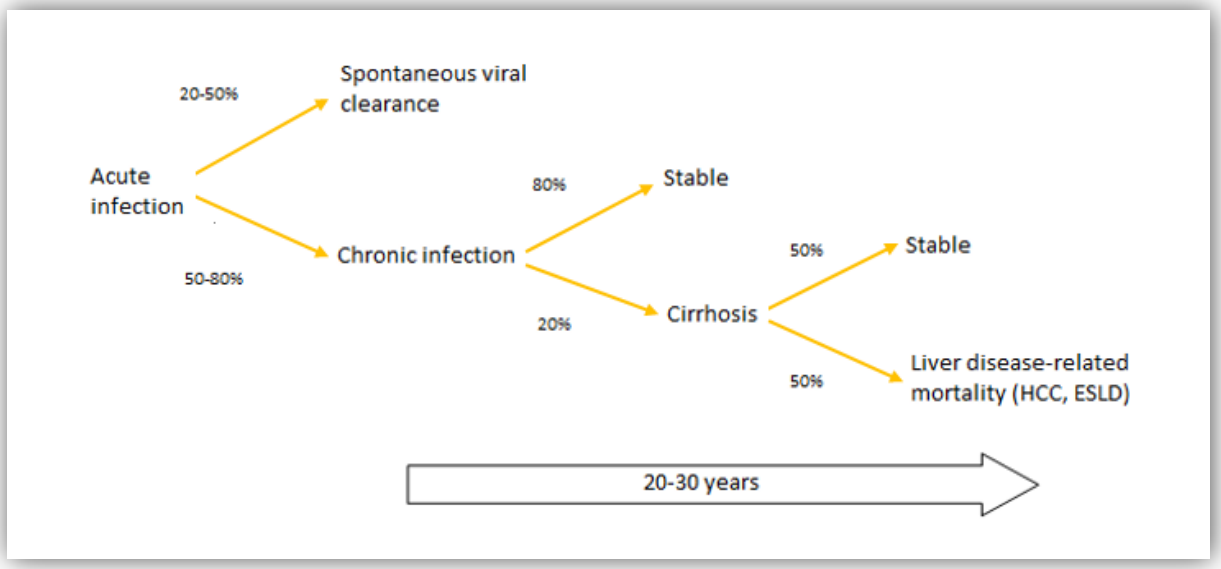


Figure 1.1 HCC – Hepatocellular Carcinoma; ESLD – End-Stage Liver Disease

1.1.3 Transmission

HCV is a blood-borne virus, therefore transmission happens through percutaneous exposure to infected blood (BMJ, 2017). The most common transmission risk factor for HCV infection is injecting drug use, with around a half of all people who inject drugs (PWID) infected with HCV (PHE, 2017a). The latest figures provided by the Needle Exchange Surveillance Initiative (HPS, 2019) in Scotland, report 57% HCV antibody positivity in PWID.

Infection transmission can also occur due to unsafe sex, in particular in people with multiple partners or at risk of sexually transmitted infections (0.4-1.8 per 100 person years) (Terrault, 2002), and due to unsafe medical practices, in particular in low and middle-income countries. In 2000, in 10 out of 14 sub-regions (according to WHO categorisation), an estimated 2 million HCV infections were caused by unsafe medical practices, accounting for 40% of new infections (Hauri et al. 2003). Percutaneous exposure to HCV-infected blood can also occur amongst healthcare staff through, for example, needle-stick injury (BMJ, 2017). Male sex is associated with lower likelihood of spontaneous clearance and with faster progression of disease compared to females. Perinatal transmission rate of the virus from HCV-infected mother to child is around 2.4%, with risk of transmission increased if the mother is co-infected with HIV (Human Immunodeficiency Virus) or has high serum titer of HCV RNA (BMJ, 2017).

Identification of HCV was scientifically challenging. Burgeoning success was only achieved in 1988, when the Chiron Corporation in the USA announced that they had discovered the virus, although details of the discovery were not published until 1989. It was then recognised that this virus was the cause of most cases of non-A non-B hepatitis (NANB) Hepatitis. Tests for the virus were developed and screening of donated blood for HCV was introduced (The Penrose Enquiry, 2015).

Prior to 1991, when screening became available due to development of the first antibody tests, blood transfusions and organ transplant had been a major risk factor for HCV infection (BMJ, 2017; The Penrose Enquiry, 2015).

1.1.4 Screening and diagnosis

Testing is offered in Scotland to people most at risk of HCV infection, namely people who inject drugs and men who have sex with men. Prevalence of HCV is higher in people who inject, people with HIV (Human Immunodeficiency Virus), people on dialysis, those incarcerated, people with tattoos, people with multiple sex partners and/or those who perform rough sex practices (BMJ, 2017).

In Scotland, testing for HCV mainly takes the form of intravenous blood samples or dry blood spot tests (DBS). Both methods will also test for HIV and hepatitis B (HBV) infections. With intravenous blood samples antibodies can be detected and, if positive, an active infection can also be diagnosed, followed by a viral count and a genotype test to characterise the virus.

DBS testing instead requires a small prick to the finger and drops of blood are deposited on a DBS card. In this way, a patient can be tested for antibodies. This has allowed testing to be exponentially increased and performed in a variety of settings, as minimal clinical skills are required to carry out the test. Support workers, nurses, needle exchange and pharmacy staff have been extensively trained in Scotland to carry out DBS testing in order to scale up testing, yearly re-testing and to find undiagnosed cases. The intensity of testing in Scotland is enabled by a positive and flexible approach and a commitment to eliminating HCV by the Scottish Government.
A reactive DBS test is usually followed by an intravenous blood sample in order to check for active infection and viral load by conducting a polymerase chain reaction (PCR) test. As mentioned above, at least 20% of people will spontaneously clear an HCV infection, which would produce a reactive DBS test result given the presence of anti-HCV antibodies but would show no active infection when checked with an intravenous blood sample.

Recent advances in testing make it now possible to test for HCV RNA PCR (active infection) from DBS tests when they are saturated with blood. This allows for a quicker diagnosis and it eliminates the need for a full blood sample unless a genotype needs to be determined. Guidelines about genotyping are in the process of changing given the introduction of pan-genotypic DAA treatment.

1.1.5 Treatments and costs to the NHS

Interferon (IFN) has been the first treatment available since the discovery of HCV. With advances in the field, HCV treatment success rate has improved throughout the decades. Sustained Virological Response (SVR), refers to the success of the treatment by measuring the level of detectable virus in the blood. Usually after a minimum of 12 weeks post treatment, blood is checked for viral load. When undetectable, the patient is regarded as treated successfully and cured. Treatment efficacy for genotype 1 (the most difficult genotype to treat) has increased steadily throughout the years: cure rates were around 10% in 1994 (IFN-only), around 30% in 1998 (IFN + Ribavirin), 44% in 2001 (Pegylated-IFN + Ribavirin), around 70% in 2011 (Peg-IFN + Ribavirin + 1st generation of Direct Acting Antivirals), and an outstanding 93-100% from 2014/2015 in the Interferon-free area of Direct Acting Antivirals (DAAs) (Pawlotsky et al. 2015).

When they were first released in the UK, DAAs were extremely expensive, with a course of treatment costing around £35,000 per patient (Hurley, 2018). Access to these drugs was therefore limited, with DAAs only offered to a specific few, while others continued to be treated with Peg-IFN, notwithstanding its inferiority in terms of SVR rates and harsh side effects. The NHS have worked tirelessly to secure deals with pharmaceutical companies producing DAAs, reducing the cost of a course of treatment to around £5,000 per patient (Hurley, 2018). With NHS boards often capping supply arrangements and treatment expenditure, lower treatment costs are essential for treatment scale up. SVR rates of close to 100% coupled with a scale up of treatment available theoretically equates to cost savings to the NHS because of substantial reductions in advanced liver diseases such as cirrhosis, decompensated liver or hepatocellular carcinoma, and related mortality (Hurley, 2018).

1.1.6 Tayside in comparison to rest of Scotland

There has been an exponential increase in HCV treatment across NHS Tayside, with clinical trials and NHS working towards the mutual goal of HCV elimination in a geographic area. Data provided by the NESI study, the Needle Exchange Surveillance Initiative that measures and monitors prevalence of BBV and characterises injecting risk behaviour in PWID in Scotland, shows that NHS Tayside and the rest of Scotland

are quite similar in terms of population characteristics, such as homeless levels and drugs used (Table 1.1) (HPS, 2019). High-risk injecting behaviours and lower Hepatitis B vaccination rates show Tayside to have slightly worse rates than the rest of Scotland (HPS, 2019). The data also shows NHS Tayside to be leading in Scotland for HCV care outcomes. In the last 12 months, the rates of testing and dispensed HCV therapy were the highest in Scotland, while the rates for needle exchange users never having been tested for HCV were the lowest in Scotland (Table 1.1) (HPS, 2019)

Table 1.1 NESI 2017/18 data comparing Tayside versus Scotland

Description	Tayside (N=211)	Scotland (N=2,130)
Homeless in last 6 months	26%	23%
Substance Injected: Heroin Cocaine Crack	 94% 11% 5%	 91% 29% 6%
Groin Injecting	59%	45%
Injecting for 15 years +	42%	58%
Hep B vaccination ever	59%	71%
HCV test in last 12 months	68%	56%
Never tested for HCV	1%	6%
HIV test in last 12 months	50%	49%
Prescribed Naloxone in last 12 months	66%	61%
Carrying Naloxone at interview	6%	13%
Prescribed methadone in last 6 months and collecting injecting equipment	49%	69%
Cleared HCV after treatment (self report)	24%	13%
Received HCV therapy	77%	50%
Received HCV therapy in community	74%	30%
Estimated Chronic HCV Prevalence	22%	31%
Soft Tissue Infection in last 12 months	22%	20%
Overdose in last 12 months	13%	15%

Source: HPS (2019) data, Mrs Donna Thain, Sexual Health & BBV MCN Manager, NHS Tayside.

1.2 Injecting risk behaviour

In Scotland, heroin continues to be the most injected substance, albeit in recent years there has been a substantial spike in the injecting use of cocaine, at times both substances being used together (HPS, 2019). Benzodiazepine use is also very common (Johnson et al. 2016), and it is associated with a number of risk-taking behaviours such

as frequent heroin injecting, cocaine injecting, non-fatal overdose, unsafe sex and syringe sharing (Tucker et al. 2016).

Injecting drug use is the principal means of transmission of HCV (PHE, 2017a), as the infection is not spread solely when sharing needles, but can be transmitted via all injecting paraphernalia: needles, barrels, pots or spoons, filters, water and tourniquets.

Despite being aware of injecting-related risks, PWID continue to carry out potential harmful injecting behaviours. Research suggests harm reduction strategies might be tackling the wrong factors, such as health motivation, as many individuals are not concerned with the health risk related to injecting, and delay discounting is common practice in PWID (Reynolds, 2006).

1.2.1 Injecting sharing behaviour at the individual level

At an individual level, different mental health and psychosocial factors have been investigated in relation to the sharing of injecting equipment. Depressive symptoms and high anxiety assessment scores have both been associated with receptive syringe sharing (Bailey et al. 2007; Perdue et al. 2003). Negative affectivity and feelings of hopelessness also influence injecting risk behaviour and reduce self-efficacy to avoid sharing (Cheng et al. 2012; Mackesy-Amiti et al. 2014). Difficulty in avoiding or refusing sharing of injecting equipment can also be a result of lack of emotional regulation, high delay discounting and impulsivity, especially when the individual is experiencing negative emotions, intoxication or withdrawal (Cheng et al. 2012; Mackesy-Amiti et al. 2014).

Self-efficacy has been found to play an important role in injecting risk behaviour among PWID (Bonar & Rosenberg, 2011; Cox et al. 2008; Gagnon & Godin, 2009; Gibson et al. 1993; Nasir & Rosenthal, 2009; Thiede et al. 2007; Wagner et al. 2010a). Different types of self-efficacy have been investigated, such as self-efficacy to always use new equipment (Gagnon & Godin, 2009), self-efficacy to avoid sharing (Thiede et al. 2007), self-efficacy to convince others to inject more safely (Cox et al. 2008). Whilst assessing constructs related to self-efficacy, Gagnon and Godin (2007) found that intention to always use new equipment was also predicted by perceived behavioural

control and attitudes towards new equipment and its perceived benefits (Cox et al. 2008; Gagnon & Godin, 2007). Perceived benefits of safer injecting is often influenced by subjective norms and the perception of peers' attitudes, as well as perceived benefits of safe behaviours. Social norms, such as believing that peers engage in injecting equipment sharing, predicted sharing of injecting equipment (Bonar & Rosenberg, 2011; Davey-Rothewell et al. 2010; Davey-Rothewell et al. 2015; Shaw et al. 2007).

Social norms, perceived susceptibility to risky consequences, such as HIV or HCV infection, and attitudes to these risks also influence individual behaviour (Bailey et al. 2007; Bonar & Rosenberg, 2011; Rhodes & Treloar, 2008; Skeer et al. 2018). HCV in particular can be perceived by PWID as an unavoidable infection, as ubiquitous and omnipresent (Rhodes & Treloar, 2008) and sometimes described as a 'common cold' for PWID by PWID (Skeer et al. 2018). These attitudes 'normalise' HCV infection. Yet, regardless of the normalisation of HCV infection in PWID, stigma towards HCV is still present both in the general population and the PWID population itself (Brener et al. 2014; Krzeczkowska et al. 2019; Treloar et al. 2013a).

Stigma is a social construct that occurs in a defined sociocultural and historical context (Becker & Arnold, 1986). It can impact both the mental and physical health of individuals (Ahern et al. 2007; von Hippel et al. 2018). Although it is considered as a phenomenon which occurs at societal level, when individuals from stigmatised groups are exposed to stigma overtime, they can start to internalise the negative attitudes towards them, thereby beginning to self-stigmatise and producing an individual-level phenomenon (von Hippel et al. 2018). Literature has previously described the relationships between internalised stigma and poor mental health and lower self-esteem (Cama et al. 2016), as well as lessened use of injecting equipment provision sites to access sterile equipment (Rivera et al. 2014), and less likelihood of disclosure of blood-borne virus status (von Hippel et al. 2018). However, a recent study found an association between high levels of implicit internalised stigma and lower rates of injecting equipment sharing (von Hippel et al. 2018). When drug users had a more positive drug using identity, internalising a positive view, they were more likely to share equipment (von Hippel et al. 2018). The influence of stigma and discrimination

on injecting behaviour practices has not only been investigated from the point of view of the individual's internalised self-stigma. PWID are a stigmatised population, and stigmatising attitudes can translate into discriminatory behaviours; but the way individual PWID perceive stigma and discrimination differs depending on who is the discriminating actor. Although PWID often report perceiving themselves as being the target of discrimination from the general population and general health workers (Brener et al. 2014; Treloar et al. 2013a; Wilson et al. 2014), this type of discrimination is not associated with injecting risk behaviour (Wilson et al. 2014). In contrast, the perception of discrimination by harm reduction staff, who are expected to be more knowledgeable, understanding and empathic about addictive behaviours, is associated with an increase in reports of sharing behaviour (Wilson et al. 2014).

1.2.2 Injecting sharing behaviour at the social level

As exemplified by the individual's own perception and consequent behaviour of wider social level factors such as stigma and discrimination, the social nature of drug use, and injecting drug use, creates a complex interplay of inter and intrapersonal factors which influence decision making and motivation in regards to injecting behaviour and injecting sharing behaviour (European Monitoring Centre for Drugs and Drug Addiction - EMCDDA, 2001). Macro-environmental and social factors such as housing and benefits policies, or the availability and purity of heroin, can affect social relationships maintained or newly formed, influencing the individual's social network, place of drug purchase, preferred dealer, use of different substance and way in which these substances are used (EMCDDA, 2001; Fraser & George, 1988; Rhodes, 2008). Micro-environmental factors such as accessibility of Injecting Equipment Provision (IEP), for example opening hours and geographical location or locations where the injecting take place, such as secluded public places or 'trap houses', will influence risk injecting practices (Adamson et al. 2017; Cloud et al. 2019; Fraser et al. 2016).

Social networks play an important role in the sharing of injecting equipment (Day et al. 2005; Fraser et al. 2016; Latkin et al. 2011; Nasir & Rosenthal, 2009; Shaw et al 2007). Networks can be formed of close friends, family and partners, or be simply convenient acquaintances that pool resources. The characteristics of these networks are predictive

of injecting risk practices. Sharing behaviour is more common in networks which are larger in size (De et al. 2007; Heimer et al. 2014a; Smith et al. 2017) and in social environments that present acceptability of sharing or social pressure related to the expectancy of sharing of injecting equipment (Bailey et al. 2007; McGowan et al. 2013; Neaigus et al. 2006). Refusing to share equipment in these networks might produce negative social consequences and individuals might therefore feel pressurised in sharing (McGowan et al 2013). Increasing resistance to peer pressure to share equipment (Magura et al 1989) and reducing the importance of the perceived negative social consequences of sharing (Thiede et al. 2007) might help promote safe injecting and might be achieved through increasing self-efficacy to refuse sharing (Cox et al. 2008; Nasir et al 2009; Thiede et al. 2007).

Interactional network characteristics, such as norms or trust between members, have been defined in the literature as social capital when they assist in enhancing action and cooperation for mutual benefits to members (Putnam, 2001). Social capital that generates from social networks such as social support has been found to be an important factor in the prevention of risk-taking in substance use (Neaigus et al. 1996). In a 2016 study (Kumar et al. 2016), members of networks who reported higher social capital, such as material aids, emotional support and social participation, were less likely to share equipment compared to individuals reporting low social capital.

However, social support, such as emotional or instrumental support, has also been positively associated with injecting equipment sharing (Lakon et al. 2006; Zapka et al. 1993). In particular, multiplex relationships such as drug using sexual partners present a variety of factors influencing injecting risk behaviour. Evidence suggests that people with an injecting drug using partner are more likely to start using illicit drugs and to be initiated to injecting (Cox et al. 2008; Fraser et al. 2016; Gossop et al. 2002; Medić et al. 2008; Roux et al. 2014). Couples who are more intimate, report having instrumental support and pool money for drugs are more likely to share injecting equipment (Shahesmaeili et al. 2018). Couples featuring intimate partner violence also show an association with sharing equipment, with recepting syringe sharing being associated with experience of psychological and physical abuse (Stoicescu et al. 2019).

Although the literature suggests social networks impact risk-taking behaviour for

injecting drug use, evidence is not clear on whether this impact is positive or negative, and the direction of this impact might be produced by individual network structural and interactional characteristics (Lakon et al. 2006). A deeper understanding of these characteristics is necessary to identify the mechanism influencing injecting sharing behaviour.

1.2.3 Theory of Planned Behaviour

One of the dominant health behaviour models which highlights the influence of attitudes, societal norms and perceived behaviour control on behaviour is the Theory of Planned Behaviour (TPB) (See Figure 1.2; Ajzen & Madden, 1986; Ajzen, 1991).

According to the TPB, behaviour is predicted by behavioural intention, which in turn can be predicted using attitudes, subjective norms and perceived behavioural control towards the behaviour (Sutton et al. 1999). Perceived behavioural control also has a direct influence on behaviour, omitting the mediating effect of the behavioural intention (Ogden, 2012). Perceived behavioural control can be divided into two main constructs: controllability and self-efficacy. Controllability refers to the external control factors, the level of control an individual has over not using shared equipment, such as accessibility to clean equipment. Self-efficacy refers to the individual's confidence in their own ability to perform an action, their internal control factors, skills and abilities to refuse sharing of equipment (Ogden, 2012).

Self-efficacy was a construct introduced by Bandura (1986) as a central feature of Social Cognitive Theory. Social cognitive theory proposes that behaviour is a result of expectancies (including self-efficacy expectancies), incentives (consequences of change in behaviour) and social cognitions (and an individual's representation of the social world (Ogden, 2012).

Figure 1.2: Theory of Planned Behaviour

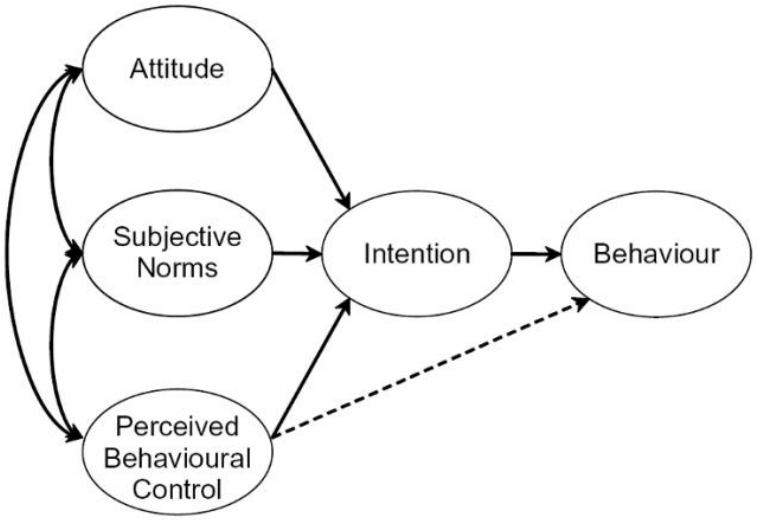


Figure 1.2: Adapted from Ogden (2012)

The TPB and other social cognitive models use social cognitive theory as the basis of their theoretical framework. The TPB has been widely applied to inform health behaviour research in a variety of settings and health topics, as explored by well-cited meta-analyses (Armitage & Conner, 2001; Trafimow et al. 2002).The TPB has also been widely criticised for being too simplistic as a social cognitive model, for not predicting behaviour when tested experimentally, for its focus on rational thinking and decision making and its lack of emotional and unconscious influences on behaviour (Ogden, 2012; Sniehotta et al. 2014).

1.2.3.1 Self-efficacy and implementation intentions

As mentioned in the paragraphs above, self-efficacy has been found to play an important role in injecting risk behaviour among PWID (Bonar & Rosenberg, 2011; Cox et al. 2008; Falck et al 1995; Gagnon & Godin, 2009; Gibson et al. 1993; Kang et al. 2004; Rácz et al 2007; Thiede et al. 2007; Wagner et al. 2010a). Intervening on self-efficacy can influence overall sharing practices, therefore reducing individuals' risks of HCV infection (Copenhaver & Lee, 2006; Latka et al .2008; Robles et al. 2004).

PWID are usually aware of the risks they incur in sharing equipment, yet when the sharing situation occurs, they are unable or unwilling to refuse (Rhodes & Treloar,

2008; Skeer et al. 2018). Previous research shows that by increasing self-efficacy and planning actions, injecting risk behaviours can be reduced (Copenhaver & Lee, 2006; Latka et al .2008; Robles et al. 2004).

Given part of the focus of the TPB is to predict behaviour from behavioural intention, the theory has been used extensively as the basis to design interventions which explore and intervene on the intention-behaviour gap. Implementation intentions have been used as an extension of the TPB to intervene on the gap between intention and behavioural action (Higgins & Conner, 2013).

Implementation intentions are self-regulatory processes that allow individuals to plan how they will perform a behaviour when a certain situation occurs, in the form of if-then plans (Gollwitzer & Sheeran, 2006; Prestwich et al. 2006). Questions have been posed about the possible effectiveness of implementation intentions in individuals under the influence of drugs (Nydegger et al. 2013), such as people presenting with a high cognitive load when in opiate withdrawal (Brandstätter et al. 2001). Brandstätter and colleagues (2001) tested the use of implementation intentions on such a population for everyday activities and found that both low and high cognitive load patients showed 'automatised' action initiation when they had formed implementation intentions.

Systematic reviews and meta-analyses assessing the effectiveness of implementation intentions to increase health-related behaviours such as healthy eating, physical activity, reducing alcohol use or smoking, have shown variable effects size, with reported standardized mean differences varying between 0.24 and 0.65 (Adriaanse et al. 2011; Bélanger-Gravel et al. 2013; Gollwitzer & Sheeran, 2006). However, some research has shown that forming implementation intentions can have negligible effects on both goal intentions and self-efficacy (Webb & Sheeran, 2008). The accessibility of the components of plans mediated the effect of implementation intentions on goal achievement (Webb & Sheeran, 2008). Using a volitional help sheet can provide participants with a structured approach to creating effective implementation intentions (Arden & Armitage, 2012). This has been shown to be an effective intervention for binge drinking and smoking cessation in student populations (Arden & Armitage, 2012).

Forming if–then plans specifying situations and associated solutions to achieve a particular goal could make an individual feel more confident about succeeding in such a task (Webb & Sheeran, 2008). The impact of implementation intentions on self-efficacy, as well as the role of self-efficacy within implementation intention interventions has been investigated by various researchers with mixed findings (Milne & Sheeran, 2002; Murray et al. 2005; Rodgers et al. 2002). Self-efficacy was investigated as a potential mediator (Armitage & Arden, 2012) and also as a moderator of the effects of the intervention (Wieber et al. 2010).

A more in depth investigation of the use of implementation intentions to change risk behaviour and self-efficacy will be presented in Chapter 2. No published study to date has investigated the use of implementation intentions to increase self-efficacy and reduce injecting sharing behaviour.

1.3 Harm Reduction

Harm reduction is a term that encompasses policies, programmes and services established to reduce harm (health, social and economic harms) to individuals and their communities associated with substance misuse (Newcombe, 1992; Scottish Parliament Information Centre - SPICe, 2017). Harm reduction interventions and services form part of the controllability aspect of individual behaviour, the external factors that influence perceived behavioural control, behavioural intention and behaviour itself. The harm reduction budget is controlled and decided by the Scottish Government. In recent years, the budget for drug and alcohol treatment and related services has been reduced quite significantly (Audit Scotland, 2019; Scottish Government, 2017; SPICe, 2017). Table 1.2 shows funding allocation for Alcohol and Drug Partnerships (ADP) in the NHS Tayside board and in Scotland between 2015 and 2018.

Table 1.2 ADP Funding allocations for Alcohol and Drug Treatment and related services in Tayside and the whole of Scotland

NHS Board	2015-16 (£)	2016-17 (£)	2017-18 (£)
Tayside	5,363,523	4,158,654	4,158,654
Total Scotland	69,209,071	53,800,001	53,800,001

Source: Scottish Government, 2017; SPICe, 2017; Audit Scotland, 2019

When the most recent drug and alcohol strategy was published in November 2018, an additional £20million per year was announced for drug and alcohol services in Scotland. The annual funding for 2018-19, 2019-20 and 2020-21 was therefore increased to a total of £73.8 million (Audit Scotland, 2019; Scottish Government, 2017; SPICe, 2017). Of the extra £20 million, £17m were specifically ring-fenced to invest in patient/peer-led service design, support families affected by addiction, to improve retention rates in treatment and reduce waiting times (Audit Scotland, 2019; SPICe, 2017). Out of the full allocation, £3 million was subdivided between a challenge fund to invest in innovative ways of working with this population and to prevent homelessness (Audit Scotland, 2019; SPICe, 2017).

Harm reduction strategies, policies, programmes and services for drug misuse which are currently being offered or considered in Scotland are hereby briefly presented and discussed.

1.3.1 Opiate Substitution Therapy

Opiate Substitution Therapy (OST) is a pharmacological intervention used to substitute illicit opiates with synthetic prescribed alternatives. They are used to treat opioid dependency to prevent withdrawals and reduce craving for illegal substances, with the aim of reaching stability and reducing prescribed amount overtime (National Institute for Health and Care Excellence - NICE, 2007a; SPICe, 2017). The British National Formulary (the BNF) recommends the use of methadone and buprenorphine as synthetic opioids for the pharmacological treatment of substance misuse (NICE,

2007a). They provide milder, less euphoric and longer lasting effects compared to heroin.

Methadone is a synthetic opioid receptor agonist with effects on the body similar to that of morphine. The usual maintenance dose that patients will receive is 60-120mg daily as an oral solution (NICE, 2007a). An oral concentrate solution, tablets and injectable solution of methadone are also available but the oral solution is the most commonly prescribed. Methadone is the most prescribed drug used for OST in Scotland at 12.13 daily doses per 1000 population per day (Information Services Division - ISD, 2018a).

Buprenorphine is both a partial opioid agonist and antagonist, and provides less euphoric and sedating effects than methadone (NICE, 2007a). It is recommended for the treatment of substance misuse with the support of medical, psychological and social care. It is available as sublingual tablets, injectable solution or transdermal patches. Sublingual tablets are the most commonly prescribed, with a maintenance dose of between 12-24mg daily (NICE, 2007a). Buprenorphine differs from methadone as it has a higher affinity with opioid receptors, occupying them for longer and rendering the use of other opioids (synthetic and heroin alike) somewhat futile. NICE (2007a) reports the potential for abuse of buprenorphine, as tablets can be crushed and injected. In Scotland, buprenorphine is prescribed at a rate of 0.56 daily doses per 1000 population per day (ISD, 2018a).

Literature comparing fixed doses of methadone maintenance therapy (MMT) and buprenorphine maintenance therapy (BMT) suggests fixed MMT doses have higher retention rates (NICE, 2007a). Literature on illicit opiate use produced mixed results on comparing MMT and BMT doses, with flexible doses showing no significant differences between the two therapies (NICE, 2007a). However, lower levels of mortality, especially related to opioid overdose, have been associated with BMT compared to MMT (NICE, 2007a; SPICe, 2017).

1.3.2 Heroin-assisted treatment

Heroin–assisted treatment was introduced in the 1990s in Switzerland and has since become an important treatment option for people for whom standard therapies such as OST or residential rehabilitation programmes have not been successful (EMCDDA, 2012). It is also referred to as supervised injectable heroin, because all doses (most typically 200mg of diacetylmorphine) are supervised by nursing staff to ensure compliance and safety, and prevent prescribed heroin entering the illicit market (EMCDDA, 2012).

A number of RCTs have been conducted on the effectiveness and safety of heroin-assisted treatment. Five were conducted in Europe (van den Brink et al. 2003; March et al 2006; Haasen et al. 2007; Perneger et al. 1998; Strang et al. 2010) and one in Canada (Oviedo-Joekes et al. 2009). The evidence from all 6 RCT supports the use of heroin-assisted treatment. All studies showed that participants in the supervised injectable heroin group, compared to the control groups, reduced their illicit heroin use, improved their physical and mental health and were involved in less criminal activity (EMCDDA, 2012).

The first heroin-assisted treatment service in Scotland opened in Glasgow at the end of 2019 and the Chief Scientific Office has funded an evaluation project to run alongside its launch (Scottish Drugs Forum - SDF, 2019). In the UK, heroin-assisted treatment has been trialled in London, Brighton and Darlington (SDF, 2019). The aim for the service in Glasgow is to treat 20 patients in year 1 and 40 patients in year 2, and once stabilised onto treatment, patients will gradually progress from intravenous prescribed heroin to an oral prescription which will allow more patients to be treated (Glasgow City Council, 2019).

1.3.3 Injecting Equipment Provision (IEP)

The provision of injecting equipment promotes safe injecting and reduces incidences of viral and bacterial infections. The first dedicated outlets were operating in the UK in 1986 as a measure to reduce the epidemic spread of HIV infections. IEP is free of charge in these outlets and is often accompanied by the provision of other harm reduction services such as dry blood spot testing or naloxone provision. The World

Health Organization defines high coverage needle and syringe provision as 60% of all people estimated to inject drugs receiving more than 200 sterile syringes per person per annum (O'Keefe et al. 2019; WHO, 2012). This target was devised by means of mathematical modelling and real-life studies to reduce the spread of HIV. The WHO has acknowledged these recommendations were calculated to limit the spread of HIV but might not be adequate to reduce newly acquired HCV infections and support the current 2030 WHO HCV elimination targets (discussed in subsequent paragraphs). An increase to 300 syringes per person per annum should instead be distributed and would be considered high coverage in order to achieve such a target (O'Keefe et al. 2019; WHO, 2016a).

The WHO targets are extremely high compared to real-life data on equipment distribution. Data on Scottish coverage in 2014/15 shows an average of 72 sterile syringes per person was distributed (ISD, 2018b). Despite equipment being free of charge and the presence of around 5 IEP outlets per 1000 people who use drugs (ISD, 2018b), levels of reported equipment sharing remains a problem. In the NESI survey, 10% reported sharing a needle and syringe in the past six months in 2017/18, whilst 26% reported sharing other injecting paraphernalia such as spoons, filters or water, down from 48% in 2008/09 (HPS, 2019). Albeit the number of people reporting sharing of equipment has reduced in the last decade, this behaviour remains the biggest concern for blood-borne virus infection transmission and one of the major challenges faced by the WHO in achieving its target for global HCV elimination by 2030.

1.3.4 National Naloxone programme

Naloxone is an opioid antagonist which reverses the effects of opioids in cases of a potential overdose. It is of paramount importance in the action taken by Scotland to tackle the rising trend of drug-related deaths (National Records Scotland - NRS, 2019). Scotland was a worldwide pioneer in introducing the National Take Home Naloxone Programme (Scottish Government, 2019). In 2011/12, only 8% of the NESI study participants had been prescribed naloxone in Scotland, increasing to 61% in 2017/18 (HPS, 2019). Despite this increase in take-home naloxone prescriptions, increases in drug-related deaths have been steadily recorded since 1996 (NRS, 2019). In Tayside,

there has also been an increase in non-fatal overdoses, which might infer the number of take-home naloxone kits prescribed to the affected population which are used. Data collected in Tayside between the 1st January 2017 and the 22nd September 2019 show a month by month increase in incidents. In 2017 there was an average of 0.77 non-fatal overdose incidents per day, with an increase to 1.8 incidences per day in 2019 (Unpublished NHS Tayside data, September 2019).

When the take-home naloxone programme was introduced, naloxone could only be prescribed by nurses, pharmacists, GPs and other healthcare staff working with the substance use population. Since the introduction of new legislation in October 2015, all staff working in drug services can administer naloxone but also provide and supply take-home naloxone, which allows a much greater number of kits to be distributed via third sector organisations. It remains a prescription only medicine, but is exempt from certain prescription only medicine requirements because it is a life-saving intervention in case of emergency. The change in legislation also allows family members to access take-home naloxone for a person at risk, without the person's knowledge or consent (PHE, 2017b).

1.3.5 Residential detoxification and rehabilitation

Residential detoxification and rehabilitation centres are an additional measure of support for people trying to become substance-free and for whom other community-based interventions have not been successful. The information provided by the Scottish Government on residential detoxification and rehabilitation facilities is not particularly current, with the last review having been carried out in 2004 (Scottish Government, 2004). Twenty-one facilities were present in Scotland with 352 beds for drug treatment (Scottish Government, 2004).

Residential detoxification aims to provide safe and humane withdrawal from the drug of dependence (Scottish Government, 2004; SPICe, 2017). It constitutes short-to-medium programmes, lasting between a few days to a few weeks (usually 1 week in NHS Tayside) and provides different types of interventions such as clinically-supervised detoxification, counselling and relapse prevention, crisis support and practical help

with housing and benefits. Completion rates are high (75-80%), yet relapse is very common (Scottish Government, 2004; SPICe, 2017).

According to Scottish Government documentation, residential rehabilitation aims to provide individuals with long-term abstinence, a drug-free lifestyle and re-integration into society (Scottish Government, 2004; SPICe, 2017). Given the more complex nature of these goals compared to detoxification facilities, these programmes tend to be medium to long-term, lasting from a couple of months to one year and providing clinically-supervised detoxification, intensive psychological support and therapeutic interventions such as counselling, group therapy and cognitive behavioural therapy, as well as employability interventions, such as upskilling and employment preparation (Scottish Government, 2004; SPICe, 2017). Completion rates are not as high, with 25% of individuals choosing to be discharged within 2 weeks and 40% within 3 months (Scottish Government, 2004; SPICe, 2017).

1.3.6 Supervised consumption facilities

Supervised consumption facilities, also referred to as drug consumption rooms or safe injecting facilities, have been implemented across European countries, Canada and Australia since 1986 (Hedric et al.2010). The aim of supervised consumption facilities is to provide a safe and hygienic place for people to inject drugs. They have been evidenced to reduce disease transmissions, as sterile injecting equipment is provided, and fatal overdoses, as emergency care is available immediately in case of need (EMCDDA, 2018). There is also an opportunity to engage and refer clients to other services such as social healthcare and substance use services (EMCDDA, 2018).

In April 2018, EMCDDA audited the number of supervised consumption rooms, with a total of 90 across Switzerland, Netherlands, Germany, Spain, Luxembourg, Norway, Denmark and France. Facilitative laws were passed in Ireland and Portugal for supervised consumption rooms to open in 2019. Belgian policy makers were also presented results from a feasibility study on drug consumption facilities in five major Belgian cities which supported the introduction of these facilities (EMCDDA, 2018). The UK government, however, continues, in spite of the available evidence, to refuse to permit this harm reduction measure.

Data published in 2019 showed that Scotland has the highest rates in Europe for drug-related deaths, at 0.16 per 1000 population, and Greater Glasgow & Clyde showing the highest rate in Scotland (0.23 per 1000 population) (National Records of Scotland, 2019). In response to this rising number of drug-related deaths and to a significant outbreak of HIV in Glasgow since 2015, the Glasgow City Integration Joint Board approved the development of a business case for piloting a safe consumption facility in Glasgow. Although health policy is a devolved power, drug laws are reserved to the UK Government in Westminster (Nicolls et al. 2019). After the business case was supported by Glasgow City Council, it was debated in April 2018 in Holyrood where MSPs voted in favour, calling Westminster to make legislation changes to the 1971 Misuse of Drugs Act or to declare a health emergency in Scotland, therefore granting Holyrood emergency powers to introduce the facility in Glasgow. The UK government blocked such an initiative (Nicolls, 2019; SDF, 2018).

1.4 Reinfection

In 2016, the World Health Organization set targets for the elimination of hepatitis B and C by 2030 (WHO, 2018a). The treatment targets set diagnostic coverage at 90%, treatment coverage at 80% of those eligible to be treated, 90% reduction in incidence of viral hepatitis chronic infections and a 65% reduction in mortality caused by viral hepatitis (WHO, 2018a). The introduction of highly effective DAA for the treatment of HCV infection has improved the perception of the WHO targets being achievable (Falade-Nwulia et al. 2018).

However, cure from HCV infection does not provide protective immunity against future infections, so people who have been treated or have spontaneously cleared the virus, can become reinfected (Falade-Nwulia et al. 2018). HCV reinfection could therefore hamper optimistic predictions on HCV elimination. Reinfection rates vary dramatically according to population. The two main populations which are being monitored for reinfection are PWID and men who have sex with men (MSM) as evidence suggests they are at the highest risk of reinfection (Islam et al. 2017). In PWID who have not injected since being treated for HCV, incidence rate is of 1.7 per 100 person-years (Midgard et al. 2016a). For PWID with ongoing risk (e.g. currently

injecting drugs) post-treatment rates vary between 4.9 per 100 person-years in Norway (Midgard et al. 2016a), to 16.7 per 100 person-years in a Spanish population who reported injecting in the past 6 months, and 18.9 per 100 person-years amongst those who reported injecting in the previous 30 days (Valencia et al. 2019). The highest rate was reported in Dundee (Scotland), a city under the remit of NHS Tayside, where those treated in the largest IEP outlet in the city was recorded as 21.5 per 100 person-years (Schulkind et al. 2019).

Among MSM, the incidence varied between 9.02 per 100 person-years in a German sample (Ingiliz et al. 2019) and 15.2 per 100 person-years in a Dutch sample of HIV-infected MSM (Lambers et al. 2011).

More recently, a meta-analysis was conducted which found the overall rate of HCV reinfection from 36 included studies was 5.9 per 100 person-years in people with recent drug use, 6.2 per 100 person-years in people who recently injected drugs and 3.8 per 100 person-years in those on OST (Hajarizadeh et al. 2020). Reinfection rates were similar among individuals treated with interferon-based therapy (5.4 per 100 person-years) and those treated with DAAs (3.9 per 100 person-years) (Hajarizadeh et al. 2020).

The risk of reinfection is not only a danger to the efforts carried out internationally to achieve viral hepatitis elimination by 2030. At an individual level, becoming reinfected would compromise the benefits of the previous treatment, such as the prevention of HCV-related liver disease (Midgard et al. 2016b) and possible psychological consequences associated with a renewed diagnosis, such as anger, depression and stigma (Janke et al. 2008). It is extremely important for healthcare professionals not to stigmatise and discriminate people who present with reinfection, as this might add barriers to accessing treatment (Midgard et al. 2016b). Healthcare professional should acknowledge reinfection, and use education and counselling coupled with harm reduction to address the risk of reinfection with patients, and by post-SVR screening, retreat HCV reinfected patients as soon as possible (Midgard et al. 2016b). The decreasing costs of DAAs have led to more health systems allowing re-treatment of people who present with HCV reinfections.

At a systemic level, reinfections alter the cost-effectiveness calculations of treatment

as prevention, with continued high costs for the NHS associated with chronic infections and HCV-related liver disease and increasing the pressure for prevention of HCV on harm reduction strategies. Therefore, acknowledgement and education on reinfection is important on a systemic level as well, with post-SVR surveillance and harm reduction still being pivotal in the fight for HCV elimination (Midgard et al. 2016b).

Reinfections can be perceived as the proof the most at-risk population is being targeted and treated and efforts should continue to diminish the virus pool present in such networks. However, sustained presence of reinfections might also highlight the disconnect between approved evidence-based governmental HCV elimination strategies and their effective implementation on the frontline. Such an example is the Scottish Government commitment to eliminate HCV by 2024 by upscaling treatment, investing financial and intellectual resource in case-findings (Scottish Health Protection Network, 2019) and ensuring people have access to optimal harm reduction services, such as access to 300 syringes per person per annum (O'Keefe et al. 2019; WHO, 2016a) to lower transmission, yet only having an average coverage of 72 syringes per person per annum (ISD, 2018b).

1.4.1 The role of health psychology

A multi-stakeholder approach must be taken if both domestic and international elimination targets are to be achieved (Lazarus et al. 2018). Combining treatment and prevention is essential (WHO, 2018a). Both of these individual strategies require different degrees of behaviour change, which is the reason health psychology can contribute to elimination efforts.

Health psychology aims to improve, promote and maintain health of individuals and populations by applying theories and models of behaviour change to practice and therefore providing an evidence-based approach to the management of illnesses (British Psychological Society, 2019). It is often applied in a multidisciplinary setting and can be helpful both at a population and an individual level.

At a systemic level, treatment scale up, testing scale up and harm reduction measures are being implemented with the help of national strategies. Thirty-six countries have developed national plans and 33 are in the process of developing such plans (WHO,

2018a). Health psychology can be applied to carry out needs assessments in a population; gather and analyse evidence to produce public health interventions; test the effectiveness of these interventions as well as strategies that are already in place; configure efficacious implementation plans and help evaluate them; train healthcare and third sector staff in behaviour change and low-tier interventions.

At an individual level, it will be difficult to achieve and maintain HCV elimination if the primary behaviour and route of transmission, sharing of injecting equipment, does not change. The roles of health psychology at a systemic level mentioned above can also be applied at an individual level for one-to-one behaviour change work with patients. This type of application of health psychology is the focus of this thesis.

1.5 Overview of the Thesis

1.5.1 Aims

In light of the higher HCV reinfection rate for people who continue to inject drugs and the role that health psychology can play in the management of HCV, the main aim of this research is to test the effectiveness of a behaviour change intervention at an individual level to reduce rates sharing rates of injecting equipment, and consequentially of HCV reinfection, by intervening on patients' self-efficacy and injecting risk behaviour.

The full thesis presents a series of studies that aim to: a) understand the current use of implementation intentions in substance use populations (Chapter 2); b) explore injecting behaviour changes, and psychosocial factors associated to these, in people who inject drugs on HCV treatment from a previous study to help inform the current intervention (Chapter 3); c) investigate the effectiveness and feasibility of implementation intentions with people who inject drugs for reducing sharing of injecting equipment and associated HCV reinfection rates and increasing self-efficacy to refuse sharing (Chapter 6); d) explore psychosocial predictors of injecting sharing behaviour (Chapter 5); e) examine patients' experience of HCV treatment and their perception of HCV as an illness (Chapter 7).

1.5.2 Research questions

Table 1.3 Research questions of this thesis

Research question	Specification of centrality	Study number & Design
Are implementation intentions effective in reducing substance use?	Primary	Study 1: Meta-Analysis
Does injecting behaviour change during HCV treatment? What psychosocial factors are associated with such change?	Primary	Study 2: Existing dataset secondary data analysis
Will implementation intentions produce changes in self-efficacy to refuse sharing of injecting equipment and injecting risk behaviour in active PWID on treatment for hepatitis C at 1-month follow-up?	Primary	Study 3: Pilot Randomised Controlled Trial
• Is there longevity of the intervention effectiveness 4 months post-intervention (and 12 weeks post-treatment)? • What type of relationship exists, if any, between measured psychosocial factors and injecting risk behaviour? • Are there any differences in psychosocial factors pre- and post-treatment?	Secondary	
What is the lived experience of patients on HCV DAA treatment?	Primary	Study 4: Qualitative study
What is the patients' illness perception?	Secondary	

1.5.3 Structure of the thesis

The research project was subdivided into 4 studies. The initial two studies were carried out to inform the latter two.

The first study is presented in Chapter 2. The aim of this study is to assess the effectiveness of forming implementation intentions to reduce substance use. The chapter briefly explores epidemiological data on substance use in general, including alcohol use, tobacco smoking and illicit drug use. It continues by presenting implementation intentions as self-regulatory processes which help achieve health-related behaviour change. A systematic search of published literature was conducted

to gather evidence on the effectiveness of the use of implementation intentions for substance use behaviours from existing studies. The findings of studies selected from this search were collated to carry out a meta-analysis in order to produce evidence for the effectiveness of implementation intentions within substance use behaviours, informing study 3.

The second study is presented in Chapter 3. The aim of this study is to investigate possible injecting behaviour changes associated with no intervention other than clinical treatment of hepatitis C. The chapter reports the results from a data analysis exercise completed in January 2018. The data was collected and provided by the Eradicate-C study group and the Chief Investigator, Professor John F. Dillon, also second supervisor to this PhD project. Eradicate-C was a single-centre clinical trial investigating the effectiveness of hepatitis C treatment in current injecting drug users (primary outcome) between 2012 and 2017. Secondary outcomes, such as behavioural and social measures, were collected during the trial to analyse any changes during treatment. These outcomes were used to characterise the population and examine any relationship between these factors and injecting behaviour change. The participants of Eradicate-C are directly comparable with the population chosen for the studies included in this thesis, as they were also current injecting drug users on treatment for hepatitis C in the same Scottish Health Board region where study 3 and 4 of this thesis took place. It was therefore considered important to analyse this data in order to inform our protocol for study 3 and 4.

The third study, ADAPT, represents the main study of this thesis. It was the study that required most resources in terms of planning, statutory and regulatory approvals, recruitment, analysis and dedicated time. Three chapters of this thesis are therefore dedicated to ADAPT: Chapter 4, 5 and 6.

Chapter 4 presents the design and methodology of the randomised controlled trial (ADAPT). It is reported in accordance with the CONSORT (The Consolidated Standards of Reporting Trials) 2010 statement for transparent reporting of trials (Schultz et al. 2010), in conjunction with the TIDieR checklist (Template for Intervention Description and Replication) for better reporting of interventions (Hoffmann et al. 2014). This chapter required updating throughout the course of the study, as three substantial

amendments were submitted during the study life. It includes a description of all the assessment scales collected and analysed for ADAPT, namely those reported in chapters 5 and 6.

In chapter 5 psychosocial factors measured during visit 1 of ADAPT (RCT) are explored as predictors of the primary outcome, injecting risk behaviour. Only measures taken on visit 1 are considered in this analysis. The chapter presents the characteristics of the sample, the mean variable score, normality testing, correlation testing to check the relationship between injecting risk behaviour and psychosocial secondary outcomes. A regression analysis is then performed with bootstrapping to test a predicting model of injecting risk behaviour as explained by injecting frequency, identification with family and identification with drug network.

Chapter 6 presents the main findings of ADAPT. This chapter explores attrition rates and randomisation, and it focuses on presenting and describing the intervention data in detail, using simple inferential statistics to investigate the effects on the use of implementation intentions with the specified population on self-efficacy and sharing of injecting equipment.

The fourth study is presented in Chapter 7. This study is classified in the ADAPT study protocol as a sub-study, as it is directly linked to the RCT and its recruitment took place from the same study sample of ADAPT. It is presented in the thesis as a separate chapter and study because of its concurrent design with the RCT and because it was answering a related but different set of research questions. This study is a qualitative investigation of the lived experience of people who inject drugs who are infected with hepatitis C. Thematic analysis was used to analyse the findings of this study. The concurrent design of study 3 and 4 was selected to ensure the qualitative data was not influenced by the quantitative study findings or vice versa.

Lastly, Chapter 8 aims to integrate the findings of study 3 and 4 into one final discussion. The concurrent design of these two studies allows the analysis of the convergence, divergence or contradiction of the findings of the two datasets in an overall discussion. It aims to provide a narrative reflection on the lessons learnt whilst planning and conducting the research with a hard-to-reach population. It will also

present the implication of the findings, the limitation of the studies and the suggestions for future research.

CHAPTER TWO: Study 1 - Meta-analysis

Effectiveness of the use of implementation intentions on reduction of substance use.

This chapter presents the first study of the thesis. It explores epidemiological data on the effects of substance use, such as alcohol, tobacco and illicit drugs, on health and mortality. It presents implementation intentions as self-regulatory processes which help achieve behaviour change. A systematic search was carried out to identify studies testing the effectiveness of implementation intentions on substance use behaviour change. Data was extracted and a meta-analysis carried out to produce pooled evidence on the effectiveness of implementation intentions. The findings of this study were used to inform Study 3 of this thesis.

2.1 Abstract

Background: Substance use, such as alcohol drinking, tobacco smoking and illicit drug injecting, has been associated to severe health conditions and an annual estimated 12% of all deaths worldwide. Implementation intentions are self-regulatory processes which help achieve health-related behaviour change. *Objectives*: To investigate the effectiveness of forming implementation intentions to reduce substance use and increase self-efficacy.

Design: Data sources: PsycINFO, MEDLINE, Psychology and Behavioural Science Collection, clinicaltrials.gov, UK Clinical Trials Gateway, Reference lists. *Inclusion criteria*: RCT of substance users forming implementation intentions to reduce consumption (active or passive control condition present). *Study appraisal and synthesis methods*: the SIGN checklist for RCT quality was used for quality appraisal, data was extracted by two reviewers.

Results: Twenty-one studies were included in the meta-analysis. The overall effect size for alcohol use was g=0.31 (95% CI: 0.21, 0.42), p< .001; for tobacco smoking g=0.31 (CI: 0.12, 0.50), p=.002; for self-efficacy g=0.16 (CI: -0.02, 0.34), p=.087); no studies were retrieved for the use of implementation intentions on illicit drug use. The interventions revealed stronger effects in the general population compared to

students for both alcohol and smoking, and when delivered in person rather than online on screen for alcohol only.

Conclusions: This review suggests that implementation intention interventions are effective in reducing some forms of substance use (alcohol and tobacco smoking), albeit revealing small effect sizes, among the general population and students in secondary and higher education. Implementation intentions also have a small non-significant effect on self-efficacy. *Review registration number*: CRD42018116170.

2.2 Background

Commonly consumed psychoactive substances such as alcohol, nicotine (within tobacco) and opioids have been linked to an astonishing amount of health conditions (World Health Organization - WHO, 2018b) and an estimated yearly 12% of all deaths worldwide (Hodder et al. 2016), amounting to around 11 million deaths a year. In the paragraphs below, the association between substance use and health is investigated and categorised by substance.

2.2.1 Alcohol use

In 2016, 43% of the worldwide population aged 15 and over had drunk alcohol in the previous year (WHO, 2018b). The WHO European Region sees the highest level of individual consumption of alcohol worldwide, with the global average of 6.4 litres of pure alcohol per capita having been consumed in 2016 in over 15s (WHO, 2018c).

In the same year, around 5.3% of deaths worldwide (equivalent to 3 million people) and 5.1% of disability-adjusted life years (DALYs) were a result of harmful alcohol use. Alcohol consumption is linked to both acute and chronic poor health outcomes (and related mortality) such as injuries, hepato-gastroenterological diseases, cardiovascular disease, infectious diseases and cancers (Bahorik et al. 2017; Schuckit, 2009; WHO, 2018b0). In addition to this, alcohol related DALYs are attributable to non-communicable conditions, mental health and injuries (WHO, 2018c). Some meta-analytical research suggests that light to moderate alcohol consumption could reduce the risk of cardiovascular disease, stroke and coronary heart disease and their related

mortality (Ronksley et al. 2011). However, health departments of countries around the world define light, moderate and harmful drinking as widely different, with recommended drinking guidelines ranging from 8g of pure alcohol mass a day in Guyana to 40g a day in Estonia, Republic of Korea, Romania, Spain and Uruguay (International Alliance for Responsible Drinking, 2018). It is therefore difficult to globally specify a consistent threshold of health-protective light to moderate drinking, leaving the debate wide open on how, if at all, to integrate this information into public health messages (Ronksley et al. 2011).

2.2.2 Tobacco smoking

Smoking of tobacco is the single leading cause of preventable deaths around the world. Cardiovascular disease, cancers, chronic respiratory disease, diabetes have all been linked to first-hand tobacco use, smoke and smokeless, and second-hand smoke exposure (WHO, 2014a). Albeit tobacco use is reported in both smoke and smokeless forms, data for smokeless use is rarely captured, with data and information reported by WHO relating almost exclusively to smoking in over 15 year olds. Globally, 7% of female deaths and 12% of male deaths are related to tobacco use. The World Health Organization had estimated that, worldwide, tobacco will be the cause of 8 million deaths per year by 2030. From 6 million deaths in 2014 (WHO, 2014a), we are now on course to reach and surpass this threshold with an estimated 7.2 million deaths related to smoking reported in 2016 (WHO, 2017b). Eight million deaths in 2030 would be equivalent to 10% of all-cause deaths (WHO 2014a).

In 2016, smoking was estimated to be prevalent in 21.9% of the global population in people over 15 years of age. Once again, the highest population average in the world is reported in the WHO European region, with a 28.7% prevalence of smoking in over 15s (WHO, 2018c).

Aside from mortality, in 2015 smoking-attributable DALYs were mainly due to 41.2% of cardiovascular disease, 27.6% cancers and 20.5% chronic respiratory diseases. Smoking remains one of the worse contributors to DALYs, with an overall 6% global estimate (Global Burden of Disease, 2015).

2.2.3 Illicit drug use

A United Nations report estimated that 275 million people in 2016 had used illicit drugs at least once, a prevalence of 5.6% of the population aged 15 to 64 years (United Nations Office for Drugs and Crime - UNODC, 2018). It suggested 192 million people had used cannabis, 34 million opioids, 34 million amphetamines and prescription stimulants, 21 million ecstasy, 19 million opiates and 18 million cocaine. Around 31 million of these people have drug use disorders and are undergoing, or requiring, treatment. These people will use drugs via different administration routes, with 11 million estimated to be injecting them. One in 8 people who inject are living with HIV and one in 2 with hepatitis C, 1 million co-infected with both (UNODC, 2018).

Illicit drug use has severe health consequences. In 2015, around 450 thousand people died as a consequence of their drug use. Just under 168 thousand deaths were associated to drug use disorders, 69 thousand people dying from opioid overdose alone each year (UNODC, 2018; WHO, 2014b); the remaining deaths are often associated to HIV and HCV infections acquired mainly via sharing of injecting equipment (UNODC, 2018).

As well as mortality, opioid use disorders have been linked to other poor health outcomes, such as arthritis, chronic pain, musculoskeletal disorders, bacterial and viral infections, cardiovascular disease, limb amputations, poor mental health (e.g. suicidality, anxiety and depression), poor oral health (Bahorik et al. 2017). Similarly, cannabis use is linked to cognitive impairment, poor mental health (e.g. psychosis, suicidality, anxiety and depression), cardiovascular disease, chronic pulmonary disease, respiratory and other cancers (WHO, 2016b).

2.2.4 Implementation intentions to promote health behaviour

Implementation intentions are self-regulatory processes which take the form of ‘if-then’ plans and facilitate the attainment of goals and behaviour change (Gollwitzer, 1993). The role of intentions in behaviour change has been explored within a variety of theories and models of behaviour change, e.g. Ajzen’s Theory of Planned Behaviour (1991). The behavioural intention variable has been largely discussed and criticised as

it can be perceived as both an excellent and poor predictor of behaviour given the 'notorious' intention-behaviour gap (Prestwich, et al. 2006; Sheeran, 2002; Sutton, 1998). The intention-behaviour gap is the relation between intending to carry out a certain behaviour and actually performing that behaviour (Hagger & Luszcynska, 2014). Correlational studies suggest a medium-to-large effect size of intention-behaviour relations, which however don't seem to translate to the same level of effects in experimental studies, which is why the relation is referred to as having a "gap" (Armitage & Conner, 2001; Hagger & Luszcynska, 2014; Webb & Sheeran, 2007). The gap might be explained by dividing into intention activation and intention elaboration (Sheeran et al. 2005). Intention activation refers to characteristics of the context in which a goal is set. A goal intention "I intend to do X" might be the victim of change of salience, direction or reprioritisation depending on how achievable the goal itself is in a particular context; intention elaboration refers to the lack of detail of action planning that people usually provide for their goals (Bélanger-Gravel et al. 2013). Previous research shows that action planning interventions (implemented either as a once-off or as repeated sessions) can be helpful in reducting substance use behaviour in both populations with diagnosed addictions (Latka et al., 2008; Robles et al., 2004) and the general population (Bolman et al., 2015). Implementation intentions are hypothesised to offer a solution to the intention-behaviour gap (Hagger & Luszcynska, 2014).

Implementation intentions have been used to recognise contextual barriers and to plan in detail how to achieve a goal: when, where and how to perform a specific behaviour. They take the form of if-then plans: "if Y happens then I will perform Z", which commits individuals to behave in a particular way (Z) when they are presented with a certain situation (Y) (Gollwitzer, 1993). This provides the individual with self-regulatory strategies that create heightened accessibility of environmental cues, allowing individuals to automatically respond to contextual cues by unconsciously initiating their planned behaviour (Aarts et al. 1999; Gollwitzer, 1993; Hagger & Luszcynska, 2014). Implementation intentions are specifically mentioned in the Behaviour Change Technique Taxonomy (Michie et al. 2013) as a theoretical framework within action planning. Action planning in the taxonomy is the technique 1.4, part of Group 1: Goals and planning. It requires prompt detailed planning,

including context, frequency, duration and/or intensity, of the performance of a behaviour; the context can be environmental or internal (Michie et al. 2013). Implementation intentions have similarities with coping planning, which is included in the taxonomy as part of the problem solving technique 1.2 (Michie et al. 2013). Both techniques specify cues-to-action relevant to the individual or population, the when and where the behaviour will be enacted, and both can take the format of if-then plans; yet coping planning involves more conscious processing in decision-making and self-evaluation (Hagger & Luszcynska, 2014).

Implementation intention interventions can assume a variety of different formats. They can be oral or in writing, on paper or on screen (sometimes online), self-generated by people completing the intervention or pre-specified by the researchers or clinicians, or pre-specified situations with self-generated solutions (Armitage 2009; Armitage 2015; Caudwell et al. 2018; Hagger et al. 2012a).

A number of studies have investigated the effects of implementation intentions on health-related behaviours, but none have been solely focused on substance misuse (Adriaanse et al. 2011; Bélanger-Gravel et al. 2013; Gollwitzer & Sheeran, 2006). In fact, implementation intentions have rarely been applied to addictions. Addiction-related behaviours are notoriously difficult to change and for any change to be maintained. The automaticity aspect of implementation intentions discussed above, however, would suggest that this type of intervention could successfully be applied to substance use behaviours such as alcohol consumption, smoking and illicit drug use. Questions have been posed about the possible effectiveness of implementation intentions in individuals with a high cognitive load, such as people in opiate withdrawal (Brandstätter et al. 2001). Albeit implementation intentions were formed for a behaviour unrelated to their substance use, Brandstätter and colleagues (2001) found that both low and high cognitive load patients showed ‘automatised’ action initiation when they had formed implementation intentions.

Forming if–then plans specifying situations and associated solutions to achieve a particular goal could make an individual feel more confident about their ability to achieve behaviour change (Webb & Sheeran, 2008). The impact of implementation intentions on self-efficacy, as well as the role of self-efficacy within implementation

intention interventions has been investigated by various researchers with mixed findings. Some studies found implementation intentions increased self-efficacy (Murray et al. 2005, Rodgers et al. 2002), whilst others found no differences between intervention and control groups (Milne & Sheeran, 2002). In addition, some research has shown that forming implementation intentions can have negligible effects on both goal intentions and self-efficacy (Webb & Sheeran, 2008). The accessibility of the components of plans mediated the effect of implementation intentions on goal achievement (Webb & Sheeran, 2008).

Given no previously published meta-analyses have focused on the effectiveness of implementation intentions on substance use reduction at the time of this study, this review aims to fill this gap in the literature.

2.2.5 Objectives

This review's objective was to investigate the effectiveness of forming implementation intentions to reduce substance use. It aimed, in more detail, to answer the following questions:

1. Does forming implementation intentions reduce alcohol consumption?
2. Does forming implementation intentions reduce cigarette smoking?
3. Does forming implementation intentions reduce illicit drug use?

A secondary question which the review aimed to answer was:

4. Does forming implementation intentions increase self-efficacy?

2.3 Methods

The methodology and reporting of this review comply with the PRISMA statement checklist for the reporting of systematic reviews and meta-analyses (Moher et al. 2009), with the Meta-Analysis Reporting Standards – MARS (American Psychological Association, 2008) and with the Scottish Intercollegiate Guidelines Network (SIGN) checklist 1: systematic reviews and meta-analysis (SIGN, 2018). The review protocol

with methods and inclusion criteria was registered in advance on the University of York's Centre for Reviews and Dissemination PROSPERO register, as CRD42018116170.

2.3.1 Eligibility criteria

Only studies written in English were considered for selection, with no limit on publication dates on the first searches carried out between April and September 2018. An update search was run in January 2019, to which restricted publication dates were applied between 2018 and 2019 only. No geographical restrictions were applied.

2.3.1.1 Participants

No restrictions were applied to study participant characteristics

2.3.1.2 Interventions

The intervention under review was the formation of implementation intentions for the reduction of substance use behaviours, such as tobacco smoking, drinking alcohol, and other drug use. Trials with more than one intervention were selected when the implementation intention was reported independently so that the effect could be measured independently.

2.3.1.3 Comparisons

All studies had to present a control group. This included passive control groups (not performing any task) and active controls (performing an unrelated time-controlled task such as filling in an extra questionnaire or creating implementation intentions for an unrelated behaviour).

2.3.1.4 Outcomes

All studies were required to report on substance use as their main outcome measures. Outcomes such as weekly consumption of alcohol units, binge drinking occasions, quantity of cigarettes smoked, nicotine dependence and other drug use consumption were all accepted primary outcomes. Secondary outcomes, such as self-efficacy, were not necessary for inclusion in the systematic review.

2.3.1.5 Study design

Randomised controlled trials (RCTs) were selected for review. Intervention follow-up length was left unrestricted for selection.

2.3.2 Information sources

The following databases were searched between April 2018 and September 2018 via EBSCOhost: PsycINFO, MEDLINE and Psychology and Behavioural Science Collection. Reference lists of all selected papers for screening were searched by hand between September and October 2018. The following clinical trial registers were searched in November 2018: Clinicaltrials.gov and UK Clinical Trials Gateway.

2.3.3 Search and study selection

The search strategy was similar across all databases, adjusting for database-specific headings. An example of the search strategy for PsycINFO is provided in Supplementary File 2.1. Reference lists were searched by hand for relevant titles; whilst research registers were searched with "implementation intentions" in the title or trial description.

One reviewer carried out the full search on the three different databases via EBSCOhost between April and September 2018. Searches were saved in an EBSCOhost folder. All selected title items were transferred into the reviewer's personal EBSCOhost list.

2.3.4 Data collection process and items

Data was extracted by 2 reviewers, both chartered health psychologists, and input into a summary table then transferred into the Comprehensive Meta-Analysis Software v3.3. The data extracted (See Table 2.2) were study design (including control group format), follow-up period, sample characteristics (size, type, age, sex), theoretical approach, behavioural goal (reduce alcohol consumption, reduce tobacco smoking), implementation intentions format (online or pen & paper, pre-specified or self-

generated, number of plans), outcome measures of substance use reduction (units/day, binge drinking occasions, cigarettes/day, tobacco smoking quitting status), and effect size (Hedge's g with specified 95% Confidence Intervals, see section 2.7 for effect size calculation). For 10 studies, the authors were contacted for data or data clarification. Authors for 8 of these studies replied, 5 of which provided the requested information.

2.3.5 Risk of bias in individual studies

Risk of bias in individual studies was assessed with the SIGN checklist 2 for randomised controlled trials (SIGN, 2018). The checklist assesses selection bias, ascertainment bias, measurement bias, attrition bias and reporting bias. Agreement for assessment of individual studies by different reviewers was calculated using Cohen's kappa coefficient of inter-rater reliability (McHugh, 2012).

2.3.6 Summary measures

2.3.6.1 Statistical analyses

The Comprehensive Meta-Analysis software (version 3.3) was used to perform all calculations, test for heterogeneity and generate forest plots. Given the assumed heterogeneity in interventions, populations and outcomes, a random-effects model was selected (Hedges & Vevea, 1998). Using a random-effect model allows for a more conservative interpretation of the findings, given the confidence intervals (CIs) for the average intervention effects obtained in this way are wider compared to CIs obtained with fixed-effect models (Sutton, 2001).

2.3.6.2 Effect size calculations

For continuous outcomes (e.g. units alcohol/day, cigarettes/day and self-efficacy score) Hedges' g with 95% confidence intervals (CIs) were calculated as the difference between the intervention groups' mean follow-up scores and the comparison groups' mean follow-up score divided by the pooled standard deviation and adjusted for sample size. Hedges' g corrects for small sample sizes, and its results are very close to Cohen's d for 20 or more samples (Borenstein et al. 2009).

For dichotomous outcomes (e.g.percentage of people who quit smoking, group differences in abstinence) the risk ratio (RR) and 95% CIs were calculated on the basis of the number of events and the number of participants in the intervention and control groups. The RR were then transformed into Hedge's g statistic, using the Comprehensive Meta-Analysis Software v3.3, to allow for comparisons across studies (Borenstein et al. 2009)

In studies where the primary outcome was investigated with more than one measure (i.e. alcohol units consumed per week and binge drinking occasions or cigarettes smoked per day and nicotine dependence score) results were combined into one overall outcome effect size (i.e. alcohol use or smoking) using the Comprehensive Meta-Analysis Software v3.3. This allowed for a more comprehensive meta-analysis, and heterogeneity checks were performed during the analysis to ensure validity of outcomes (Puhan et al. 2006).

Alternative statistics (e.g. t-test, F-statistic, odd ratio or p-value and sample size) were used to calculate Hedge's g when studies did not provide means, standard deviations and proportions (Borenstein et al., 2009).

Effect sizes were coded so that positive scores signified favourable intervention effects such as lower alcohol use or smoking, with values of 0.20 considered small effects, 0.50 as medium and 0.80 as large (Cohen, 1988).

Separate analyses were conducted for studies that targeted alcohol, smoking or self-efficacy and those that included adjusted or unadjusted effect estimates, as some studies adjusted for baseline differences.

2.3.7 Synthesis of results

2.3.7.1 Assessment of heterogeneity

The I^2 and Q statistic tests were used to analyse heterogeneity between studies. I^2 indicates the heterogeneity percentage across the studies. The magnitude of heterogeneity was categorised as 1) I^2 =0% -25%, low heterogeneity; 2) I^2 =26% -50%, moderate heterogeneity; 3) I^2 =51%=75%, substantial heterogeneity; and 4) I^2 =76%-

100%, considerable heterogeneity (Higgins, 2011). Sensitivity analyses were performed to explore potential sources of heterogeneity.

2.3.8 Risk of bias across studies

2.3.8.1 Assessment of publication bias

Three techniques were used to determine the extent to which publication bias impacted on the results of the overall sample. Funnel plots were created to explore the presence of publication bias. The Egger regression asymmetry test and the Begg and Mazumdar adjusted rank correlation test (Begg & Mazumdar, 1994) were performed to measure the extent of the funnel plot asymmetry, with $p<0.05$ indicating a statistically significant publication bias. Finally, the Duval and Tweedie's trim-and-fill method (Duval & Tweedie, 2000), in which the studies are 'trimmed' from the right of the funnel plot and entered on the left side to address funnel plot asymmetry, was used to formalise the result of the funnel plot.

2.3.9 Additional analyses

2.3.9.1 Subgroup analyses

Subgroup analyses were conducted to explore potential sources of heterogeneity among studies for the alcohol and smoking outcomes using the following characteristics: quality of the study, type of implementation intention (self-generated or pre-specified), format of implementation intention (in person or online) and population (students or general population). In the alcohol use outcome, 2 of the 16 studies presented adjusted data. Unadjusted data of 14 studies was analysed for the main analyses, whilst the 2 studies presenting unadjusted data were analysed as a subgroup. The 16 studies were then combined to check for similarity of results. No subgroup analyses were performed for self-efficacy due to the small number of studies.

2.3.9.2 Sensitivity analyses

Sensitivity analyses were performed to determine the robustness of intervention effects by evaluating whether the overall effect size was sensitive to inclusion of any

individual study (Higgins and Green, 2011). One sensitivity analysis was carried out. Effects were explored to determine robustness when only studies with low risk of bias scores were retained in the analyses. These analyses were carried out by excluding studies with high risk of bias (Borenstein et al., 2009; Cooper et al. 2009).

2.4 Results

2.4.1 Study selection

AM carried out the full search on the three different databases via EBSCOhost between April and September 2018 (for full database search strategy see Supplementary File 2.1 at the end of chapter). Searches were saved in an EBSCOhost folder. Duplicates were removed manually. The reviewer screened 1756 titles and selected 79 relevant results for abstract selection. All selected title items were transferred into the reviewer's personal EBSCOhost list. Duplicates were removed manually before the abstract screening process. Abstracts were again screened by the same reviewer, who selected 29 relevant studies according to the eligibility criteria. Full texts were downloaded and divided by database. Twelve studies were excluded with reason (See Table 2.1) and 18 were selected for quality appraisal and inclusion in the analysis. A further 9 studies were found via reference list searches, 2 excluded after abstract screening, 3 excluded after full-text assessment with reason (See Table 2.1), and 4 selected for quality appraisal. An extra 2 studies were selected for abstract screening after searching Clinicaltrials.gov and UK Clinical Trials Gateway. One was retained for full-text assessment and included in the study.

After re-running the searches in January 2019, an extra 104 studies were screened by title, 8 selected for abstract screening, 4 were removed as duplicates and 3 selected for full-text screening. All 3 were excluded with reason (See Table 2.1).

Overall, a total of 1906 were identified in the search for this review: 94 were screened through their abstract, 40 selected for full-text assessment, 18 excluded with reason (See Table 2.1), 22 selected for quality appraisal, and 21 included in the meta-analysis (See Figure 2.1).

Table 2.1 Full-text reasons for exclusion

Reason for Exclusion	Paper
Protocol paper	Caudwell et al. 2016
Creation of implementation intention not completed by all intervention participants	Epton et al. 2014 Cameron et al. 2015
No formation of implementation intentions (e.g. coping skills training)	Steven & Hollis, 1989 Avants et al. 2000 Borlard et al. 2015 Dolan et al. 2013 Sugarman et al. 2010 Walters et al. 2014 Zetterlind et al. 2001 Elfeddali et al. 2012
No Control group	Elfeddali et al. 2013 Buitenhuis et al. 2018 Leightely et al. 2018
Not an intervention study	Hooper et al. 2013
Implementation intentions if-then plans not formed substance use	Brown et al. 2019 Chatzisarantis and Hagger, 2010
Unsuitable Implementation intention format	DeStasio et al. 2018

One study was included in the qualitative synthesis but excluded from the meta-analysis (Conner & Higgins, 2010). The study presented interval follow-up period of 4 to 48 months; however, the authors, after being contacted for unadjusted 4 month follow-up data, suggested the exclusion of their paper on the basis of the multi-level nature of their data.

2.4.2 Characteristics of the studies

Among the 22 studies selected for the review, 15 studies were RCTs on interventions to reduce alcohol consumption, whilst the remaining 7 RCTs aimed to reducing cigarette smoking (Table 2.2). One paper (Armitage & Arden, 2016) reported 2 different studies which were treated as separate studies for the analysis, whilst another divided results by nationality of the sample (Hagger et al. 2012b) bringing the total number of studies reviewed for the alcohol use outcome to 18. All studies had suitable explanation about the randomisation procedure, albeit details on which online software or website was missing when papers described their randomisation as being

online. All studies reported behavioural outcomes; some studies (*k*= 6) reported self-efficacy comparison outcomes at follow-up.

The three main outcome analyses were run on studies with a follow-up of between 2 weeks and 3 months (*k*= 19), with a mean follow-up period of M= 5.68 weeks (SD= 4.8). These were all considered short follow-up timeframes, given healthy habits tend to require around 6 months to become established (Armitage et al. 2011).

Two studies with, respectively, 1 week and 6 months follow-up (Norman & Wrona-Clarke, 2016; Norman et al. 2018) were included in the meta-analysis in the subgroup analyses of adjusted data on alcohol use (*k*=2).

The papers selected for the meta-analysis (*k*=21) reported an initial sample total of N= 6655. The analysed sample total was 2758, with some papers performing an intention-to-treat analysis (*k*= 13).

This meta-analysis only analysed the effect of implementation intentions on substance use behaviour. Some of the studies selected were comparing control conditions to implementation intention groups and other intervention groups, such as Theory of Planned Behaviour messages (Table 2.2). The participants included in these groups do not feature in this analysis, increasing the difference between total and analysed sample. In total, a sample of 2055 was analysed for the alcohol use outcome, 703 for the smoking outcome, and 468 for the self-efficacy outcome (albeit the self-efficacy outcome had included repeated participants from the alcohol and smoking studies but for a different outcome).

Figure 2.1: PRISMA flow diagram of study selection

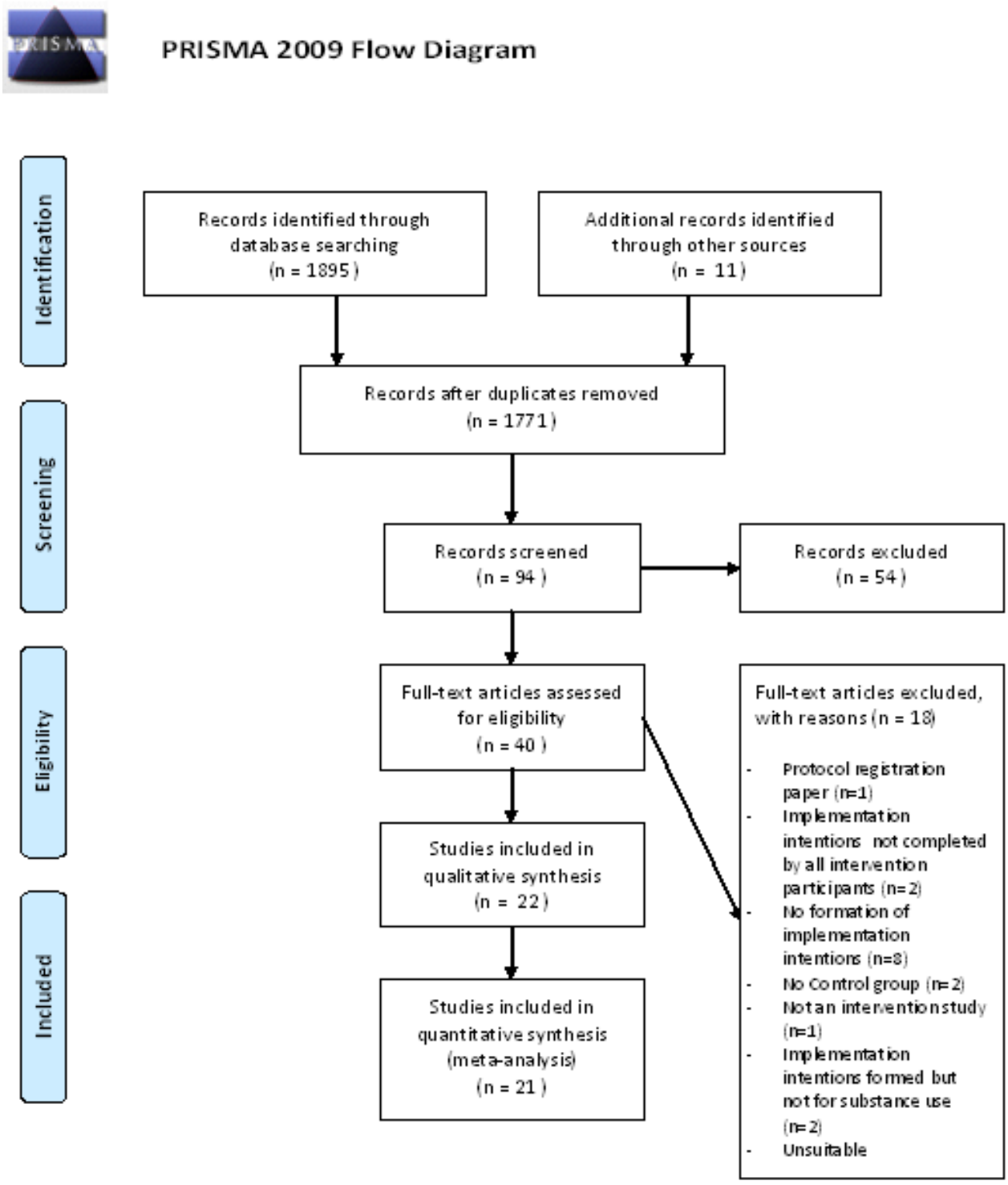


Table 2.2: Summary table of characteristics of studies included in the review (N=22)

Authors (year)	Study Design (group types)	Follow-up period	Sample characteristics	Theoretical approach	Behavioural goal	Implementation intentions format	Measures of substance use reduction	Effect size (Hedge's g) [95%CI]
Arden & Armitage (2012)	RCT (2x control groups and 1x II)	2 weeks	56 students; UK Age: 20.57y (1.9); 66.1% ♀	SOC	Reduce alcohol consumption	Pen and paper, pre-specified situation and solutions.	Alcohol consumption Units/week, binge drinking occasions	Combined g= 0.64 [0.21; 1.07]
Armitage (2007)	RCT	2 months	90 adults; UK Age: 33y (13); 45.56% ♀	TPB	Reduce smoking	Pen and paper for one self-generated plan.	Nicotine dependence, N of quitters	Combined g=0.47 [0.08; 0.85]
Armitage (2008)	RCT (2 intervention x2 control)	1 month	193 adults; UK Age: 37y (14.6); 51.8% ♀	SOC	Reduce smoking	Pen and paper, pre-specified situation and solutions.	Cigarettes/day, nicotine dependence N of quitters	Combined g=0.57 [0.23; 0.9] Self-efficacy: g= 0.26 [-0.14; 0.66]
Armitage (2009)	RCT (2 intervention x2 control)	1 month	248 adults; UK Age: 38.4y (15.46); 50.4% ♀	SOC	Reduce alcohol consumption	Pen and paper form. Plans pre-specified/self-generated in the written form	Alcohol consumption Units/day	g= 0.30 [-0.06; 0.66]
Armitage (2015)	RCT (Intervention, Active control)	1 month	65 adults; UK Age: 33.77y (9.69); 56.9% ♀	SOC	Reduce alcohol consumption	Pen and paper form. Control asked to tick pre-specified VHS, intervention to link	Alcohol consumption Units/week	g= 0.13 [-0.35; 0.61]

Armitage (2016)	RCT 4 groups (if-then, when-then, 2 x control)	1 month	168 adults; UK Age: 33y (12.30), 47.01% ♀	SOC	Reduce smoking	Pen and paper, pre-specified situation and solutions.	Quitting, cigarettes/day	g=-0.01 [-0.43; 0.41]
Armitage & Arden (2008)	RCT (2x control groups and 1x II)	2 months	350 adults; UK Age: 36.20y (14.3); 50.6% ♀	SOC	Reduce smoking	Pen and paper, self-generated plan	Quitting and nicotine dependence score	Combined g= 0.46 [0.26; 0.67]
Armitage & Arden (2012)	RCT (2 CP (multiple or single) x II x active control	3 months	69 adults; UK Age: 38.51y (16.34); 52.2% ♀	SOC	Reduce alcohol consumption	Pen and paper, pre-specified situation and solutions.	Alcohol consumption in Units	g= 0.54 [-0.13; 1.2] Self-efficacy g= 0.36 [-0.3; 1.02]
Armitage & Arden (2016)	2-study RCT	1 month	Adults & students; UK <u>Study 1</u>: N= 85 Age 23.69y (3.61); 62.38% ♀**;** <u>Study 2</u>: N= 58 Age: 19.38y (0.9); 75.86% ♀**;**	Self-affirmation Theory	Reduce alcohol consumption	Self-affirming pre-specified intention	Alcohol consumption in Units/Week	<u>Study 1</u> g= 0.59 [0.16; 1.02] Self-efficacy g= -0.09 [-0.51; 0.33] <u>Study 2</u> g= 0.47 [-0.04; 0.99] Self-efficacy g= 0.49 [-0.02; 1.01]

Armitage et al. (2011)	RCT (2 experimental, 1 control)	1 month	278 adults; UK Age Range 16-74; 66.2% ♀	Self-affirmation theory	Reduce alcohol consumption	Pen and paper form. Pre-specified plans but participants had to write them down as one sentence	Alcohol consumption in Units/Day	g= 0.57 [0.28; 0.86]
Armitage et al. (2014)	RCT (experimental and control group)	2 months	67 adolescents; UK Age: 17.09y (0.38); 55.22%	Self-affirmation theory	Reduce alcohol consumption	Pen and paper form. Pre-specified plans but participants had to write them down as one sentence	Alcohol consumption in Units/Day	g=0.19 [-0.29; 0.66] Self-efficacy g= -0.13 [-0.61; 0.34]
Caudwell et al. (2018)	RCT (2 autonomy support x 2 II)	4 weeks	202 students; Australia Age: 20.95y (4.02); 73% ♀	SDT and TPB	Reduce alcohol consumption	Online, to use example given or elf-generate plan.	Weekly pre-drinking summed to create monthly score	g=0.07 [-0.43; 0.56]
Conner & Higgins (2010) *	RCT (II, self-efficacy intervention, 2 control conditions)	48 months	1551 adolescents; UK No mean age reported; 48.9% ♀	NR	Reduce smoking	Pen and paper, 5 x pre-specified plans	Jarvis (1997) self-report smoking measure or objective carbon monoxide breathalyser.	g=0.24 [-2.64; 3.12]
Ehret & Sherman (2018)	RCT (II, self-aff, control, II+self-aff)	2 weeks	293 college students; USA Mean age NR; 70% ♀	Self-affirmation theory	Reduce alcohol consumption	On screen in lab. Self-generated plans.	Typical drinking week measured with Daily Drinking Questionnaire;	g=0.26 [-0.08; 0.59]
Hagger et al. (2012a)	Cluster RCT 2x2 (mental simulation; II)	1 month	238 undergraduate students; UK Age: 20.35y (2.51); 58% ♀	HAPA/TPB	Reduce alcohol consumption	Online, self-generated plans + self-affirmation manipulation.	Alcohol consumption in Units/Week & binge drinking occasions	Combined g=0.25 [-0.16; 0.66]

Hagger et al. (2012b)	Multi-centred Full-factorial RCT 2x2 (mental stimulation; impl intentions)	1 month	718 undergraduate students (240 Estonia, 194 Finland, 284 UK); Age: 21.37y (SD range= 2.7-4.28); 74% ♀	HAPA/TPB	Reduce alcohol consumption	Pen and paper, self-generated plans.	Alcohol consumption in Units/week and binge drinking occasions	UK sample Combined g= 0.35 [0.06; 0.65] Estonian sample Combined g= 0.31 [0.02; 0.6] Finnish sample Combined g= -0.16 [-0.49; 0.18]
Matcham et al. 2014	RCT 2x2 (effectiveness booklet and/or/not II)	4 weeks	160 adults; UK Age: 43.7y (14.2); 54.4% ♀	NR	Reduce smoking	Pre-specified plans written on paper but repeated orally.	Self-report 4-week quit status (and CO breath test where possible)	g= 0.06 [-0.4; 0.53]
Murgraff et al. (2007)	RCT	8 weeks	347 students; UK Age: 26y (SD NR) 73.2% ♀	TPB	Reduce alcohol consumption	Recommended daily units + normative misperceptions + self-efficacy statements + 6 pre-specified plans.	Alcohol consumption on Friday (units)	g=0.44 [0.09; 0.8] Self-efficacy g=0.21 [-0.14; 0.56]
Norman & Wrona-Clarke (2016)	Cluster RCT 2x2 (mental simulation; II)	1 week	348 undergraduate students; UK Age: 22.58y (6.31); 64.1% ♀	Self-affirmation theory	Reducing alcohol consumption	Online, self-generated plans + self-affirmation manipulation.	Alcohol consumption in Units/Week and binge drinking occasions	Combined g=0.19 [-0.04; 0.42] Adjusted data
Norman et al. (2018)	RCT (2 self-affirmation x 2 TPB messages x 2 II)	6 months	2682 students; UK Age: 18.76y (1.94); 53.8% ♀	TPB	Reduce alcohol consumption	Online, self-generated plans.	Alcohol consumption in Units/week and binge drinking sessions	Combined g= -0.03 [-0.23; 0.17] Adjusted data

Rivis et al. (2013)	RCT (2 II x 2 stereotype evaluation)	1 month	202 pupils; UK Age: 16.62y (0.68); 55.4% ♀	TPB	Reduce alcohol consumption	One pre-specified plan on paper read by participant 3 times	Binge drinking sessions	g=0.2 [-0.08; 0.47]
Webb et al. (2009)	RCT (1 intervention, 1 control)	1 month	172 students; UK Age: 18.49y (SD NR); 43% ♀	NR	Reduce smoking	Pen and paper. 4 pre specified situations, subjective solution. Seat belt control group.	Cigarettes/day	g= 0.11 [-0.19; 0.41]

Note: RCT - Randomised Controlled Trial; II - Implementation intentions; SOC - Stages of Change Model; TPB - Theory of Planned Behaviour; HAPA - Health Action Process Approach; SDT - Self-Determination Theory; VHS - Volitional Help Sheet; NR – Not reported. *= Study included in the review but not included in the meta-analysis.

2.4.2.1 Characteristics of the participants

The two main populations recruited within the selected studies were adolescents and undergraduate students (*k*=11), and the general population (*k*=10). The total mean age of the sample ranged from 16.6 to 43.7 (M= 26.97, SD= 8.69, *k*= 20). A slightly higher percentage of women was generally included in the studies, ranging from 43 to 76% (M= 59.03%, SD=9.95, *k*= 22).

2.4.2.2 Characteristics of substance use outcomes

Most studies measuring alcohol use outcomes used self-reported weekly or daily consumption or binge drinking occasions (*k*=14). One study (Ehret & Sherman, 2018) used the Daily Drinking Questionnaire (Collins et al. 1985). The studies measuring smoking outcomes tended to use a mixture of self-report on cigarettes a day and quitting status (*k*=6), nicotine dependence score (*k*=3) and objective carbon monoxide (CO) breath tests (Matcham et al. 2014), a non-invasive procedure used for data validation.

2.4.2.3 Characteristics of implementation intention interventions

All studies referred to Gollwitzer's (1993) principles of implementation intentions. Implementation intentions were characterised mainly by two features. All implementation intentions were delivered after other questionnaires, such as demographic information or self-affirmation messages. The first feature to characterise the intervention was the type of implementation intention: self-generated (k=10) or pre-specified plans (*k*=12). The second feature was the mode of delivery: online on a computer screen (in person or remotely; *k*=5) or delivered in person on paper (*k*=17).

2.4.3 Risk of bias within studies

Risk of bias in individual studies was assessed with the SIGN checklist 2 for randomised controlled trials (SIGN, 2018). One reviewer (AM) completed the quality appraisal for all studies. A second reviewer (R2) appraised 13 studies, whilst a third reviewer (R3) appraised 10 studies (Table 2.3).

Table 2.3: Risk of bias of selected studies

	Randomisation sequence concealment (selection bias)	Allocation concealment (selection bias)	Blinding of subjects and investigators (ascertainment	Similarity in groups at baseline (selection bias)	Relevant, valid and reliable outcomes (measurement bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting	Overall quality
Arden & Armitage 2012	+	+	?	+	?	+	+	++
Armitage 2007	+	+	+	+	+	+	+	++
Armitage 2008	+	+	+	+	+	+	+	++
Armitage 2009	+	+	+	+	+	+	?	++
Armitage 2015	+	+	+	+	+	+	+	++
Armitage 2016	+	+	+	+	+	+	+	++
Armitage & Arden 2008	+	+	+	-	+	+	+	++
Armitage & Arden 2012	+	+	+	+	+	+	?	++
Armitage & Arden 2016	+	+	?	+	+	?	?	++
Armitage et al. 2011	+	+	+	+	+	+	+	++
Armitage et al. 2014	+	+	+	+	+	+	+	++
Caudwell et al. 2018	+	+	?	+	+	-	+	++
Conner & Higgins, 2010	+	+	-	-	+	-	+	+
Ehret et al. 2018	+	+	?	+	+	+	-	+
Hagger et al. 2012a	+	+	+	-	+	-	?	-
Hagger et al. 2012b	+	+	+	+	+	-	?	+
Matcham et al. 2014	+	-	-	?	+	?	+	+
Murgraff et al. 2007	+	-	?	?	?	-	?	-
Norman & Wrona-Clarke 2016	+	+	+	+	+	+	-	+
Norman et al. 2018	+	-	-	+	+	-	+	+
Rivis & Sheeran, 2013	+	?	?	+	?	-	?	-
Webb et al. 2009	+	+	+	+	+	+	+	++

Note: Quality assessed as: ++ (High quality); + (Acceptable); - (Low quality); ? (Can't say/Does not apply)

A Cohen's Kappa coefficient (*K)* was calculated for the reviewers to assess inter-rater agreement (McHugh, 2012). There was a substantial inter-rater agreement between AM and R2, with *K*=0.64, p<.001 (n=143), and a moderate inter-rater agreement between AM and R3, with *K*=0.54, p<.001 (n=110). Disagreement or discrepancies were resolved by discussion (See Table 2.3).

2.4.4 Synthesis of results

The effectiveness of implementation intention was analysed by behavioural outcome and described in the paragraphs below. The intervention effectiveness was calculated between-groups at follow-up.

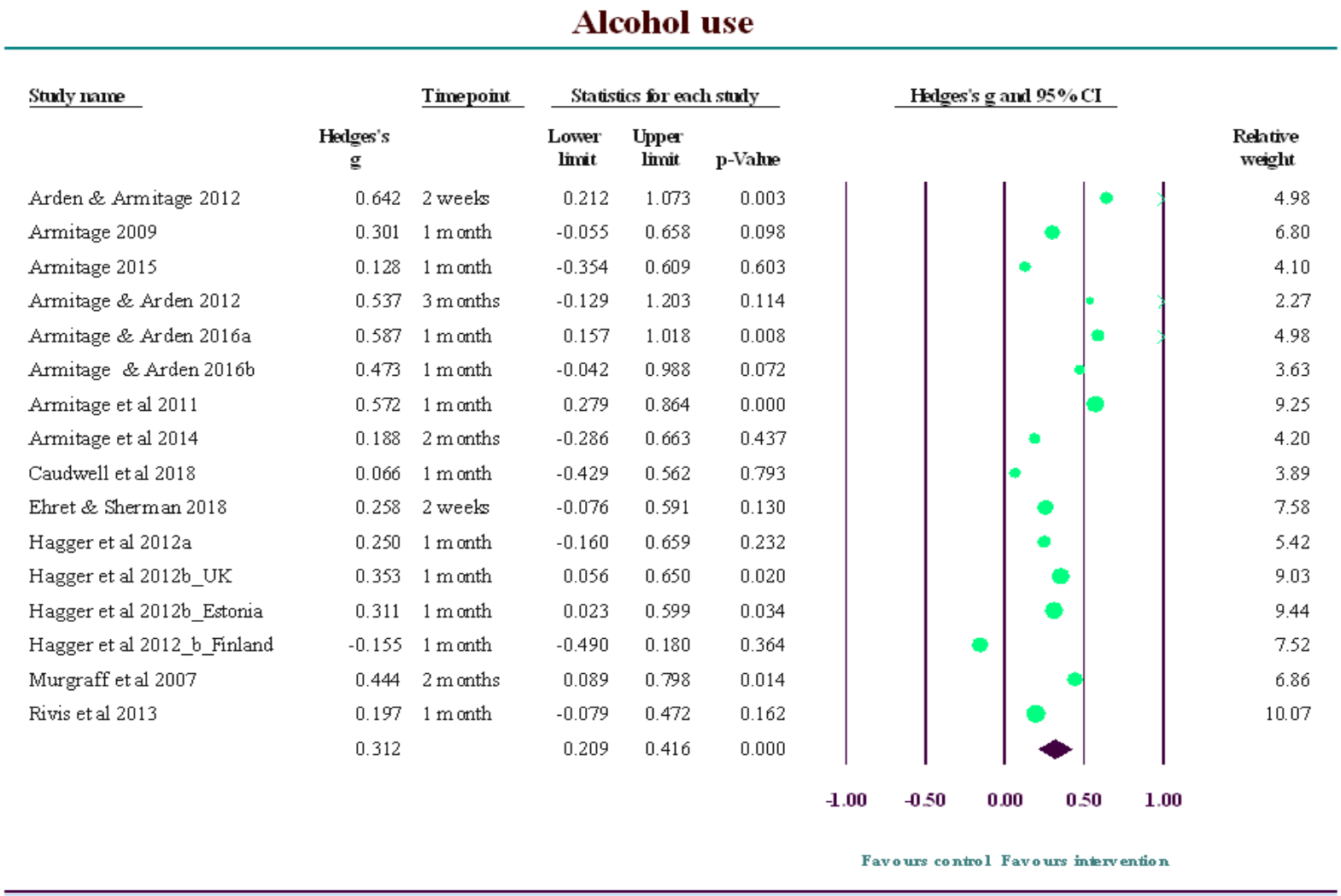
2.4.4.1 Alcohol consumption

Firstly, data was pooled from 16 studies that reported unadjusted data (Arden & Armitage, 2012; Armitage, 2009; Armitage, 2015; Armitage & Arden, 2012; Armitage & Arden, 2016a; Armitage & Arden, 2016b; Armitage et al. 2011; Armitage et al. 2014; Caudwell et al. 2018; Ehret & Sherman, 2018; Hagger et al. 2012a; Hagger et al. 2012b (3 samples); Murgraff et al. 2007; Rivis et al. 2013) and included 2055 individuals (students and general population). The effect size for alcohol use was g=0.31 (CI: 0.21, 0.42), p< .001, indicating that implementation intentions had a small but significant effect in reducing alcohol consumption (Figure 2.2). The statistical heterogeneity across the studies was not significant ($Q_{statistic}$= 18.39; df=15; I^2 = 18.41 %; p= .24).

2.4.4.2 Tobacco smoking

Data was pooled from 6 studies (Armitage, 2007; Armitage, 2008; Armitage, 2016; Armitage & Arden, 2008; Matcham et al. 2014; Webb et al. 2009) and included 703 individuals. A small effect size was detected, with g=.31 (CI: 0.12, 0.5), p=.002, indicating that implementation intentions had a small effect on reducing smoking (Figure 2.3). The homogeneity analysis suggested a moderate, yet non-significant degree of statistical heterogeneity ($Q_{statistic}$= 9.9; df= 5; I^2 = 49.49%; p= .08).

Figure 2.2: Forest plot of the effect of implementation intentions on alcohol use at follow-up.



2.4.4.3 Illicit drug use

No studies that fitted the inclusion criteria were found in the present systematic search for the use of implementation intentions on reduction of illicit drug use. Literature suggests implementation intentions should be employed to prevent and treat addiction (Prestwich et al. 2006), yet more research is undoubtedly needed in this area. The lack of literature on this topic could also be due to publication bias, favouring publication of significant results.

2.4.4.4 Self-efficacy

Six studies evaluated the impact of implementation intentions on self-efficacy scores, with g ranging from -0.2 to 0.494 (Armitage, 2008; Armitage & Arden, 2012; Armitage & Arden, 2016a; Armitage & Arden, 2016b; Armitage et al. 2014; Murgraff et al. 2007). The pooled studies, which included 468 individuals (adult and student population), resulted in an effect size of g=0.16 (CI: -0.023, 0.342, p=.087), indicating that implementation intentions had a very small, non-significant effect in improving self-efficacy scores. One study (Norman et al. 2018) provided adjusted data so it was not included in this analysis (Figure 2.4). The statistical heterogeneity across the studies was neither important nor significant ($Q_{statistic}$= 5.07; df= 5; I^2 = 1.373%; p= .407).

2.4.5 Risk of bias across studies

2.4.5.1 Assessment of publication bias

Funnel plots for the studies reporting alcohol, smoking and self-efficacy follow-up effect sizes were visually inspected to assess publication bias, with no bias detected (see Figures 2.5, 2.6 and 2.7). Eggers regression test (Egger et al. 1997) also showed no evidence of publication bias among the studies reporting alcohol use (intercept=0.4; SE=1.25; CI= 2.28, 3.08), among those reporting tobacco smoking (intercept=-2.33; SE=1.89; CI= -7.57, 2.91) and those reporting self-efficacy (intercept=-2.64; SE=1.14; CI= -0.28, 5.57). The trim and-fill method (Duval & Tweedie, 2000) suggested that no missing studies were needed to make the plot symmetric for the smoking outcome, yet it suggested the inclusion of an extra 2 studies for greater symmetry for both the alcohol and self-efficacy outcomes.

Figure 2.3: Forest plot of the effect of implementation intentions on tobacco smoking at follow-up.

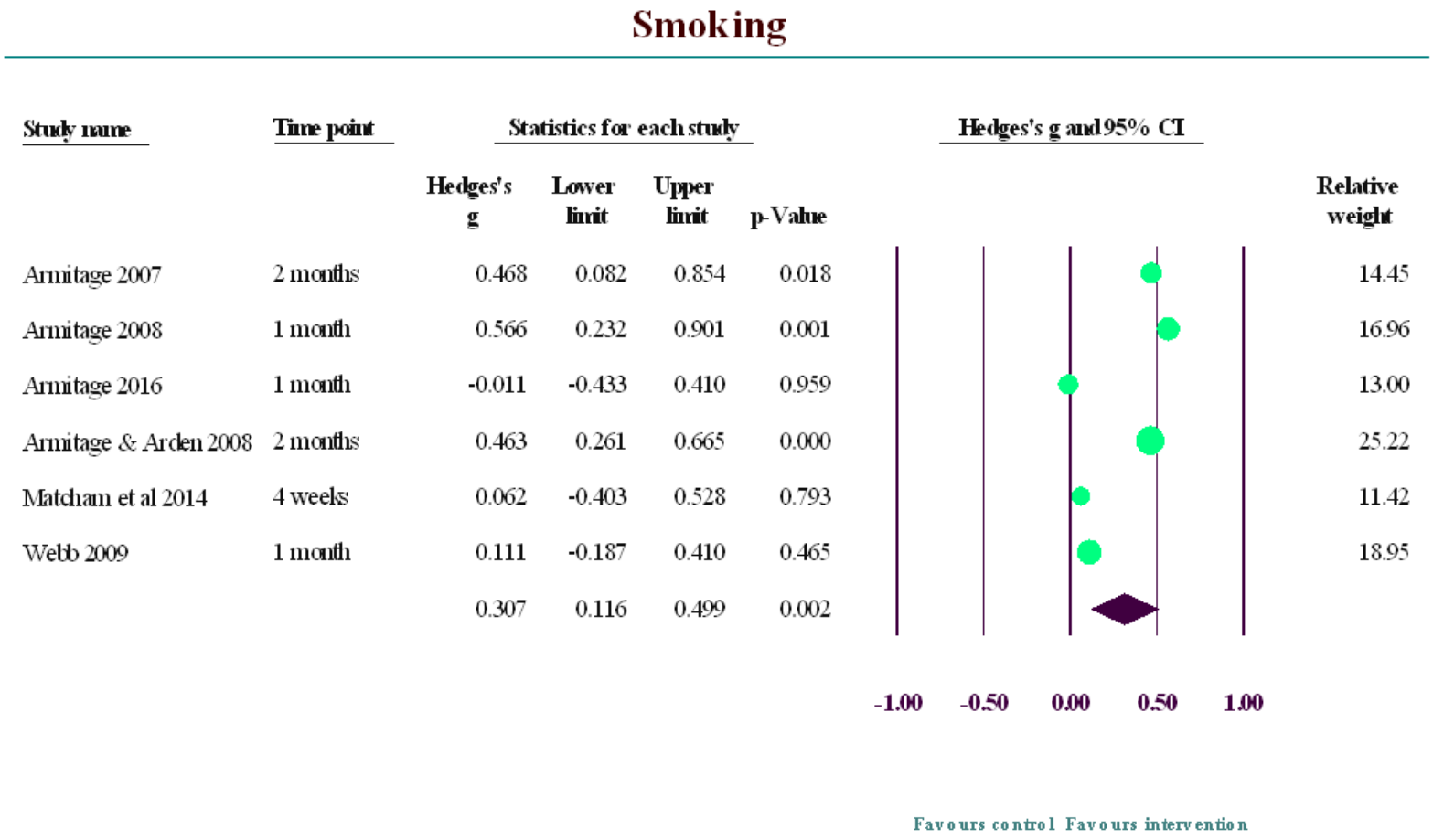


Figure 2.4: Forest plot of the effect of implementation intentions on self-efficacy at follow-up.

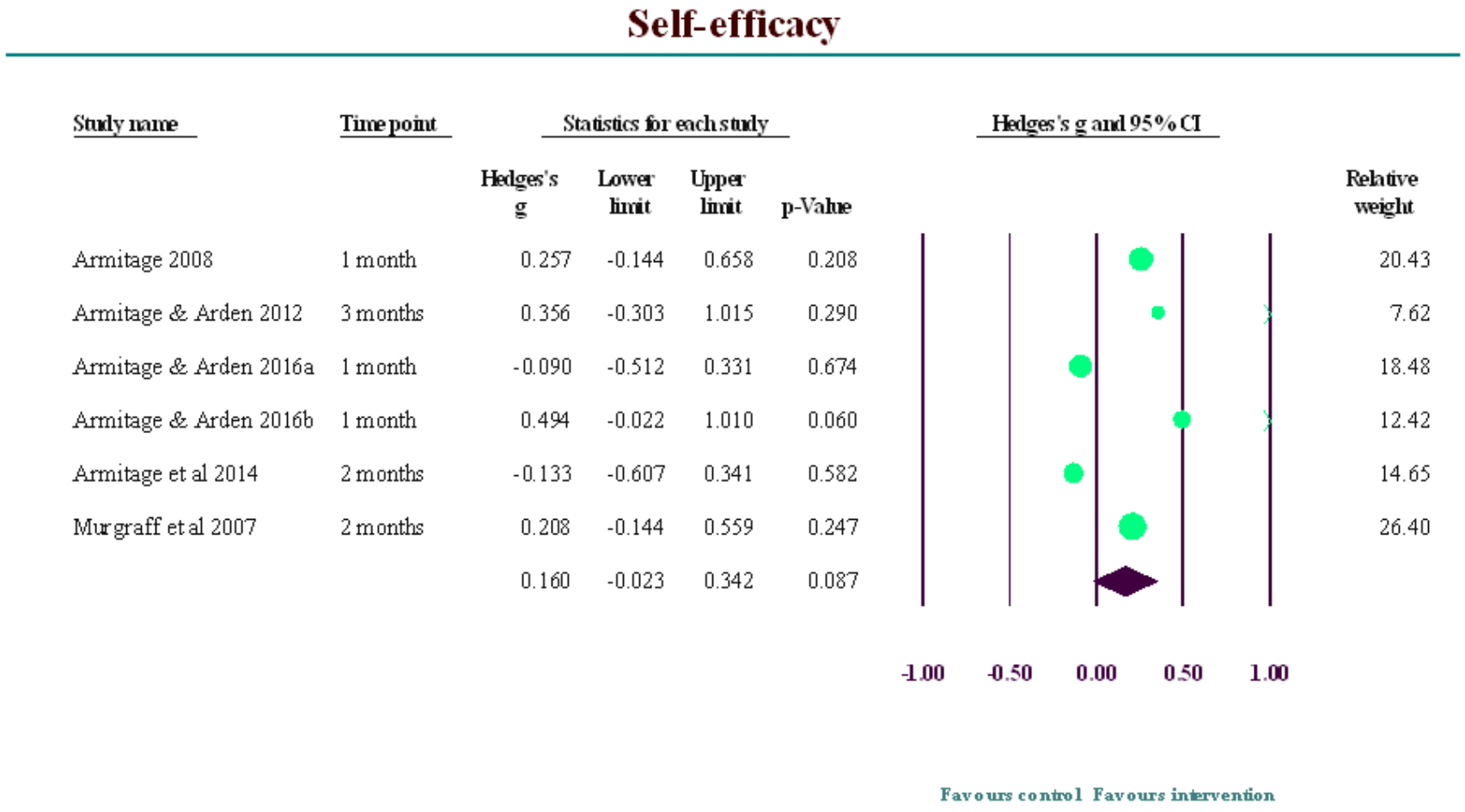


Figure 2.5: Publication bias analysis for alcohol use

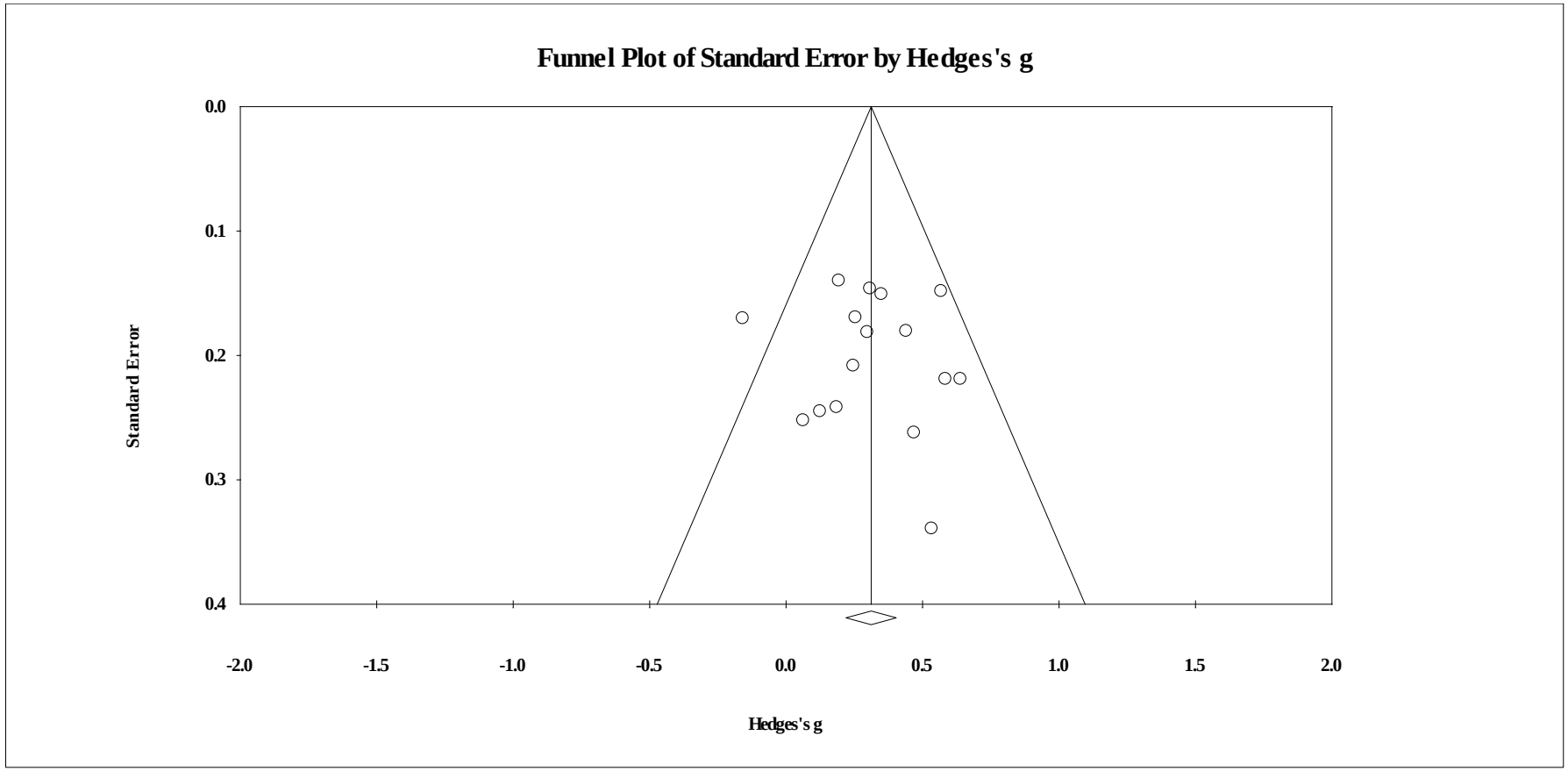


Figure 2.6: Publication bias analysis for tobacco smoking

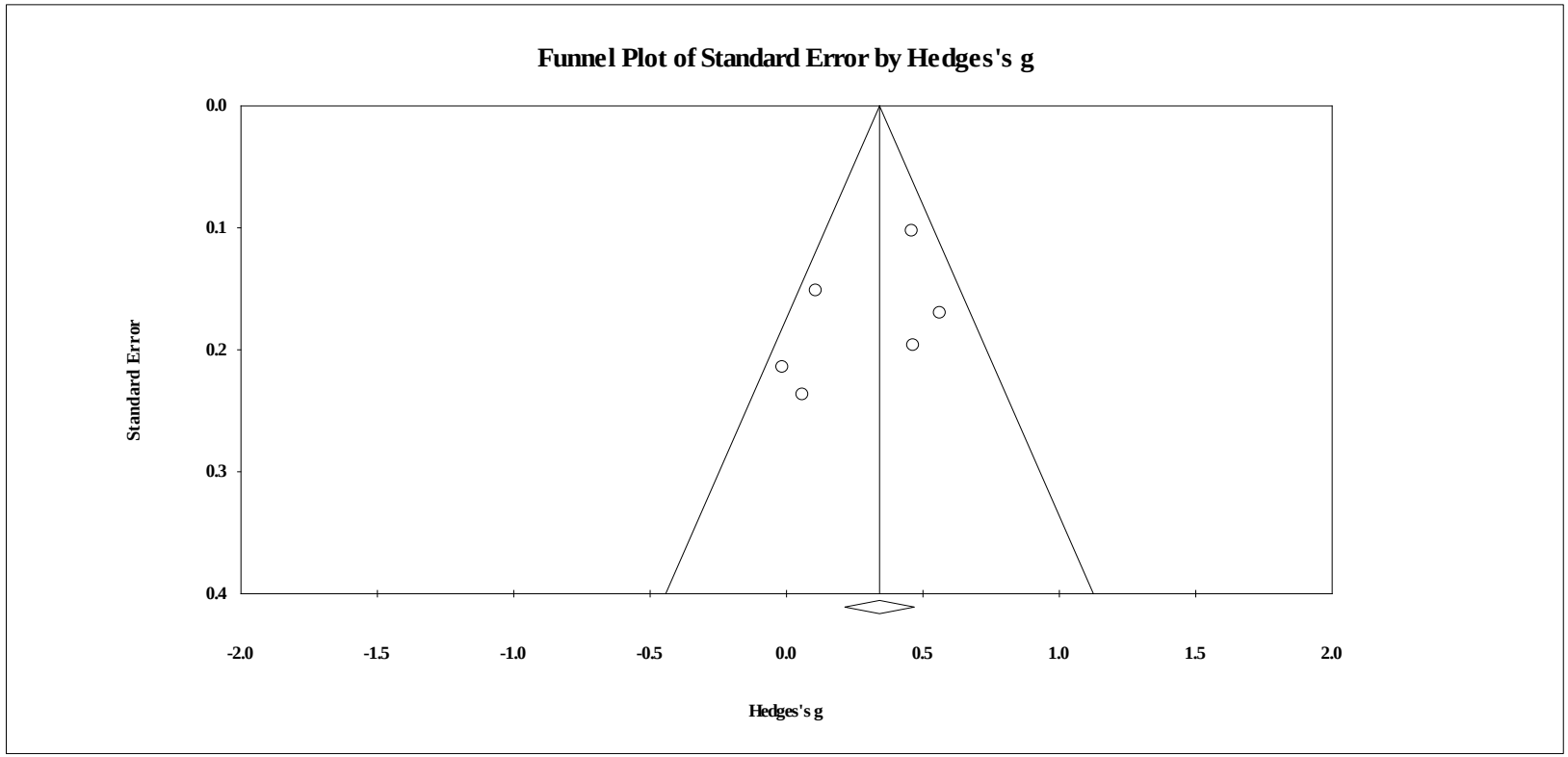
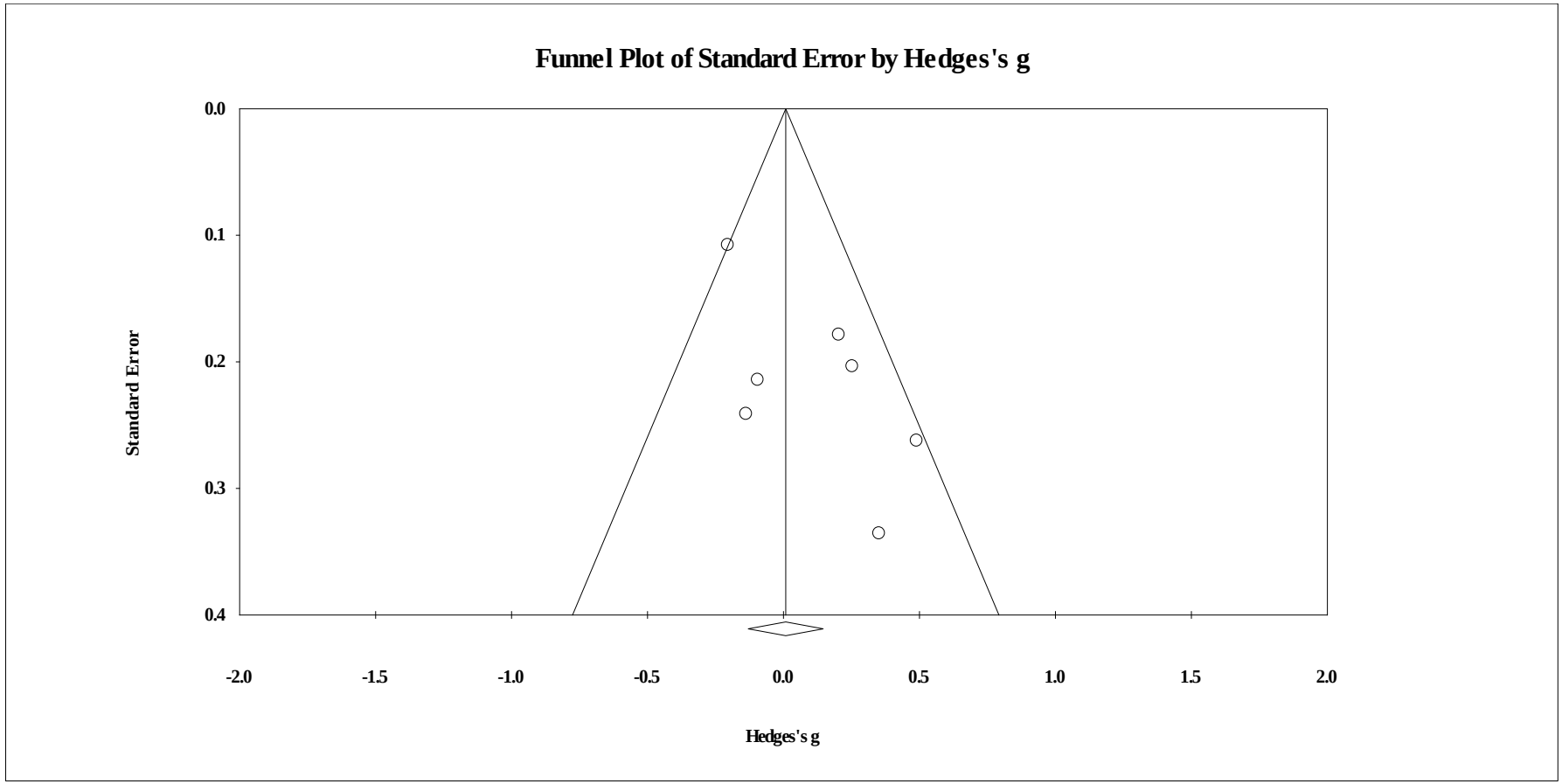


Figure 2.7: Publication bias analysis for self-efficacy



This simply estimates that the addition of 2 unpublished studies would increase the symmetry of the funnel plot, showing slight publication bias towards studies with positive medium effect sizes.

2.4.6 Additional analysis

2.4.6.1 Sensitivity analyses

Sensitivity analyses were used to remove individual studies with high relative weight to investigate the robustness of the overall results. For the alcohol outcome, one study (Rivis et al 2013) was found to influence the meta-analysis results more than other studies. When Rivis et al. (2013) was omitted from the analysis, a slight increase in the pooled effect size was observed, g=0.33 (0.21, 0.44), p<.001.

For the tobacco smoking outcome, one study (Armitage and Arden 2008) was omitted, providing a slightly smaller effect size, g=0.25 (CI: 0.02, 0.48), p=.031.

For the self-efficacy, one study (Murgraff et al. 2007) was omitted, resulting in a very slight reduction in effect size, g=0.15 (CI: -0.09, 0.39), p=0.23.

2.4.6.2 Subgroup analyses

Subgroup analyses were run where possible ($k \geq 2$ in each subgroup) for all outcomes (Table 2.4). Self-efficacy did not present a sufficient number of studies per subgroup to allow any comparison. Subgroup analyses on the alcohol outcome showed that the effect of implementation intentions differed according to mode of delivery (in person or online), type of implementation intention (self-generated or pre-specified), population (general population or students) and by the studies' methodology quality (with high quality differing from acceptable or low quality). The two studies (Norman & Wrona-Clarke, 2016; Norman et al. 2019) presenting adjusted data revealed a lower effect size compared to the unadjusted analysis reported in the main results, resulting in a slightly lower overall effect size when all studies were combined.

The only two subgroup analyses obtainable for the smoking outcome were population and type of implementation intention. Both revealed differences in effect sizes between subgroups (Table 2.4).

Table 2.4: Effect sizes at follow-up using moderators of effect of implementation intention on alcohol use and tobacco smoking.

	Alcohol use		Tobacco smoking	
Factor	**No. of studies**	**Pooled g (95% CI)**	**No. of studies**	**Pooled g (95% CI)**
Mode of delivery				Number of studies per subgroup not sufficient to allow comparison.
In person	13	0.335** (0.211, 0.458)		
Online	3	0.214 (-0.015, 0.443)		
Type of implementation intention				
Pre-specified	9	0.389** (0.258, 0.520)	3	0.229 (-0.158, 0.616)
Self-generated	7	0.232** (0.082, 0.383)	3	0.352* (0.119, 0.584)
Population				
Students	10	0.254** (0.129, 0.379)	2	0.097 (-0.154, 0.348)
General	6	0.447** (0.278; 0.615)	4	0.406** (0.199, 0.613)
Quality				Number of studies per subgroup not sufficient to allow comparison.
Low	3	0.281* (0.089, 0.473)		
Acceptable	4	0.201 (-0.02, 0.422)		
High	9	0.413** (0.271, 0.556)		
Effect estimate				
Adjusted analysis	2	0.115 (-0.011, 0.241)		
Unadjusted analysis	16	0.312** (0.209, 0.416)		
Overall	18	0.272** (0.175, 0.369)		

Note: *p< .05; **p≤ .001

2.5 Discussion

This meta-analysis reviewed the evidence of the effectiveness of implementation intention on the reduction of substance use. It found a small, yet significant, effect size for both alcohol use and tobacco smoking. The Hedges' g values reported in this meta-analysis are smaller than the medium effect size of *d* = 0.65 reported in a highly cited meta-analysis of behaviour change studies (Gollwitzer & Sheeran, 2006). The results are, however, similar to other meta-analyses investigating the effectiveness of implementation intentions on specific health behaviour, such as promoting physical activity, SMD= 0.24 (Bélanger-Gravel et al. 2013), and reducing unhealthy eating, d=0.29 (Adriaanse et al. 2011).

The results of this meta-analysis suggest that implementation intentions have been successfully applied to some substance use behaviours such as alcohol consumption and tobacco smoking, implying that the automaticity aspect of implementation intentions could function as the mechanism of behaviour change. The results for the alcohol use outcome were consistent throughout the subgroup and sensitivity analyses, suggesting a degree of confidence in the strength of the findings. The number of studies included for this outcome (*k*=16) and the general high quality of the studies presented, contributed to the strength of the findings.

The strength of the findings on the tobacco smoking and self-efficacy outcomes were less consistent due to the low number of studies identified for the meta-analysis (*k*=6 for either outcome). The tobacco smoking results were mostly homogeneous, with only one study reporting a negligible effect of implementation intentions on the outcome (Armitage, 2016). The results for the self-efficacy outcome, however, presented a small effect size with confidence interval overlapping zero. Not only was the number of studies small, but the degree of variation in the promotion of action-specific self-efficacy was obvious in these results. As with previous studies investigating self-efficacy and implementation intentions (Milne et al. 2002; Murray et al. 2005, Rodgers et al. 2002; Webb & Sheeran, 2008), the findings of this study show inconsistency and further research on this area is recommended. However, the overall findings on alcohol use and tobacco smoking remain in line with previously published literature on implementation intentions (Adriaanse et al. 2011; Bélanger-Gravel et al. 2013; Kwasnicka et al., 2013).

In some studies, implementation intention interventions were coupled with other behaviour change techniques (BCTs), such as self-affirmation manipulations, social comparisons and information about social and environmental consequences or mental rehearsal of successful performance. Since the introduction of the Behaviour Change Technique Taxonomy (Michie et al. 2013) and the TIDieR checklist (Template for Intervention Description and Replication) for better reporting of interventions (Hoffmann et al. 2014), there have been advances in the way behaviour interventions are reported. However, it is possible that the effect sizes reported in the findings of this review might have been influenced by more than one BCT. This is the nature of

social and health psychological research, which includes research with possible confounders given 'laboratory' experimental conditions are unnatural and arguably lack ecological validity (Orne, 1962).

Regrettably, this review was unable to analyse whether implementation intention interventions can reduce illicit drug use. The lack of identifiable studies on this subject is surprising, highlighting a need for this type of research to be conducted. Given the interest this topic had raised in previous years (Brandstätter, Lengfelder & Gollwitzer, 2001; Churchill & Jessop, 2010; Prestwich, Conner & Lawton, 2006; Verdejo-García, Lawrence & Clark, 2008), it is possible studies have been conducted, but have been victim of publication bias, where studies with no significant effects have failed to be published and distributed to the wider scientific community.

2.5.1 Subgroup analyses

Subgroup analyses revealed little difference between subgroups, with most effect sizes remaining small to medium and significant (Table 2.4). The most notable differences were observed in the target population subgroups. For both alcohol use and smoking, implementation intentions showed a much stronger medium effect size in the general population compared to student/adolescent populations. These results might be due to adolescents usually being less future-orientated than adults (Siu et al. 2014), suggesting planning future actions results in weaker plans and greater observed delayed discounting in the present moment (Steinberg et al. 2009).

2.5.2 Implications for policy and practice

The damaging effects on health of substance use and misuse, such as alcohol and tobacco smoking, and their related mortality rates, were explored in detail at the start of this chapter. Implementation intentions are a brief, one-off and inexpensive intervention that can be provided by primary and secondary care healthcare providers alike. They provide individuals with self-regulatory strategies to automatically initiate action planning after experiencing environmental cues. Given the small significant effect sizes, and the characteristics of study participants, it is unclear what the

implications from this review may be for clinical practice. Therefore future research on implementation intentions should test them as part of clinical practice with patients in alcohol use, smoking cessation settings and with people in substance misuse services.

2.5.3 Limitations

At a study level, this review did not exclude studies with high risk of bias. Only RCTs were included in the review, in order to minimise risk of bias and increase confidence in the overall findings. However, studies which were found to have low methodological quality were retained in the review, which could have increased the risk of bias at review level. Equally, excluding these studies might have increased the risk of bias at review level by reporting only high-quality studies. A decision was made to keep all studies despite their individual risk of bias, as there was an identified need to translate the findings into real-world clinical application, allowing therefore for some methodological imperfections.

At review level, other limitations were also identified. Only 3 databases were searched for literature, no grey literature was reviewed and only one reviewer conducted the searches and identified the studies for quality appraisal. Grey literature is not peer reviewed and therefore was purposefully not included. Two clinical trial databases were searched for ongoing RCTs, yet only published trials were identified with this search. Reference list searches were conducted and proved fruitful.

All populations included in the studies analysed were from Western societies. High-income Western countries may have a very different cultural relationship with substance use compared to low- and middle-income countries in other parts of the world. Further research which elucidates whether the automaticity of action planning initiation following environmental cues can differ between cultures should be conducted.

Lastly, the reviewers observed some heterogeneity with regards to implementation intentions intervention delivery (e.g. pen and paper, paper and oral repetition, online self-generation), yet when I^2 and $Q_{statistic}$ tests were run to assess heterogeneity between studies, two of the outcomes did not demonstrate any heterogeneity, whilst

the smoking outcome showed a somewhat moderate level of non-significant heterogeneity. Subgroup analyses clearly showed that the population targeted in the intervention (students or general population) was the source of this heterogeneity. All data was checked to be correct and this analysis was reported, as some degree of heterogeneity is to be expected in meta-analysis (Higgins, 2008).

2.5.3 Conclusions

This meta-analysis suggests that implementation intention interventions show significant small effects in reducing some forms of substance use (alcohol use and tobacco smoking) among the general population and students in secondary and higher education. The evidence of the effectiveness of this intervention could be improved by standardising implementation intention interventions (oral or written, self-generated or pre-specified, implementation intention seen once or with repeated exposure). Generalisability could be improved by conducting interventions in clinical populations and in low- to middle-income countries with different cultural views on substance use. Future research efforts should also be applied on the use of implementation intentions to reduce illicit drug use, whether or not the effect of this intervention is significant and on the use of implementation intentions in clinical practice.

Supplementary File 2.1: Systematic review searches

PsycINFO via EBSCOhost - 23 April 2018

Search ID	Search terms	Hits
S1	TI (implementation intention* OR coping strateg* OR goal planning) OR AB (implementation intention* OR coping strateg* OR goal planning)	18384
S2	TI (action OR goal OR plan) OR AB (action OR goal OR plan)	390,959
S3	AB (coping OR cop* OR barrier* OR obstacle* OR shield*) OR TI (coping OR cop* OR barrier* OR obstacle* OR shield*)	188327
S4	S1 OR S2 OR S3	556753
S5	TI ((subtance OR drug)) AND TI ((abuse OR misuse OR use OR disorder* OR addict* OR dependen*)) OR AB ((subtance OR drug)) OR AB ((abuse OR misuse OR use OR disorder* OR addict* OR dependen*))	1,281,538
S6	TI (alcohol OR drink* OR bing*) OR AB (alcohol OR drink* OR bing*)	125138
S7	TI ((smok* OR cigarette* OR cannabis OR marijuana OR grass OR pot OR dope)) OR AB ((smok* OR cigarette* OR cannabis OR marijuana OR grass OR pot OR dope))	66,963
S8	TI ((drug* OR heroin OR opioid OR opiate OR opium OR cocaine OR stimulant* OR methamphetamine OR amphetamine OR crack OR hash OR brown OR gear)) OR AB ((drug* OR heroin OR opioid OR opiate OR opium OR cocaine OR stimulant* OR methamphetamine OR	239497

	amphetamine OR crack OR hash OR brown OR gear))	
S9	TI ((inject* OR intravenous*)) OR AB ((inject* OR intravenous*))	65,215
S10	TI ((reduc* OR impair* OR decreas* OR eliminat* OR diminish* OR cut* OR quit* OR cessation OR stop OR moderat*)) OR AB ((reduc* OR impair* OR decreas* OR eliminat* OR diminish* OR cut* OR quit* OR cessation OR stop OR moderat*))	924,587
S11	S5 OR S6 OR S7 OR S8 OR S9 OR S10	1,926,788
S12	S4 and S11	265,373
S13	TX ((randomi?ed control* trial OR trial OR rct)) OR TI ((randomi?ed control* trial OR trial OR rct)) OR AB ((randomi?ed control* trial OR trial OR rct))	180281
S14	S12 AND S13	15,007
S15	S1 AND S14	360
Selected through Title		35
Minus duplicates		n/a (first database search)
Selected through Abstract		19
Selected through Full-Text		9

Medline via EBSCOhost - 04 May 2018

Search ID	Search terms	Hits
S1	TI (implementation intention* OR coping strateg* OR goal planning) OR AB (implementation intention* OR coping strateg* OR goal planning)	11,961
S2	TI (action OR goal OR plan) OR AB (action OR goal OR plan)	906,226
S3	AB (coping OR cop* OR barrier* OR obstacle* OR shield*) OR TI (coping OR cop* OR barrier* OR obstacle* OR shield*)	711,540
S4	S1 OR S2 OR S3	1,584,771
S5	TI ((subtance OR drug)) AND TI ((abuse OR misuse OR use OR disorder* OR addict* OR dependen*)) OR AB ((subtance OR drug)) OR AB ((abuse OR misuse OR use OR disorder* OR addict* OR dependen*))	4,726,923
S6	TI (alcohol OR drink* OR bing*) OR AB (alcohol OR drink* OR bing*)	313,307
S7	TI ((smok* OR cigarette* OR cannabis OR marijuana OR grass OR pot OR dope)) OR AB ((smok* OR cigarette* OR cannabis OR marijuana OR grass OR pot OR dope))	309,815
S8	TI ((drug* OR heroin OR opioid OR opiate OR opium OR cocaine OR stimulant* OR methamphetamine OR amphetamine OR crack OR hash OR brown OR gear)) OR AB ((drug* OR heroin OR opioid OR opiate OR opium OR cocaine OR stimulant* OR methamphetamine OR amphetamine OR crack OR	1,557,128

	hash OR brown OR gear))	
S9	TI ((inject* OR intravenous*)) OR AB ((inject* OR intravenous*))	912,742
S10	TI ((reduc* OR impair* OR decreas* OR eliminat* OR diminish* OR cut* OR quit* OR cessation OR stop OR moderat*)) OR AB ((reduc* OR impair* OR decreas* OR eliminat* OR diminish* OR cut* OR quit* OR cessation OR stop OR moderat*))	5,796,228
S11	S5 OR S6 OR S7 OR S8 OR S9 OR S10	9,776,504
S12	S4 and S11	884,035
S13	TX ((randomi?ed control* trial OR trial OR rct)) OR TI ((randomi?ed control* trial OR trial OR rct)) OR AB ((randomi?ed control* trial OR trial OR rct))	1,459,786
S14	S12 AND S13	76,559
S15	S1 AND S14	964
Selected through Title		51
Minus duplicates		36
Selected through Abstract		11
Selected through Full-Text		7

Psychology and Behavioural Science Collection via EBSCOhost - 06 September 2018

Search ID	Search terms	Hits
S1	TI (implementation intention* OR coping strateg* OR goal planning) OR AB (implementation intention* OR coping strateg* OR goal planning)	2917
S2	TI (action OR goal OR plan) OR AB (action OR goal OR plan)	64882
S3	AB (coping OR cop* OR barrier* OR obstacle* OR shield*) OR TI (coping OR cop* OR barrier* OR obstacle* OR shield*)	47442
S4	S1 OR S2 OR S3	108419
S5	TI ((subtance OR drug)) AND TI ((abuse OR misuse OR use OR disorder* OR addict* OR dependen*)) OR AB ((subtance OR drug)) OR AB ((abuse OR misuse OR use OR disorder* OR addict* OR dependen*))	238255
S6	TI (alcohol OR drink* OR bing*) OR AB (alcohol OR drink* OR bing*)	24086
S7	TI ((smok* OR cigarette* OR cannabis OR marijuana OR grass OR pot OR dope)) OR AB ((smok* OR cigarette* OR cannabis OR marijuana OR grass OR pot OR dope))	16383
S8	TI ((drug* OR heroin OR opioid OR opiate OR opium OR cocaine OR stimulant* OR methamphetamine OR amphetamine OR crack OR hash OR brown OR gear)) OR AB ((drug* OR heroin OR opioid OR opiate OR opium OR cocaine OR stimulant* OR methamphetamine OR amphetamine OR crack OR hash OR brown OR gear))	55410
S9	TI ((inject* OR intravenous*)	12253

	) OR AB ((inject* OR intravenous*))	
S10	TI ((reduc* OR impair* OR decreas* OR eliminat* OR diminish* OR cut* OR quit* OR cessation OR stop OR moderat*)) OR AB ((reduc* OR impair* OR decreas* OR eliminat* OR diminish* OR cut* OR quit* OR cessation OR stop OR moderat*))	159363
S11	S5 OR S6 OR S7 OR S8 OR S9 OR S10	358745
S12	S4 and S11	47976
S13	TX ((randomi?ed control* trial OR trial OR rct)) OR TI ((randomi?ed control* trial OR trial OR rct)) OR AB ((randomi?ed control* trial OR trial OR rct))	170027
S14	S12 AND S13	13472
S15	S1 AND S14	408
Selected through Title		15
Minus duplicates		8
Selected through Abstract		1
Selected through Full-Text		1

CHAPTER THREE: Preliminary behavioural analysis of equivalent population

Change in injecting behaviour among people treated for hepatitis C virus.

This chapter reports the results from a data analysis exercise completed in January 2018, which informed a substantial amendment to the study protocol. The data was collected and provided by the Eradicate-C study group and the Chief Investigator, Professor John F. Dillon, also second supervisor to this PhD project. Albeit the Eradicate-C was a single-centre clinical trial investigating the effectiveness of hepatitis C treatment in current injecting drug users (primary outcome), behavioural and social measures were taken as secondary outcomes to analyse any changes during treatment. The participants of Eradicate-C are directly comparable with the population chosen for this PhD project. It was therefore considered important to analyse this data in order to inform our protocol. Below is the research paper report of the data analysis, published in the Journal of Viral Hepatitis.

3.1 Abstract

Background: Injecting behaviour in people who inject drugs is the main risk factor for hepatitis C virus (HCV) infection. Psychosocial factors, such as having a partner who injects drugs and living with other drug users, have been associated with increases in injecting risk behaviour. This study aimed to investigate injecting behaviour changes during treatment for HCV infection whilst exploring the role of psychosocial factors on patients' injecting behaviour.

Methods: Eradicate-C was a single centred clinical trial investigating the effectiveness of HCV treatment within the injecting drug use population between 2012 and 2016. A total of 94 participants completed up to 24 weeks of treatment, with social and behavioural measures taken at different intervals throughout. Data for 84 participants was analysed retrospectively to explore mechanisms of potential behavioural changes which had occurred during treatment.

Results: Injecting frequency reduced significantly between baseline (week 1) and every 4-weekly interval until week 26. Not being on Opiate Substitution Therapy (OST) was associated with a statistically significant decrease in injecting frequency, χ^2 (1) = 10.412, p=.001, as was having a partner who also used drugs, in particular when that partner was also on treatment for HCV infection, Z= -2.312, p=.021.

Conclusions: Treating a 'chaotic' population for HCV infection is not only possible, but also bears health benefits beyond treatment of HCV alone. Enrolling couples on HCV treatment when partners are sero-concordant has shown enhanced benefits for reduction in injecting behaviour. Implications for practice are discussed.

3.2 Introduction

Over 170 million people worldwide are infected with the hepatitis C virus (Hanafiah et al. 2013; World Health Organization - WHO, 2011). The burden is axiomatic, with an estimated HCV-related mortality rate of 350 thousand people a year (Mann et al. 2013; Palmateer et al. 2007; Public Health England, 2014; WHO, 2010). The most common transmission route remains injecting drug use, with an estimated 60-80% of the HCV-positive population having acquired the virus via injecting risk behaviour (Aspinall et al. 2013; Mcdonald et al. 2014; Nelson et al. 2011). A variety of psychosocial factors have been associated with injecting risk behaviour: injecting frequency, poly-drug use, having a sexual partner who also injects, trust and risk perception to name a few (De et al. 2007; Dunn et al. 2010; Shaw et al. 2007). Despite the continued injecting risks carried out by people who inject drugs, many studies have shown that fears of non-adherence and low sustained-virological response (SVR) rates are unjustified, with people who inject drugs (PWID) showing both successful adherence and high SVR rates (Aspinall et al. 2013; Hellard et al. 2009; Wolfe et al. 2015).

Psychosocial factors such as social support, romantic partnerships and living situation seem to have conflicting effects on injecting risk behaviour and HCV treatment success. Published literature reports an association between HCV treatment success rates and social support (Janda et al. 2017). Peers help to increase motivation, self-care, feelings of hope and strength to complete treatment, feelings of being listened to, accepted and understood, as well as decreasing internalised stigma and shame

related to HCV and substance misuse and reducing use of substances itself (Batchelder et al. 2015; Rance et al. 2017). Yet, historically, close relationships with other PWID, such as romantic partnerships and living with other drug users, are among the factors most strongly linked to continued injecting risk behaviour (De et al. 2007; Dunn et al. 2010; Shaw et al. 2007). These polar effects of psychosocial factors on injecting risk behaviour and HCV treatment might be due to the function of romantic, and other, partnerships of PWID as sources of social care and protection, in a hostile and 'chaotic' environment where the behaviours of vulnerable adults are influenced negatively by partners, whilst also increasing a sense of acceptance, belonging and self-worth (Rance et al. 2017). Integrated models of behaviour change attempt to explain how couple dynamics can influence risk and health behaviours (Lewis et al. 2006).

HCV treatment itself seems to have a wider effect on PWID than curing hepatitis C alone. It has been associated with a decrease in ancillary injecting equipment sharing after treatment completion (Alavi et al. 2015), suggesting treatment might impact the HCV as well as impacting injecting behaviour. Midgard and colleagues (Midgard et al. 2017) investigated changes in behaviour during and after treatment, and reported a decrease in recent injecting drug use and alcohol use and an increase in opiate substitution therapy (OST) uptake throughout HCV treatment and at follow-up. However, they found no changes in daily injecting, use of sterile or shared equipment (Midgard et al. 2017).

Only a few studies have investigated the effects of HCV treatment on risk behaviour (Alavi et al. 2015; Midgard et al. 2017) and no literature to date has investigated the role of psychosocial factors such as romantic partnerships and living situation on risk behaviour during and following HCV treatment.

The Eradicate-C study was carried out to investigate the effectiveness of interferon-based HCV treatment on current PWID, characterised by a 'chaotic' lifestyle and erratic engagement with healthcare services. This study aimed to investigate changes in injecting behaviour during treatment, examining the role of psychosocial factors on hypothesised injecting behaviour change.

3.3 Methods

3.3.1 Study design

Eradicate-C was a single centred clinical trial investigating the effectiveness of HCV treatment within the injecting drug use population between 2012 and 2017. Participants were seen on a weekly basis for 26 consecutive weeks. The nurses, starting on visit 2 of treatment, provided a weekly injection of 180µg pegylated interferon α (PEG-IFNα) and supplied participants with a week's worth take-home daily dose of between 400 – 1400 mg (weight based) of self-administered ribavirin. Patients presenting with a genotype 1 infection also received protease inhibitors: telaprevir or simiprevir. The study treatment mirrored the standard of care treatment duration of 24 weeks for genotype 1 infections and of 16 weeks for genotypes 2 and 3 infections. All participants completed behavioural and social measures at different time points during the 26 visits of treatment.

The study was conducted in accordance with the Declaration of Helsinki and the principles of good clinical practice. The study was co-sponsored by the University of Dundee and NHS Tayside, and was ethically reviewed and approved by the East of Scotland Research Ethics Service REC 2. It was also registered with the National Institute for Health Research (NIHR) on UK Clinical Trials Gateway as ISRCTN27564683.

3.3.2 Outcomes

The primary outcome of the Eradicate-C study was to analyse SVR12 in the PWID population, which resulted in 84.2% genotype 1 and 85.2% genotype 2 & 3 achieving SVR (Johnston et al. 2017). The total SVR12 rate for all participants was 84.8%. The abstract hereby referenced shows a slightly lower SVR12 rate of 83.1% because it was submitted before the end of the study, with 5 patients SVR12 results still pending.

In this paper, the outcomes of interest were the behavioural and social measures collected during treatment. The primary outcome was injecting frequency throughout treatment (collected at visit 1, 4, 8, 12, 20, 24 and 26). Independent variables analysed were OST, living situation, living with other drug users, having children, having a partner, having a partner who used drugs/alcohol and the EQ5D scores. These

measures were taken at visit 1 and visit 26, with the exception of OST which taken every visit from visit 2 to follow-up (visits 27 and 28).

3.3.3 Study participants

A total of 94 participants completed up to 24 weeks of treatment between January 2013 and December 2016 within the largest Injecting Equipment Provision (IEP) service in Dundee (Scotland, UK). Participant inclusion criteria were: being aged between 18 and 70; active HCV infection - genotyped and confirmed by Polymerase Chain Reaction; current illicit drug use (confirmed through self-report and injection sites inspection); if female of child-bearing age, provision of a negative pregnancy urine test and fitting of Long-Acting Reversible Contraception (LARC). Exclusion criteria were: inability to provide informed consent; aggressive or violent behaviour; features of decompensated liver; evidence of primary hepatocellular carcinoma; if female, being pregnant, breastfeeding or pre-menopausal not on LARC; contraindications to using PEG-IFNα or Ribavarin; previous treatment with PEG-INFα, Ribavarin or Telaprevir criteria; participation in other drug study within past 30 days. The current study analysed behavioural and social data from visit 1 and visit 8 of treatment. Not all 94 participants who completed treatment provided data for both visits, reducing the pool of participants to 84 for the present analysis.

3.3.4 Analysis

Data was analysed using IBM SPSS Statistics 22. Descriptive analyses were run to obtain characteristics of the sample. If data was available for immediately preceding and subsequent weeks (e.g. visits 7 and 9), an average score was used for the required missing data (e.g. visit 8). If immediately preceding and subsequent visit scores were not available, data was considered missing. The null hypothesis (no difference in injecting frequency at different time points) was tested with a non-parametric Friedman test, and subsequent post-hoc analyses using Wilcoxon Signed Ranked tests were run to identify where differences lay. Non-parametric testing was selected following data testing for violation of normality, which showed skewed data with kurtosis at all time points. A square root transformation was attempted to normalise

distribution and eliminate outliers, but distribution remained skewed. Outliers were included in analysis as non-parametric use of medians signifies outliers hold less influence over test results.

Once identified that the largest injecting frequency difference was observed between week 1 and week 8 of the study, this difference was used to create a new dependent variable of injecting change, used in the analysis both as a categorical variable, to allow for Crosstab explorations using multiple categorical social factors, and as a continuous variable, to allow investigation of significant differences between the most important categorical social factors using Mann-Whitney U tests.

3.4 Results

A total of 106 participants consented to treatment. Two never completed baseline measures: 1 participant did not meet inclusion criteria and 1 participant died before starting treatment and completing baseline data. Of the remaining 104 consented, 94 completed treatment, but only 84 had completed behavioural and social data. So a total of 20 participants were lost to follow-up for this sub-study. Ten participants never commenced treatment: 3 spontaneously cleared the infection, 4 were lost to follow-up, 2 were treated on standard pathway after becoming drug-free and 1 was in prison outwith the catchment area. The remaining 10 consenting participants who completed treatment had data missing for the visit 8 follow-up. Characteristics of participants at enrolment are presented in Table 3.1.

Table 3.1: Participants' characteristics

Characteristic	**Study population (N=84)**	**Lost to Follow-up (N=20)**
Female Sex (%)	26 (31)	2 (10)
Age, median (IQR)	34 (23-45)	33 (25.25-40.75)
Legal situation: none (%)	49 (58.3)	11 (55)

Table 3.1 continued	Study population	Lost to Follow-up
Living situation		
Homeless (%)	16 (19)	6 (30)
Living in own or rented accommodation (%)	61 (72.6)	13 (65)
Living alone (%)	38 (45.2)	12 (60)
Living with partner (%)	25 (29.8)	4 (20)
Living with parents (%)	12 (14.3)	1 (5)
Living with other drug users (%)	30 (35.7)	5 (25)
Romantic relationships		
Has partner (%)	42 (50)	5 (25)
Partner uses drugs (% of Has partner)	34 (81)	4 (80)
Has children (%)	50 (59.5)	7 (35)
Healthcare-related measures		
EQ5D Health state score, median (IQR)	50 (20-80)	45 (20-70)
On OST (%)	60 (71.4)	4 (20)
Methadone dose, median (IQR)	70 (45-95)	75 (61-89)
Weekly injecting frequency, Mean (STD)	9.39 (8.87)	11.35 (11.37)

Only 32 of the 84 participants presented a complete set of data on injecting frequency at the 8 time points. A Friedman test for differences in weekly injecting frequency among the time points gave a significant result, χ_F^2 (7) = 36.44, p< .001. The median for week 1 was 4.5, for week 4 was 2, and thereafter for weeks 8 to 26 the median was 1. The range for the 8 time points remained between 0-14 and 0-30. Post hoc Wilcoxon Signed Rank Tests were applied to the differences between Week 1 and each of the other 7 time points. Bonferroni's correction reduced the significance level to p< .007. The results and effect sizes are shown in Table 3.2. Effect size *r* was calculated with Rosenthal's formula $r = \frac{Z}{\sqrt{N}}$ (Rosenthal, 1991), where Z is the post hoc Wilcoxon Signed

Rank Test score and N is the number of observations. The coefficient *r* is more commonly used as a correlation coefficient to measure the strength of a relationship; however, it is a versatile coefficient and it is used, especially within non-parametric testing, as a measure of experimental effect (Field, 2018).

Table 3.2: Post-Hoc comparisons

	Z	p *	*r* †
Weeks 1-4	-3.534	< .001*	-.63
Weeks 1-8	-5.459	< .001*	-.97
Weeks 1-12	-5.265	< .001*	-.93
Weeks 1-16	-4.759	< .001*	-.84
Weeks 1-20	-3.768	< .001*	-.67
Weeks 1-24	-3.225	.001*	-.57
Weeks 1-26	-4.495	< .001*	-.80

* Significant at p < .007 with Bonferroni correction
† Effect size *r* : Small = .1, Medium = .3, Large= .5

Week 8 was the time point at which the largest decrease in injecting was observed. To explore the decrease in injecting further, a new variable was computed. The difference between week 1 and week 8 injecting frequency was computed and categorised as 'Better' for a difference of ≥ 7or 'Not Better' otherwise. This was because a reduction in injecting frequency of at least once a day was judged to have some clinical significance. Figure 5.5.1 shows the difference in injecting frequency between week 1 and week 8 of treatment among the grouping variables analysed above.

Chi-Square tests were run to explore associations between participant characteristics and injecting behaviour change as judged by the new variable Better or Not Better (Table 3.3). Living situation, having children and healthcare-related measures showed no significant association with injecting behaviour change. However, having a partner who used drugs was significantly associated with being 'Better' (i.e. to reducing of weekly injecting), χ^2 (1) = 4.43, p =.035, Fisher's Exact test p =.043. Not being on OST

on week 2 of treatment was also significantly associated with being 'Better', χ^2 (1) = 10.412, p =.001, Fisher's Exact test p =.003 (See Table 3.3).

Table 3.3: Chi Square Tests for association

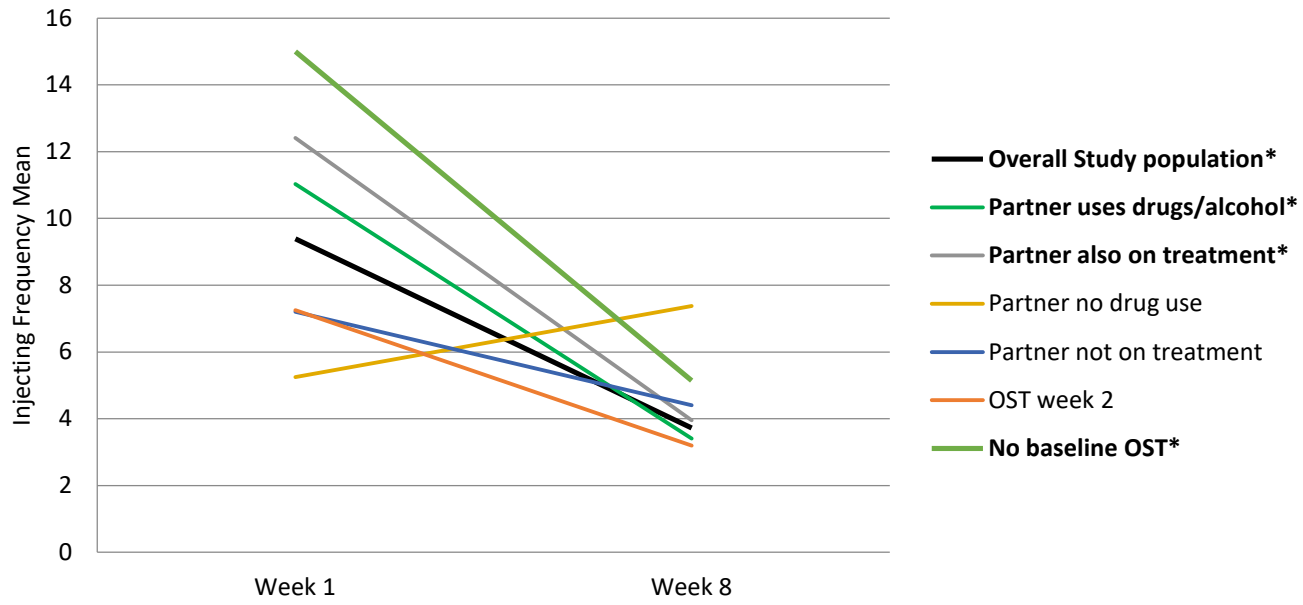
Characteristic	**χ^2 (df)**	**p ***	**Fisher's Exact Test ***
Legal situation	4.254 (4)	.373	na
Living situation	1.361 (3)	.715	na
Accommodation	.04 (2)	.98	na
Living with other drug users	2.007 (1)	.157	.21
Romantic relationships			
Has partner	.023 (1)	.880	1
Partner uses drugs*	4.43 (1)	.035*	.043*
Has children	.067 (1)	.795	.813
Healthcare-related measures			
EQ5D Mobility	.05 (1)	.823	1
EQ5D Self-care	1.088 (1)	.297	.368
EQ5D Activity	.621 (2)	.733	na
EQ5D Pain	.905 (2)	.636	na
EQ5D Anxiety	1.159 (2)	.56	na
On OST week 2*	10.412 (1)	.001*	.003*

* Significant at p < .05
na: not available

The association between having a partner who uses drugs and a reduction in weekly injecting frequency was quite surprising. A possible explanation may be that couple members were on treatment together, i.e. Partner who uses drugs is also on treatment study. The trial nurses identified N=22 participants as couples on the study (26.2% of total study sample, 52.4% of those with partner who used drugs/alcohol).

A Mann-Whitney U test showed that those who had a partner who used drugs and was also on treatment for HCV (N=22) reduced their injecting frequency significantly more than those whose partner was not on treatment (N=20), Z= -2.312, p=.021, medium effect size *r* =0.36. The mean weekly injecting difference was M = 5.65 (95% CI: -0.23 to 11.54), just short of one injection per day difference between the two groups (Figure 3.1).

Figure 3.1: Injecting frequency change by grouping



***** Significant at p < .05

These results were confirmed by analysing the association between the injecting frequency difference between week 1 and week 8 in couple members. Couples were assigned a couple ID (N=22, hence 11 couples on the study). All couples were heterosexual. The male-female Pearson's correlation coefficient was *r* = .629, p = .038, which meant that when males reduced their injecting, so did their female partners and vice versa.

3.5 Discussion

The findings of this paper show a significant reduction in injecting frequency between baseline, i.e. before the start of HCV treatment, and every other time point. The largest reduction was recorded between week 1 (baseline) and week 8, with injecting frequency stabilising thereafter whilst on treatment. Possible mechanisms of behaviour change were explored using baseline social factors.

3.5.1 Benefits for non-OST patients

Firstly, not being on OST on week 2 of treatment (first treatment visit recording this information) was found to be associated with a significant reduction in injecting frequency. It has been widely demonstrated that OST impacts injecting drug use (Gowing et al. 2008; Kemode et al. 2011; Kimber et al. 2010; Turner et al. 2011). Meta-analysis and pooled analysis of the effect of OST and IEP on incidence of HCV infections (Turner et al. 2011) reported a mean injecting frequency reduction of 20.8 injections per month (95% CI: -27.3 to -14.4), though OST did not reduce lifetime timeframe duration of injecting (Kimber et al. 2010). So it is possible that the patients who were on treatment for HCV and were already enrolled on OST, had previously reduced their injecting frequency before starting HCV treatment. Previous studies however, have attributed decreases in ancilliary injecting equipment and decrease in recent injecting drug use to enrolment in HCV treatment (Alavi et al. 2015; Midgard et al. 2017). Enrolment on OST might therefore attenuate the effects of receiving HCV treatment on injecting behaviour.

On the other hand, those who were not on OST on week 2 of Eradicate-C had not experienced the behavioural benefits of OST before their engagement with HCV treatment. It is well recognised that PWID are reluctant to access healthcare services, generally due to a lack of material resources, complicated and lengthy referral pathways, experience of stigma and poor relationship with healthcare providers (Ahern et al. 2007; Day et al. 2011; Morgan et al. 2015; Neale et al. 2008). For these individuals who were not on OST, engagement with HCV nurses might have been the only contact with any healthcare provider. Given the regular and considerate nature of this contact, a therapeutic relationship with the nurses providing the HCV treatment

might have functioned as a behaviour change mechanism these patients had not experienced because not enrolled on OST. Unfortunately therapeutic alliance was not measured in this study, but previously published literature attests for the importance of this factor on healthcare outcomes relating to this population (Haber et al. 2009; Meier et al. 2005; Schneider et al. 2004; Simpson et al. 1997). Meta-analyses have shown positive therapeutic alliance to increase patients' engagement and retention within drug services, as well as motivation, treatment readiness and treatment experience (Meier et al. 2005). The results of this study show that engagement in HCV treatment has increased health-related benefits, i.e. reduction in injecting frequency, for those patients who are not in contact with other healthcare services.

3.5.2 Behaviour change in intimate partnerships

The observed reduction in weekly injecting frequency was also, and more interestingly, linked to drug-using status of romantic partners. Those who had a partner who used drugs were more likely to reduce their injecting frequency, a reduction difference of more than 9 injections a week, equalling more than one injection a day (mean injecting difference = 9.74, SE = 3.56). This finding was surprising, as previous literature associated having a partner who uses drugs, in particular those injecting, with increased frequency of injecting and of sharing of injecting equipment (De et al. 2007; Dunn et al. 2010; Rance et al. 2017; Shaw et al. 2007). A variety of papers have been published on the power imbalance and social inequalities that drive injecting risk behaviour in heterosexual couples, in particular in women who inject drugs, who often rely on their male partner to acquire, prepare and inject the drugs (El-Bassel et al. 2014; Harvey et al. 1998; Wagner et al. 2013). Disregard of injecting risk occurs as a consequence of emotional closeness, intimacy, trust and commitment (El-Bassel et al. 2014; Rance et al. 2017; Simmons et al. 2012). Yet those who were in an intimate partnership involving drug use on this study were the principal drivers of injecting frequency reduction throughout treatment.

Given the high level of sero-concordance in people who inject drugs in intimate partnerships (Rance et al. 2017), the study team identified patients in dyadic intimate partnerships who had both been enrolled on the Eradicate-C trial. The final study

findings confirmed that members of couples both treated for HCV on Eradicate-C were significantly more likely to reduce their injecting than other individuals, i.e. those in drug using romantic partnership but whose partner was not on treatment for HCV and those who did not have a drug using partner. This effect was explored through models of behaviour change explaining the influence of partners on each other's health-related behaviour. The Interdependence model of couple communal coping and behaviour change (Lewis et al. 2006), explores couple dynamics and their influence on motivation and health behaviour change.

In the general population, the health benefits of being married or in a committed intimate relationship are well documented (Lewis et al. 2006; Rance et al. 2017). People in romantic partnerships tend to be healthier, engage with health care services and show a longer lifespan (Lewis et al. 2006). The role of intimate partnerships within the drug using population, however, has often been linked to increased risk-taking behaviour and generally as a bad influence on health (El-Bassel et al. 2014; Harvey et al. 1998; Rance et al. 2017; Simmons et al. 2012; Wagner et al. 2013). Qualitative studies have shown that HCV management within couples could help consolidate a relationship, introducing sentiments such as feeling valued and cared for (Rance et al. 2017). PWID generally experience hostile social environments, and intimate partnership which involve sentiments such as those above might represent one of the only types of meaningful social support and care that PWID encounter (Rance et al. 2017). Social support is regarded as an essential part of HCV treatment, with many care pathways for PWID involving the role of a peer support worker as integral part of the treatment (Bonnington et al. 2017), providing empathy and trustworthiness to patients on treatment. However, it is not simply individualistic social support perception that has to be considered to explain the study findings.

Lewis' couples' interdependence theory (Lewis et al. 2006) explains how motivation transformation can occur when partners experience a health event which is not only significant for the self, but has cognitive and emotional significance for the relationship. The attribution of significance of the health event to the dyad rather than the individual is the result of automatic consideration of partnership roles, subjective norms, commitment, quality of the relationship, and trust (Lewis et al. 2006). HCV

infection is a health threat that has both emotional and cognitive implications on the relationship and on each partner. These implications help transform motivation from 'individual-focused' to 'relationship-focused', adding a layer of complex interplay between intrapersonal and interpersonal behaviour change processes. Once motivation has become 'relationship-focused', couples work together through communal coping to achieve better health through shared action to manage the health threat (Lewis et al. 2006; Lyons et al. 1998). Communal coping requires shared beliefs that joint effort is advantageous to combat HCV, communication about HCV infection between partners and cooperation between partners to manage HCV and its treatment. Communal coping impacts health behaviour through the processes of outcome efficacy and couple efficacy (Lewis et al. 2006; Lyons et al. 1998). The couple's belief about the effectiveness of the coping/action strategies, i.e. HCV treatment, coupled with the couple's confidence about engaging in joint coping, i.e. reducing injecting frequency will ensure HCV is less likely to recur in the couple, will influence the behavioural outcome. The responsibility of the couples' (and individual's) health therefore lies equally on both partners, enabling the couple to become the unit for risk-reducing behaviour change (Lewis et al. 2006; Rance et al. 2017). Associations between changes in self-perception and self-care have been identified before (Batchelder et al. 2015; Jauffret-Roustide et al. 2012). Often these self-perceptions are intended as the 'self' as an 'addict' becoming the 'self' as a 'patient worthy of HCV treatment' (Batchelder et al. 2015; Rance et al. 2017). A similar process of psychological alteration might take place within the couple, with the couple's identity changing from 'drug-using partners' to 'HCV-treated partners, who coped with effects of treatment and achieved SVR as a unit', presenting a shared sense of 'self'.

3.5.3 Conclusions

This study shows that treating a 'chaotic' population for HCV infection is not only possible, but also bears health benefits beyond treatment of HCV alone. Enrolling people who are not on OST and/or couples on HCV treatment when partners are sero-concordant, has shown enhanced benefits for reduction in injecting behaviour and it is therefore recommended for practice. A complex interplay of relationship-focused

motivation transformation, outcome efficacy, couple efficacy and communal coping might improve patients' injecting risk-behaviour.

A few limitations are recognised within the study. Firstly, albeit the initial sample size seemed promising, missing data at different time points and the selection of different grouping variables considerably reduced the sample size for some of the analyses (N=42). However, the majority of clinical trials experience missing data (Dziura et al. 2013) and the analyses were performed taking this into consideration. Secondly, the effect of the results might not be as large for DAA treatment. Interferon-based treatment was notoriously harsh and communal coping within the couples might have developed strongly as a consequence of this. With the advent of DAA treatment, communal coping might become less necessary and prominent, therefore reducing health-enhancing behaviour change. However, the notion of HCV treatment alone might be enough to kick-start the motivational transformation within an intimate partnership and effects on communal coping and risk-behaviour reduction could still be observed in the DAA treatment era.

Chapter Four: Methodology

This chapter presents the design and methodology of the pilot randomised controlled trial (ADAPT). It is reported in accordance with the CONSORT (The Consolidated Standards of Reporting Trials) 2010 statement for transparent reporting of trials (Schultz et al. 2010), in conjunction with the TIDieR checklist (Template for Intervention Description and Replication) for better reporting of interventions (Hoffmann et al. 2014).

4.1 Development of the protocol

The conceptualisation of the protocol commenced prior to the Principal Investigator's (PI) enrolment onto the Psychology PhD programme. A systematic review conducted in 2015 for the Qualifications in Health Psychology Stage 2 informed the initial development of the PhD proposal, submitted to the University in December 2016. The protocol was initially created in April 2017 and developed throughout four months under the supervision of the PI's first and second PhD supervisors and the other members of the monitoring committee from NHS Tayside. Substantial amendments to the protocol were submitted throughout the lifetime of the study as informed by studies 1 and 2 of this thesis. Details of the substantial amendments applied to the protocol are reported in this chapter. The study was registered on ClinicalTrials.gov (NCT03293576).

4.2 Sponsor and ethical approval

The protocol was submitted at the start of August 2017 for sponsor comments and approval at Tayside Medical Science Centre (TASC). The study was registered at the same time with the local Research and Development (R&D) management office. The sponsor required clarifications and changes to be applied to the protocol and the rest of the study documents, such as informed consent form and participant information sheet, over the course of the following 3 months. At the end of October 2017 the study received sponsorship and insurance, study agreements were signed and the completed Integrated Research Application System (IRAS) form, study checklist with uploaded documentation

and R&D package were all submitted and the Research Ethics Committee (REC) review meeting was booked for the 8th December 2017.

The PI, first supervisor and one of the members of the monitoring committee attended the REC review meeting at the start of December 2017. The review meeting was a good professional experience for the PI (PhD student), who had not attended one of these meetings before, to learn about typical enquiries and requirements of ethics committees and how to answer or query them appropriately.

The REC provided a provisional favourable opinion a week after the review meeting, requiring further clarifications and a few changes. These were applied, and a full favourable opinion was provided on the 21st December 2017. On the same day, R&D approval was also obtained, therefore allowing the study to start recruitment.

4.2.1 Substantial Amendment AM01

In January 2018 a change to the participants' case report form (questions on romantic partners) was applied and the PI contacted the sponsor to notify of this change. The sponsor suggested this would have to be submitted as a substantial amendment (Substantial Amendment 1 – AM01) and that changes to the protocol and participant information sheet had to take place. After these changes were applied, the sponsor approved the documents and a substantial amendment form was submitted to REC and R&D. R&D approval was received on the 30th January 2018, whilst REC favourable opinion was provided after further small clarifications on 12th February 2018.

4.2.2 Substantial Amendment AM02

In April 2018, after 2 months of recruiting, it became apparent some of the variables being tested were too repetitive for participants, and that 5 visits (including a 6-month follow-up) would be hard to achieve with this population, given dropout rates between visits were high. So the CI, PI and first supervisor revised the structure of the trial to include 4 visits and reduce the number of repeated measures for each construct to a maximum of 3 times. The PI contacted the sponsor to notify of this change. The sponsor suggested this

would have to be submitted as a substantial amendment (Substantial Amendment 2 – AM02) with appropriate changes to the protocol and participant information sheet. After these changes were applied, the sponsor approved the documents and a substantial amendment form was submitted to REC and R&D. Both REC and R&D approval was received on the on 8th May 2018.

4.2.3 Substantial Amendment AM03

In June 2019, the research team agreed further changes to the protocol would allow the PI to conduct a small qualitative sub-study to explore the lived experience of people who inject drugs diagnosed with hepatitis C who were, or had been, on treatment. The concurrent design of this small qualitative study would allow a discussion of comparison of results with the main quantitative pilot RCT. The PI contacted the sponsor to notify of this change. The sponsor suggested this would have to be submitted as a substantial amendment (Substantial Amendment 3 – AM03) and that changes to the protocol, participant information sheet had to take place, plus the PI had to submit new documents: interview schedule, informed consent form for the sub-study, participant information leaflet for the sub-study. After these changes were applied, the sponsor approved the documents and a substantial amendment form was submitted to REC and R&D. R&D approval was received on the 8th August 2019, whilst REC favourable opinion was received on 9th August 2019.

4.3 Trial Design

The study was a single centre, longitudinal, unblinded, time-controlled, parallel-group trial conducted between April 2017 and January 2020 in injecting equipment provision services across Tayside (Scotland, UK). It was set to investigate differences in self-efficacy and sharing behaviour between the intervention arm compared to the control arm within the population.

The data collection was carried out over four visits in private clinic rooms within the services, with the intervention taking place on visit 2 (See the treatment trial schedule:

Table 4.1). All of the visits coincided with times at which the participants were seeing nurses or pharmacists for their hepatitis treatment.

On visit 1, informed consent was taken from participants and, subsequently, baseline measures were completed by participants with the help of the researcher (reading the questions). The baseline measures were: Injecting Risk Questionnaire (IRQ), Group Identification Scale (GIS), Patient Health Questionnaire (PHQ-9), General Anxiety Disorder (GAD-7), Post Traumatic Stress Disorder (PC-PTSD-5), Illness Perception Questionnaire (B-IPQ). This visit occurred between week 0 and week 3 of participants' HCV treatment.

Table 4.1: Treatment trial schedule

Treatment trial schedule					
Time / Measures	V1 Consent – Start of treatment	V2 Randomisation and Intervention	V3 Repeated measures – End of treatment	Qualitative Interview appointment	V4 3-month Follow-up
Demographic information	x				
Injecting risk questionnaire	x		x		x
Self-efficacy		x	x		x
Volitional help sheet (intervention)		x			
Time Perspective (Control)		x			
Subjective Norms Scale		x	x		
Social Connectedness Scale	x				
Group Identification Scale	x		x		x
Depression (PHQ-9)	x		x		
Anxiety (GAD-7)	x		x		
PTSD (PC PTSD-5)	x				
Working Alliance Inventory (WAI)			x		
Illness Perception Questionnaire	x		x		x
Qualitative interview				x	
Approx Time	30 mins	25 mins	30 mins	30 mins	25 mins

On visit 2, participants were allocated to the intervention or control group. As well as the intervention (Volitional help sheet) or control task (Zimbardo's Time Perspective Inventory), participants spent approximately 15 minutes filling in further baseline measures with the researcher's help: Self-Efficacy Scale (SES), Social Connectedness Scale (SCS), Social Norms Scale (SNS). This visit occurred between week 3 and week 7 of participants' HCV treatment as data shows injecting behaviour stabilises after 4 weeks of treatment (see Chapter 3: Preliminary behavioural data analysis of population).
On visit 3, follow-up measures were captured with participants filling in measures with the help of the researcher: IRQ, SES, SNS, GIS, PHQ-9, GAD-7, Working Alliance Inventory (WAI) and B-IPQ. This visit occurred between weeks 7 and 12 of treatment, around the time participants terminated their HCV treatment.
Visit 4 was the 3-month follow-up visit, when participants were seen by the nurses for the last blood sample, during which three measures were collected again: IRQ, SES and B-IPQ.
A full blank Case Report Form and Questionnaire collection can be found in the Appendices of the thesis.

4.3.1 Qualitative sub-study

Towards the end of their treatment, 6 participants were asked to opt in for a qualitative interview to understand factors that led to injecting risk behaviour and HCV infection and explore their experience of HCV diagnosis, treatment and therapeutic alliance. Five participants consented. Interviews were conducted in the needle-exchange services and pharmacies across Tayside where participants had received treatment. The interviews were digitally recorded. All audio transfers were conducted via NHS encrypted USB sticks, and encrypted and secure software (e.g. from audio recorder to NHS encrypted laptop). Given the interviews were arranged for a time out with standard care, participants were reimbursed for the travel cost and time with £10 cash.

4.3.2 Patient and public involvement

In May 2019, five patients on treatment for HCV were asked what type of reimbursement they would prefer if they were invited to attend the needle-exchange for a 30 minute interview outwith their standard care. Their preference was recorded using a simple feedback form. The options presented included: Bus fare (£3.70), Bus fare + 5 protein drinks, £10, Bus fare + £5 high street voucher, £5 + 5 protein drinks and £10 high street voucher. Three patients expressed their wish to be reimbursed with £10 cash, one patient express the wish to be reimbursed with £5 cash and 5 protein drinks and one to be reimbursed with a £10 voucher. One of the patients said cash would be easier as voucher for shops might be invalid since this population are sometimes banned from certain shops and hence might not be able to spend the voucher. In light of this, the PI decided that reimbursement for time and travel would consist of £10 cash.

4.4 Participants

4.4.1 Eligibility

This study aimed to investigate the effectiveness of the behavioural intervention in active PWID who were infected with HCV in Tayside and were on HCV treatment to clear their infection. Eligible participants were all adults over 18 years of age, presenting with a chronic HCV positive infection, making use of illicit drugs (established through participants' self-report), currently on treatment for HCV provided by the NHS, who spoke English and who provided informed consent. Exclusion criteria were inability to provide informed consent, aggressive or violent behaviour, presenting with a chronic HCV positive infection without being on treatment to clear the infection and the inability to communicate in English. Ineligible and non-recruited participants were thanked for their interest in the trial and were given a clear explanation as to why they were ineligible.

4.4.2 Identification and enrolment

All study participants were recruited through standard pathways of NHS care within substance misuse services, IEP enhanced services and community pharmacies. Participants who were in the process of being enrolled onto HCV treatment were approached directly by the treatment nurses with information about the study. Potential participants were provided with information on the trial verbally and via the Participant Information Sheet, and were given at least 24 hours to consider participation and to ask any questions on the study, in line with good clinical practice. On their return visit for screening for their HCV treatment, the patients interested in the study were interviewed by the researcher and asked to sign an informed consent form once they were satisfied that they had had adequate explanation about the study and had had the opportunity to ask any unanswered questions.

The informed consent procedure was regarded as a continuous and ongoing process as part of the full study (over 4 visits), in line with good clinical practice principles, and it was conducted in compliance with TASC SOP07: Obtaining Informed Consent from Potential Participants in Clinical Research.

4.5 Study settings

Recruitment took place in the main IEP site in the Tayside region in Dundee and in the main IEP service in Perth from February 2018 to January 2020. Clients were seen in clinical rooms on a one-to-one basis. The Cairn Centre Hub where participants were recruited in Dundee, is a partnership between NHS Tayside, Gowrie Care, Dundee City Council and other voluntary sector partners. The Hub aims to support people with their recovery from drugs and/or alcohol, aiding with assessment for alcohol and drug treatment, BBV testing and treatment and IEP. It is, in fact, the IEP with the highest number of clients in Tayside, with 1237 registered identity codes as of 2017 and an average of 420 transactions a month. The total population of PWID in Tayside is estimated to be approximately 2800. A note of caution in reading these figures: identity codes for needle-exchanges (NEO ID) represent a majority of opiate injectors, but in recent years there has been a significant

rise in injectors of Image and Performance Enhancing Drugs (IPED), in some areas as high an increase as 600% since 2005 (Fast Forward, 2016), and IPED users are not included in the estimated 2800 PWID population.

The study recruited patients on treatment for hepatitis C in the IEP service. During the recruitment period (2018-2020), the IEP was hosting a clinical trial investigating medicinal products for the treatment of hepatitis C called ADVANCE (Inglis et al. 2019). ADVANCE dispensed HCV medication on a fortnightly or daily basis according to their randomisation. ADAPT recruited a sub-sample from ADVANCE, irrespective of their dispensing regime. The Cairn Centre, where recruitment took place, is located in the city centre in Dundee. Patients on treatment for hepatitis C came from all over the Tayside region. Some, fortnightly dispensed, were keen to attend appointments, whether they lived within walking distance or not. Those who were on daily dispensing direct-observe therapy, had more difficulty attending appointments unless they lived close by, but daily travel expenses from outside the city centre postcode area were covered by the HCV treatment study (ADVANCE) which aided attendance to treatment. Participants were also incentivised with protein drinks, which had proven very popular with this population in the past.

The IEP in Perth is located in one of the main health centres of the city, Drumhar Health Centre, and the IEP room is situated in the same corridor as the substance use service. Both the IEP service and the substance use service had recently moved to this location prior to the treatment trial and the ADAPT trial commencing. The dynamic between the services (substance use, IEP, harm reduction nursing and viral hepatitis care) was peculiar. This will be discussed in the later chapters of this thesis. Participants for the HCV treatment and ADAPT trials, some dispensed fortnightly and others daily, were incentivised to attend with paid travel expenses and with protein drinks.

4.6 Intervention

The intervention entailed completing the volitional help sheet with the participants on visit 2. This brief intervention lasted around 20 minutes in a clinic room in the needle-

exchange services and pharmacies across Tayside. The participants and the researcher read through the list of real-life solutions the participants might find applicable to them. They then read through the list of situations one by one. The participant drew a coloured line between the situation and the solution which seemed more appropriate to them. This created implementation intentions, which are self-regulatory strategies taking the form of "if-then" plans (i.e. situation-solution plan). The volitional help sheet belonged to participants once completed; no copy was required by the researcher for data analysis as the volitional help sheet was the intervention and did not constitute analysable data. In the final visit of the study, participants were asked if they had kept (in visible or non-visible place), discarded or lost the volitional help sheet for the duration of the study.

To control for contact-time, participants in the control group spent approximately 20 minutes with the researcher on visit 2 exploring Zimbardo's time perspective constructs (ZTPI, Zimbardo & Boyd, 1999) and completing the short Zimbardo's time perspective inventory (Orosz et al. 2017). The inventory was selected because the cognitive processes involved in accessing time constructs were activated in the intervention group for the planning of coping strategies and goal achievement during future injecting risk situations. The intervention is reported below (Table 4.2) using the TIDieR checklist (Hoffmann et al. 2014), which is an extension of the CONSORT 2010 statement (Schultz et al. 2010). The checklist was developed in response to Hoffman and colleagues' (2013) analysis of 137 non-drug interventions, which showed very poor rates of adequate intervention description. It is conceptualised as an extension of the CONSORT statement to improve the quality and completeness of reporting of more non-specific interventions, allowing for greater replicability of studies.

The development of the checklist involved a panel of experts reviewing CONSORT's statement, reporting items of interest, as well as relevant literature on other checklists and research on intervention reporting guidance, which generated a list of 34 items. The panel then used a modified two-round Delphi consensus survey, which involved international experts and stakeholders. These were authors of research, clinical trial experts, journal editors, statisticians and similar experts in the field. The survey

participants were asked to rate the 34 items in an ordinal fashion, as 'omit', 'possible', 'desirable' and 'essential' for the final inclusion in the checklist. They were allowed to comment on the items and their wording and to suggest further items. The survey identified 13 items to be included and a further 13 items to be discussed. A consensus meeting was then held in person to discuss such items, with a range of experts from difference health disciplines in attendance. The drafted checklist was then piloted with 26 researchers. Clarifications and elaborations were made and the final 12-item checklist was published (Hoffman et al. 2014).

Table 4.2: TIDieR Checklist

TIDieR Checklist (Hoffmann et al. 2014)	
Item	**Item No**
Brief name	1 ADAPT
Why	2 The new HCV treatment oral regimens present a substantial reduction in side effects and remarkable Sustained Virological Response rates. The National Health Service incurs considerable costs to fund patients' HCV treatment, since this is cost-effective within the model of treatment as prevention. Once treated, there is the chance patients may become reinfected with HCV if they encounter further risk of transmission. In Tayside the rate of reinfection within the PWID treated population reaches 10%. This study aims to deliver a behaviour change intervention to reduce rates of HCV reinfection by intervening on patients' self-efficacy and injecting risk behaviour.
What	3 Materials: the intervention instrument was a volitional help sheet. It was used to create implementation intentions, which are self-regulatory strategies taking the form of "if-then" plans (i.e. situation-solution plan). The volitional help sheet can be found in the Supplementary File 4.1 at the end of this chapter
	4 Procedures: the participants and the researcher read through the list of real-life solutions the participants might find applicable to them. They then read through the list of situations one by one. The participant drew a coloured line between the situation and the solution which seemed more appropriate to them.
Who provided	5 The Principal Investigator who is also a PhD student and a qualified Health Psychologist, delivered both the intervention and the time-control activity. Her expertise and training background focus on health behaviour change, sexual health, substance misuse and drug-related risk behaviours.
How	6 Describe the modes of delivery: the intervention was provided face-to-face on an individual basis. Tea and coffee was offered to participants to help them settle and feel appreciated for their time.

Where	7 Describe the location(s): the intervention was delivered in the main IEP sites in the Tayside region. Clients were seen in clinical rooms. The Cairn Centre Hub where most participants were recruited from, aims to support people with their recovery from drugs and/or alcohol, and aids with assessment for alcohol and drug treatment, BBV testing and treatment and IEP.
When and How Much	8 The intervention was delivered on one occasion only during the course of the participant's enrolment in the study. It was delivered on visit 2 of the 5 visits planned to complete the study, and it would last approximately 20 minutes. The volitional help sheet (intervention) would then belong to the participant, who could decide whether to keep it or discard it.
Tailoring	9 No individual tailoring was required.
Modifications	10 Although the protocol was modified during the course of the study (See section 4.2 Sponsor and Ethical approvals on Amendments 1, 2 and 3), the intervention itself was not modified in any way.
How well	11 Planned: intervention adherence or fidelity was not assessed, as the intervention was a one-off activity carried out with the researcher.
	12 Actual: N/a

4.7 Outcomes

Primary and secondary outcomes of the study are described below and are listed in Tables 4.3 and 4.4. Most study outcomes were collected using previously developed and validated measures. Where previously published scales were not available or appropriate, adaptations of validated scales were made to ensure the quality of the measurements collected. It is important in healthcare research to use the best measurements available to ensure research funding and time is not wasted on unreliable measurements of constructs, and to allow more scientific evidence to be collected, disseminated and critically evaluated (McDowell, 2006).

The Case Report Form also contained SVR12 and HCV reinfection clinical data as dichotomous outcomes collected as standard practice in NHS services providing HCV treatment, and were provided to this trial by the nurses and research teams delivering HCV treatment.

All outcomes, apart from clinical outcomes such as SVR12 and HCV reinfection rates, were assessed by the Principal Investigator (PhD student), who is a registered Health Psychologist.

Table 4.3: Primary objectives and outcome measures

Primary Objective:	Outcome Measure:	Timepoint of outcome measured
To assess levels of injecting risk behaviour and self-efficacy scores in patients on treatment for hepatitis C creating implementation intentions compared to patients assigned to the control group.	Injecting Risk Questionnaire	Visit 1, Visit 3, Visit 4,
	Self-efficacy Scale	Visit 2, Visit 3, Visit 4,

Table 4.4: Secondary objectives and outcome measures

Secondary Objective:	Outcome Measure:	Timepoint of outcome measured
To assess the variability in injecting risk behaviour as explained by mental health, illness perception, subjective norms, social connectedness and group identification constructs;	Injecting Risk Questionnaire	Visit 1, Visit 2, Visit 3, Visit 4,
	Patient Health Questionnaire	Visit 1, Visit 3
	General Anxiety Disorder	Visit 1, Visit 3
	Post-Traumatic Stress Disorder	Visit 1
	Illness Perception Questionnaire	Visit 1, Visit 3 ,Visit 4
	Subjective Norms Scale	Visit 2, Visit 3
	Social Connectedness Scale	Visit 1
	Group Identification Scales	Visit 1, Visit 3, Visit 4
	Qualitative interview	Sub-study visit
To assess the longevity of the intervention effectiveness 4 months post-intervention (and 12 weeks post-treatment).	Injecting Risk Questionnaire	Visit 1, Visit 3, Visit 4,
	Self-efficacy Scale	Visit 2, Visit 3, Visit 4,
	Injecting Risk Questionnaire	Visit 1, Visit 2, Visit 3, Visit 4,
To assess any differences in psychosocial factors pre- and post-treatment	Patient Health Questionnaire	Visit 1, Visit 3
	General Anxiety Disorder	Visit 1, Visit 3
	Illness Perception Questionnaire	Visit 1, Visit 3
	Subjective Norms Scale	Visit 2, Visit 3
	Group Identification Scales	Visit 1, Visit 3

4.7.1 Injecting Risk Questionnaire

The Injecting Risk Questionnaire – IRQ (Stimson et al. 1998) was selected as a primary outcome to evaluate the efficacy of the behavioural intervention. The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) lists the IRQ as a validated instrument of evaluation. It has been referenced in a variety of published studies on HCV epidemiology and surveillance, harm reduction, addictions, recruitment strategies and behavioural interventions (Marsden et al. 1998; Platt et al. 2006; Rhodes et al. 2004; Rotily et al. 2001). While the scale is slightly out of date, its wording remains relevant to contemporary research. Contact was made with the principal author to ensure no copyright restrictions limited the use of the scale.

The scale was developed by Stimson and colleagues in 1998 for drug users who had injected within the previous 4 weeks. It has 19 items, rated with a 4-point Likert scale, exploring different features of injecting equipment sharing, with questions such as: - During the last 4 weeks, how often have you done any of the following things: 4) given or lent used needles/syringes to a friend or acquaintance; 6) injected with needles/syringes that had already been used by a sexual partner; 12) put a used needle into a container or spoon that was then used by someone else; and so on. It explores both risks to self, as well as risks to others through a variety of risk-taking injecting practices.

The questionnaire was checked for its acceptability with the population, test-retest reliability, inter-rater reliability, internal reliability and construct validity. Product moment correlation, principal component analysis and Cronbach's alpha (α) were investigated as statistical testing. The scale items were deemed acceptable, with close to 100% response rate to all questions. The test-retest correlations were all positive and significant at $p < .001$, with no differences by age, gender or main drug injected. Correlations for inter-rater reliability were calculated for subjects who were interviewed by both agency staff and field workers, showing a high degree of consensus. Internal reliability was tested at Time 1 and Time 2 with a resulting Cronbach's alpha value of between .88 and .90. Items loading was high at > .32 on one factor, accounting for 42% of the total variance.

Scoring: Although the questionnaire data responses varied from 1=frequently to 4=never, the scores for all items and all participants were reversed to 1=never to 4=frequently. This was executed in order to have scores in ascending order (Score=1 never shared in past 4 weeks / Score >1 shared in past 4 weeks). The score was computed as:
IRQ_Score= (1+2+3+4+5+6+7+8+9+10+11+12+13+14+15)/15
A categorical score was also computed with dummy variables 0 and 1 where 0= IRQ_Score of 1 (participant Not Sharing) and 1= IRQ_Score>1 (participant Sharing).

4.7.2 Self-Efficacy Scale

The Self-Efficacy Scale – SES, adapted from Martin (1995) was selected as a primary outcome because of the relationship between self-efficacy and behaviour (Ajzen, 1991). Martin's (1995) Self-Efficacy Scale for Drug Avoidance is reported on the EMCDDA as a validated evaluation instrument. Its adaptation for the trial was carried out because of its low applicability to the trial population (heroin users). It has been used to measure self-efficacy in different populations of substance misuse: medication adherence in psychiatric outpatients (Magura et al. 2012), mindfulness for relapse prevention in prison settings (Lee et al. 2010) , cognitive behavioural therapy for abstinence in adolescents (Jafari et al. 2012), and for addiction severity studies (Butler et al. 2006; Heydari et al 2014). Contact was made with the authors to ensure permission for the use of the scale.
The scale, developed by Martin and colleagues (1995), was created to specifically measure self-efficacy in drug users. The original scale had 16 items, for example "1) Imagine that you are going to a party where you will meet new people. You feel drug/alcohol use will relax you and make you more confident. Could you avoid drug/alcohol use?", with 7-point Likert responses. The typology of responses was kept the same, but the scale had to be adapted from polydrug/stimulants-orientated scale, to a scale focused on heroin use and injecting equipment sharing, with items like "8) Imagine that you have run into 2 friends who have drugs on them they offer to share. You have no clean equipment on you. Could you resist the urge to join them and share their works?". The adapted scale had 14 items, given some of the items from the original scale had situations which were completely

unrealistic for the heroin-using population. The adapted scale was first checked for validity with harm reduction nurses, then its validity was investigated with members of the population itself by piloting it for comments with clients of a needle-exchange.
The original scales' reliability tested high, with Cronbach's α= .91, and showed high predictability, with scale scores predicting future substance use behaviour. Construct validity was checked through the association of the scale scores with other concurrent measures of drug use and self-efficacy changes, which resulted in statistically significant correlations.
Scoring: The scale scored items as 1=Certainly yes to 7=Certainly no. In order to have ascending scores (the higher the score, the more confidence in one's ability to avoid sharing), items 1, 3, 4, 5, 8 ,11, 12 were reverse-scored. The score was computed as: SES_Score= (1Rev+2+3Rev+4Rev+5Rev+6+7+8Rev+9+10+11Rev+12Rev+13+14)/14.

4.7.3 Social Norms Scale

The Social Norms Scale – SNS was also adapted from previous literature (Glanz et al. 2002; Ajzen, 2002a). This construct was important to measure as a secondary outcome because of its effect on behavioural intention and risk behaviour (Ajzen, 1991; Bailey et al. 2007; McGowan et al. 2013; Neaigus et al. 2006). Given it had to be adapted specifically to injecting risk behaviour, this measure is non-validated. The construct was measured with 4 questions to ensure reliability, with a 7-point Likert scale with items such as: "1) Most people who are important to me think it is ok to share injecting equipment".
Subjective norms have been investigated in a variety of health-related behaviours and settings, from children's health to adult exercise (Courneya & McAuley 1995; Walsh et al. 2009) and has been used extensively in substance misuse populations (Hohman et al. 2014; Latkin et al. 2003; Rivis & Sheeran, 2003), though not applied to sharing of injecting equipment.
Scoring: The scale scored items as 1=Strongly Agree to 7= Strongly Disagree. In order to have ascending scores (the higher, the score the stronger the social norm to share

equipment), items 1, 2 and 3 were reverse-scored. The possible score ranged between 4 and 28. The score was computed as:

SocialNorms_Score= 1Rev+2Rev+3Rev+4.

4.7.4 Social Connectedness Scale

According to published literature, social connectedness is associated with injecting risk behaviour (Bailey et al. 2007; Bloor et al. 2008; Broz et al. 2010; Cepeda et al. 2012; Heimer et al. 2014b; McGowan et al. 2013; Neaigus et al. 2006; Roux et al. 2014), hence this construct being selected as a secondary outcome. The scale used for this construct, Social Connectedness Scale – SCS, was a validated instrument, published by Lee & Robbins (1995). The authors were contacted for permission to use the scale.

The scale and construct has been used in a variety of settings investigating health and wellbeing (Hendrickson et al. 2011; Williams & Galliher, 2006), but has not been extensively used in substance misuse settings (Buckingham et al. 2013; Hunt & Burns, 2017), in particular with opiate injectors.

There are different versions of the scale, the one selected presents 8 items, such as: "2) Even around people I know, I don't feel that I really belong", with items rated on a 6-point Likert scale. The 8 items were selected to principal component analysis, with all selected items showing factor correlations of above .677, and none correlating with other factors above with a .261 correlation. The scale showed high internal reliability with Cronbach's α = .91. Test-retest reliability over a 2-week period also showed positive results, with a correlation score *r* of .96.

Scoring: The scale scored items as 1=Strongly disagree to 6= Strongly agree. A high score meant a high sense of social connectedness. The possible score ranged between 8 and 48. The score was computed as:

SocialConnectedness_Score= 1+2+3+4+5+6+7+8.

4.7.5 Group Identification Scale

As well as social connectedness, the sense of an individual's social identification to selected groups was regarded as a possible predicting factor of injecting risk and health. Therefore, the Group Identification Scale – GIS (Sani et al. 2015a), a validated instrument, was selected to measure this construct as a secondary outcome of the research trial. The senses of belonging to a family nucleus and to an injecting network were explored in the study. The GIS scale was therefore repeated twice to obtain results on identification with both groups.

The scale has been previously used in mental health settings exploring depression in adolescents and post traumatic stress in cancer patients (Miller et al. 2017; Swartzman et al. 2017), but it has never been used with people who inject drugs.

The GIS is a short 4-item scale, each rated on a 7-point Likert scale. The items, such as "3) I have a sense of belonging to my family" were adapted for the assessment of belonging to different groups (family and to injecting drug network), as suggested by the authors (Sani et al. 2015a). The scale presents good internal reliability with Cronbach's α ranging between .85 and .92 depending on the population and group identification under investigation. It has good convergent validity, showing good correlations with other group identification scale, divergent validity, showing only moderate correlations with scales which do not measure the exact construct of group identification but measure other social aspects of group factors. Test-retest reliability was also high, with Pearson's correlation *r* coefficient on family group of .91.

Scoring: The scale scored items as 1=Strongly Agree to 7= Strongly Disagree. In order to have ascending scores (the higher the score, the stronger identification with a social group), all items were reverse-scored. A score of less than 3 signified the individual was not identified with the specific social group. The score was computed as:

GIS_Family and GIS_DrugNetw computed the same way= (1Rev+2Rev+3Rev+4Rev)/4.

4.7.6 Brief Illness Perception Questionnaire

Perception of HCV risk was another secondary outcome which emerged from review of the literature (Bailey et al. 2007; Fairnbairn et al. 2010; McGowan et al. 2013; Wagner et al. 2010b). The Brief Illness Perception Questionnaire – B-IPQ (Broadbent et al. 2006) is a validated scale adaptable to any illness. Its adaptation to hepatitis C was therefore straightforward, allowing the retention of the integrity and validity of the measure.

The published paper on the B-IPQ has been cited around 1500 times, it has been used in a variety of health settings with reviews concluding that illness perception is associated with illness and treatment outcomes (Petrie et al. 2007). Some research also focused on illness perception and hepatitis C, showing its influence on treatment outcomes, coping and adjustments (Langston et al 2016; Langston et al. 2017; Langston et al. 2018; Zalai et al. 2015).

The scale presents 9 total items, 8 of which require a response to a 10-point Likert scale, e.g. "1) How much does your Hepatitis C affect your life?", and the 9th item asking participants to rank the three most important factors that cause the illness. Test-retest analysis showed good reliability, with Pearson's correlations on items ranging between r = .42 and r = .75, and all statistically significant. Concurrent validity was tested using a revised version of the scale, showing statistically significant correlations. The scale showed good predictive validity, with variance in rehabilitation attendance in MI recovery patients explained by higher identity scores ($F(39,1) = 5.11$, $p = .03$). Higher concern and treatment control beliefs were associated to slower return to work ($r = .43$, $p = .03$ and $r = .44$, $p = .03$ respectively). Discriminant validity was tested exploring differences between B-IPQ scores in different illnesses, showing statistically significant differences able to distinguish patients' scores between different illnesses.

Studies in which the scale has been utilised, and its properties have been tested, have shown good internal reliability, with Cronbach's α in ranges between .72 and .85 (Karataş et al. 2017; Løchting et al. 2013).

<u>Scoring</u>: Items 3, 4 and 7 were reverse-scored so that a high score signified a more threatening perception of the illness. The score was computed as:

BIPQ_Score= 1+2+3Rev+4Rev+5+6+7Rev+8.

Scale author (Broadbent et al. 2006) assigned different sub-construct to each item: 1=Consequences of illness; 2=Timeline; 3=Personal control; 4+ Treatment control; 5= Identity; 6=Concern; 7=Coherence; 8=Emotional representation.

4.7.7 Mental health variables

Mental health variables have been found, by most literature, to be associated to injecting behaviour and injecting risk behaviour (Bailey et al. 2007; Broz et al. 2010; Cepeda et al. 2012; Gossop et al. 2002; Heimer et al. 2014b; Neaigus et al. 2006, Roux et al. 2014). Depression, anxiety and trauma are extremely common mental health issues with which the injecting drug use population presents. These variables could therefore show a ceiling effect, but given previous literature, it was important to collect them and control for their effects on the intervention effectiveness.

The Patient Health Questionnaire – PHQ-9 (Spitzer et al. 1999) was selected because of its wide use within clinical settings as a depression screening instrument. Papers on the development of the PHQ-9 have been cited over 18 thousand times in literature, showing its vast and extended use (Kroenke et al 2001; Kroenke & Spitzer, 2002; Spitzer et al. 1999). Pfizer lifted the copyright restricting the use of the scale in 2010, allowing free public access. Not surprisingly, the PHQ-9 shows excellent internal reliability, with Cronbach's α of 0.89 and excellent test-retest correlations with $r = 0.84$. Its 9 items are based on the nine criteria used for diagnosis of depressive disorders in the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, APA, 2000). The items, such as: "Over the last 2 weeks, how often have you been bothered by any of the following problems?: 2) Feeling down, depressed, or hopeless."

The scale was also tested for construct validity, showing significant positive correlations with other depressive symptom screening tools, and criterion validity, assessed comparing the PHQ-9 screening results to independent mental health professional assessments in 580 patients.

Scoring: All items were summed to calculate the score. Scoring instruction identified scores as: 0-5 Mild depression; 6-10 Moderate; 11-15 Moderately severe; 16+ Severe. The score was computed as:
PHQ9_Score= 1+2+3+4+5+6+7+8+9.

The Generalized Anxiety Disorder – GAD-7 (Spitzer et al. 2006) was also selected because of its vast use within clinical settings as a screening tool for anxiety symptoms, showing thousands of citations. In 2010, Pfizer lifted the copyright restricting the use of this scale, allowing free public access. The 7-items in the scale, such as "Over the last 2 weeks, how often have you been bothered by any of the following problems?: 2) Not being able to stop or control worrying." showed excellent internal reliability, with a Cronbach's α of .92. Test-retest reliability showed a correlation coefficient of r = .83. Construct validity was demonstrated with significant pairwise comparisons between GAD-7 scores and SF-20 mental health and social functioning scale scores. Convergent validity was also reported, with correlations of r between .72 and 74 with other anxiety measures.
Scoring: Exactly like the PHQ-9 scoring, all items were added for the final score. Score=0-5 Mild depression; 6-10 Moderate; 11-15 Moderately severe; 16+ Severe. The score was computed as:
GAD7_Score= 1+2+3+4+5+6+7.

The Primary Care Post-Traumatic Stress Disorder scale – PC-PTSD-5 (Prins et al. 2016) was developed as an update to the previous version, PC-PTSD-4, in conjunction with the update of the DSM to its fifth edition (APA, 2013). The scale was developed with the help of military veterans, but for use in primary care. This was because of the high prevalence of PTSD in this population. It consists of a preliminary question "Have you ever experience a traumatic event?", followed by 5 items to aid diagnostic value, for example: "1) Had nightmares about it or thought about it when you did not want to?". All the items are answered as Yes/No, and the scale score is also treated as a dichotomous variable (symptoms of PTSD with scale score of 3 or more, no symptoms with score of 2 or less).

The scale's use has been discussed in fields such as substance misuse (Matthieu et al. 2017), PTSD in children victims of sexual abuse (Cummings & O'Donohue, 2018) and in the LGBT population (Hurley et al. 2017).

The scale's inter-rater reliability was tested by two independent raters who obtained 100% agreement on diagnosis of PTSD and excellent reliability at scale-item level (k > .95). Weighted k coefficients are used for better agreement between scale results and diagnosis. The diagnostic accuracy (AUC) for the PC-PTSD-5 was .941 (95% CI: .912 to .969).

Scoring: Dummy variables assigned to the questionnaire responses: Yes=1; No=0. The items were summed to compute the score. The higher the score the more the person was showing symptoms of PTSD. According to scale scoring instructions, a score of less than 3 meant No PTSD symptomatology was present. The score was computed as:

PTSD_Score= 1+2+3+4+5

4.7.8 Working Alliance Inventory

This questionnaire (Hovart & Greenberg, 1989; Hatcher & Gillaspy, 2006) was collected to inform the ADVANCE trial (a clinical trial of medicinal products to treat hepatitis C). Given the ADAPT researcher was independent from the ADVANCE trial the measure was collected in order to assess therapeutic alliance among three different treatment-dispensed groups. This measure will therefore not be discussed or analysed in this thesis.

4.7.9 Zimbardo's Time Perspective Inventory – Short Revised

In addition, the Zimbardo's Time Perspective Inventory short revised version – ZTPI-SR (Orosz et al 2017) will be completed as the time-control activity in the control group only, and data will be used as a secondary outcome for this group. The full ZTPI has 56 items, so short versions of the scale have been tested and used in other forms of addiction, such as internet and social addiction (Przepiorka & Blachnio, 2016). The 17-item scale has been used in academic settings (Orosz et al. 2016). A short version of the inventory was necessary for the population in this study and considering the other tasks taking place in

visit 2, to keep all visits to around 30 minutes. This short version of the ZTPI was also selected because of the similar response time to the study's behavioural intervention (around 20 minutes); this allowed the researcher to control for time and contact effect with the study population.

This short version of the ZTPI had 17 items, between 3 and 4 items for each sub-construct dimensions. Examples of items for each dimension are as follows: Future "1) Meeting tomorrow's deadlines and doing other necessary work comes before tonight's play"; past positive "3) Happy memories of good times spring readily to mind"; past negative "5) I've taken my share of abuse and rejection in the past"; present fatalistic "11) My life path is controlled by forces I cannot influence"; and present hedonistic 8) Taking risks keeps my life from becoming boring".

Orosz and colleagues used confirmatory factor analysis to reduce the number of items from the original ZTPI of 56 to a minimum of 17 for the model to have a good fit (2017). Four items were identified for the past negative (PN) dimension, three items for past positive (PP), three items for present hedonism (PH), three items for present fatalism (PF) and four items for future (F). The internal consistency was good or borderline: $\alpha PN = 0.84$; $\alpha PP = 0.68$; $\alpha PH = 0.73$; $\alpha PF = 0.69$; $\alpha F = 0.70$. The test-retest reliabilities of the subscales for all dimensions were between .70 and .80. The five dimensions were inter-correlated, with small, yet significant, *r* values.

Scoring: The items were scored as 1= Very Untrue to 5= Very True. The higher the score the stronger the trait characteristic. Scale items divided into different time perspectives and scores were computed as:

ZTPI_PastNegative= (5+6+9+17)/4

ZTPI_PastPositive= (2+3+7)/3

ZTPI_PresentHedonistic= (8+14+16)/3

ZTPI_PresentFatalistic= (10+11+12)/3

ZTPI_Future= (1+4+13+15)/4

4.8 Sample size

A power calculation was conducted with G*Power 3.1.9.2 (Faul et al. 2007) to estimate the required sample size for a MANOVA between-within interaction. The desired effect size value of 0.35 was estimated from previous literature on psychological and psychosocial interventions in substance misuse (Copenhaver et al. 2006; Luty, 2015; Tanner-Smith et al. 2013; Webb & Sheeran, 2008). Alpha was set at 0.05 and desired power at 0.8. The calculation was based on the primary outcomes Self-Efficacy and Injecting Risk Behaviour, measures repeated 3 times during the course of the trial. The resulting required sample size was of 67. Dropouts and patients reinfected during the course of the trial were to be counted as part of the outcome as unsuccessful interventions. This sample will be recruited and divided into experimental and control groups for the psychosocial intervention on self-efficacy. The power calculations were checked by the PI and an honorary statistician in the School of Social Sciences at the University of Dundee.

The required sample for the qualitative sub-study is of 5 (to reach theme saturation) from either arm of the study.

4.9 Randomisation

Eligible and consenting participants were randomised to either intervention or control group (See Figure 4.1: Study flowchart). A computerized random number generation to the two trial groups was carried out by a member of the research team external to the study process, using the website Randomization.com (Dallal, 2008: www.randomization.com). The randomisation was generated in blocks of 20 with a 1:1 ratio assignment to either of the two groups; the PI was aware of the block size. Stratification was not used for the randomisation process.

Figure 4.1: Study flowchart

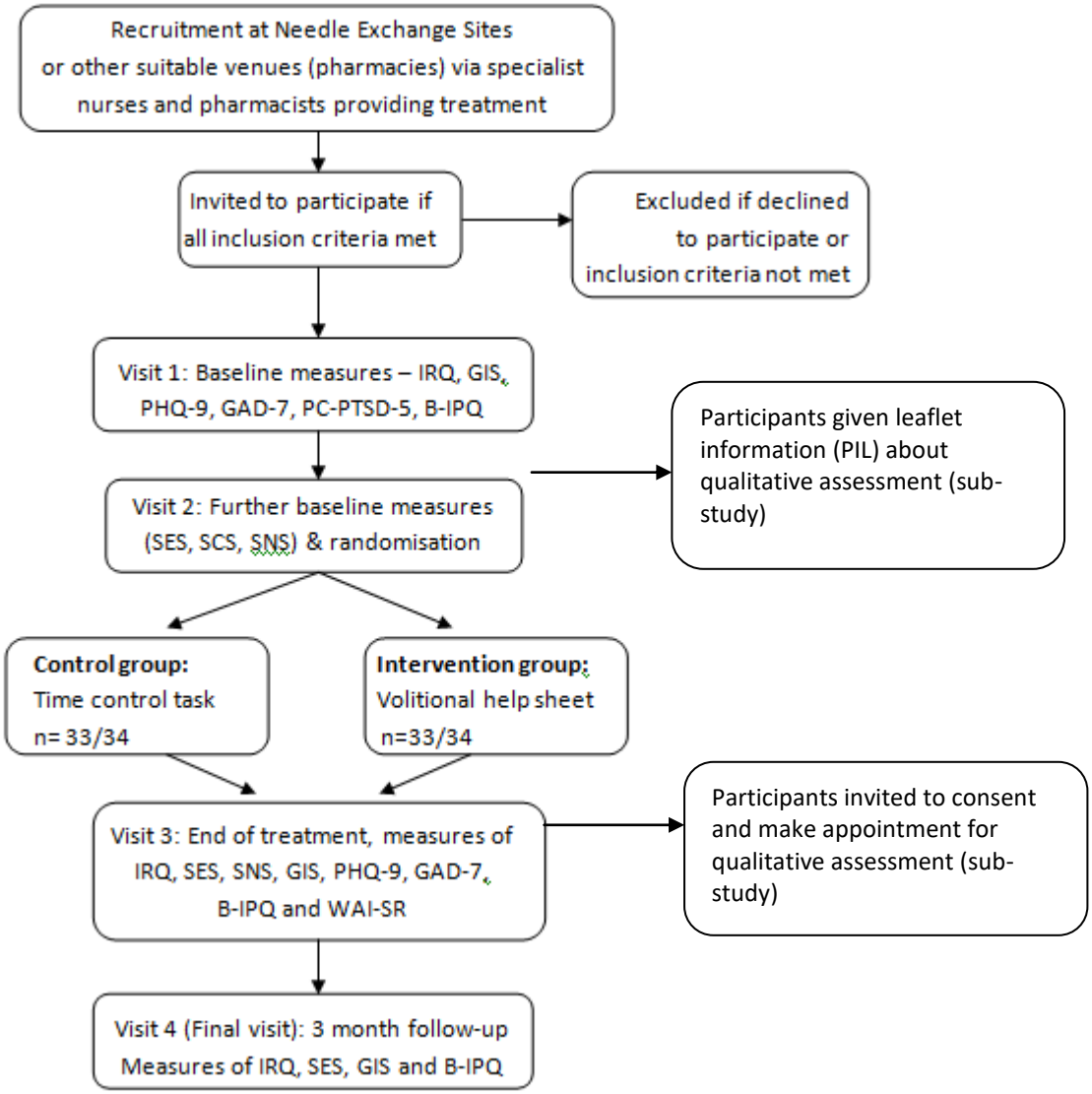


Figure 4.1

To prevent code breaking and ensure allocation concealment, sealed envelopes were produced and sequentially numbered by the independent research team member. The envelopes were opaque, brown and non-see through when held up to the light. Once the research team member had run the sequence generator and concealed allocation, the sealed envelopes were handed to the PI to bring to the recruitment site. Once a patient

had consented, the PI providing the intervention or control task, opened the patient's corresponding ID numbered envelope to allocate them to either intervention or control group. Participants and treatment nurses and pharmacists were not aware of which arm patients were allocated to, given the time and contact-control task for the control group participants.

For the sub-study, no randomisation procedure will be necessary. Participant in their second visit will be given information about the sub-study and during visit 3 they will be asked if they wish to participate.

4.10 Blinding

Given the nature of the study, it was not possible to blind the data collector to the study group allocation. The PI's role was that of study planning, sponsorship and ethical permissions acquirement, information provision to potential participants, participant enrolment, data collection, intervention provision, outcome assessment, data entry, data analysis and report write-up. It was therefore essential for the PI to be un-blinded to participant allocation in order to provide the intervention or the control task. Allocation to study group remained unknown to the PI until after participant enrolment, when the randomisation sequence was implemented by opening the sealed envelope which corresponded to the participant's ID.

4.11 Statistical methods

The data was analysed on a modified intention to treat basis, meaning that those who performed the intervention or control task and were lost to follow-up were treated as no-changers. A factorial analysis to assess the validity of the scales used was not possible given the small sample size. Reliability analyses were run on all scales.

4.11.1 Primary analyses

The primary objective was to increase self-efficacy (SES) in individuals who inject drugs who are on treatment for HCV in order to reduce sharing of injecting paraphernalia and reduce HCV reinfection rates. It was hypothesised that, by increasing self-efficacy, individuals who inject drugs would report a decrease in sharing instances at follow-up. This was achieved by using a volitional help sheet to implement intentions. A mixed between-within MANCOVA was performed to compare baseline, end of treatment, 1- & 3-month follow-up data to assess the effectiveness of self-efficacy enhancement as a behaviour change technique to reduce injecting risk behaviour (IRQ). Mental health (PHQ-9, GAD-7, PTSD-5), illness perception (B-IPQ) and psychosocial factors (Subjective norms, SCS, GIS) were set as covariates.

4.11.2 Secondary analyses

The psychosocial predictors measured at baseline were tested as predictors of injecting risk behaviour using a multiple regression.

Differences in time (baseline and follow-up) for psychosocial variables were tested in the sample using Wilcoxon Signed Ranks.

4.11.3 Sub-study analyses

For the qualitative sub-study, data was analysed using thematic analysis. Thematic analysis is one of the most widely used methods of qualitative data analysis as it allows the researcher to identify and analyse patterns and themes in the datasets (Braun & Clarke, 2013).

4.12 Missing data

The nature of this trial was to assess the applicability of this model in the real world, so incomplete data that impacted on the primary outcome was assumed to be consistent with failure of the intervention. Modified intention-to-treat analysis might be required to exclude participants lost to follow-up after visit 1, who did not receive the intervention as per protocol, and for whom assumptions of intervention failure could not be made (Abraha & Montedori, 2010).

Supplementary File 4.1

Volitional Help Sheet

Situations

1. If I am tempted to share equipment when I am in withdrawal and I am offered heroin
2. If I am tempted to share equipment when I am with others who are injecting
3. If I am tempted to share equipment when things are not going my way
4. If I am tempted to share equipment when I am feeling down
5. If I am tempted to share equipment when other people encourage me to share
6. If I am tempted to share equipment when I am very anxious
7. If I am tempted to share equipment when offered equipment by someone
8. If I am tempted to share equipment when things are going really well for me
9. If I am tempted to share equipment when I am upset
10. If I am tempted to share equipment when I am under the influence of other drugs
11. If I am tempted to share equipment when I have no clean equipment with me

Solutions

- Then I will avoid situations that encourage me to share equipment
- Then I will reward myself when I do not give into my urge to share equipment
- Then I will use alternatives to calm myself
- Then I will do something else instead of injecting
- Then I will seek out someone who listens when I want to talk about my feelings
- Then I will seek out social situations where people respect the rights of others not to inject/share equipment
- Then I will remember that I have strong feelings about how much my injecting and sharing has affected the people I care about
- Then I will remember the information that people have personally given me on the benefits of not sharing equipment
- Then I will think about how my emotions affect me when I think about consequences of sharing equipment
- Then I will tell myself that I can choose to change or not to change
- Then I will tell myself that if I try hard enough I can say no to sharing equipment
- Then I will think about the type of person I will be if I am in control of my injecting
- Then I will always make sure I have enough clean equipment

CHAPTER FIVE: Study 3 – ADAPT Results 1

The predicting role of psychosocial factors on injecting risk behaviour.

This chapter reports the baseline results from the main study in the thesis, Study 3. The chapter aims to explore the RCT sample characteristics and to investigate the psychosocial predictors of injecting risk behaviour.

5.1 Abstract

Background: Injecting behaviour in people who inject drugs is the main risk factor for hepatitis C virus (HCV) infection. Psychosocial factors such as having a partner who injects drugs and living with other drug users have been associated with increases in injecting risk behaviour. The risk of HCV reinfection in people who inject drugs (PWID) treated for HCV remains high when sharing of injecting equipment continues to occur post-treatment. This study investigates the role of psychosocial factors on risk behaviour during HCV treatment.

Methods: This cross-sectional study included 50 participants on treatment for HCV. Correlation analyses informed the association of group identification, mental health and illness perception with sharing injecting equipment. Only factors with a good correlation to sharing behaviour were included in the model. A multiple linear regression tested the model under investigation.

Results: Correlation analyses showed sharing behaviour to be significantly associated with injecting frequency and group identification with drug network. The bootstrapped multiple linear regression model was statistically significant, $F(3,46)= 5.67$, $p= .002$. The model explained 27% (R^2) of the variance in injecting risk behaviour. Group identification with drug network had a substantial and statistically significant impact on injecting risk behaviour.

Conclusions: Identification with a social group, usually associated with improved health, may pose health risks depending on the type of group an individual identifies with. Interventions on social networks are recommended to reduce sharing of injecting equipment.

5.2 Introduction

As explored in Chapters 1 and 3, drug injecting behaviour in Scotland continues to be mostly associated with heroin injecting, although concomitant use of heroin with cocaine and/or benzodiazepines has increased in recent years (Johnson et al. 2016; HPS, 2019; Tucker et al. 2016). Sharing of injecting equipment, such as needles, syringes, pots, filters, water and tourniquets, is the principal means of transmission of blood-borne viruses (Public Health England, 2017a). Literature suggests psychosocial factors influence injecting risk behaviour, whilst social identity isolation is linked to poor physical and mental health (Latkin et al. 2011; Sani et al. 2015a). A number of psychological and social factors have been associated with injecting risk behaviour and were thoroughly explored in chapters 1, 3 and 4. The rationale and theory used to develop this study were explored in chapters 1 and 2. The aim of this part of the study, and therefore this chapter, is to explore the characteristics of the study sample and investigate the psychosocial predictors of injecting risk behaviour.

5.3 Methods

The methodology employed to carry out Study 3 was the focus of Chapter 4, reported in accordance with the CONSORT 2010 statement (Schultz et al. 2010) and the TIDieR checklist (Hoffmann et al. 2014) so it will not be repeated here. All regulatory approvals (University of Dundee sponsorship, NHS East of Scotland Research Ethics Committee, Research & Development NHS Tayside) were received in December 2017. Data collection took place between February 2018 and January 2020. The total sample size was 52. The data and results reported in this chapter only refer to visit 1 of the pilot RCT, the baseline visit, allowing for cross-sectional exploration of the sample's data. This section will focus on the participants and the statistical analyses carried out to explore the baseline data and investigate the predicting factors of injecting risk behaviour.

5.3.1 Analysis

Data was analysed using IBM SPSS Statistics 25. Descriptive analyses were run to obtain characteristics of the sample at baseline and mean scores of all measured variables at visit 1. Cronbach's α reliability analysis was run to check consistency of construct measuring on all scales used at visit 1. A correlation analysis was run to explore baseline factors associated to injecting risk behaviour. The variables which were found to be significantly correlated to injecting risk behaviour were then used in a regression model. A multiple linear regression was performed to investigate possible predictors of injecting risk behaviour.

5.4 Results

5.4.1 Sample Characteristics

Exploration of the baseline data was carried out to characterise the sample (Table 5.1).

Table 5.1: Characteristics of the sample

Characteristics		**Full sample (N=50)**	
		M	**SD**
Age (years)		37.4	6.9
Weekly injecting frequency at baseline		7.1	9.13
		N	**%**
Sex:	Female Male	12 38	24 76
Recruitment site[1]	Cairn Centre Drumhar	44 6	88 12
Intervention group	Control Intervention	23 27	46 54
HCV Genotype	Genotype 1 Genotype 3	20 30	40 60
Partner	Yes No	19 31	38 62
If Yes		**(N=19)**	**Valid %**
1.Partner injects	Yes No	10 9	52.6 47.4
2. Partner on treatment	Yes No	6 13	31.6 68.4

Table 5.1 continued Characteristics		N	%
Treatment pathway[2]	DOT	21	42
	2/52	16	32
	2/52+	11	22
SVR12 Achieved[3]	Yes	40	80
	No	10	20
Drugs Injected	Opiates	45	90
	Opiates + Cocaine	5	10

[1]Sites= Cairn Centre is the main IEP in Dundee; Drumhar is the main IEP in Perth.
[2]Treatment pathways: DOT= Daily Observed Therapy; 2/52= Fortnightly observed therapy; 2/52+ = Fortnightly observed therapy with Psychological intervention (Adherence).
[3]SVR12 Achieved= Sustained Virological Response (HCV undetectable, patient cured).

5.4.2 Exploration of variables

Means, standard deviations and reliabilities of measures were calculated for all variables and presented in Table 5.2. An exploratory factor analysis on all the measures was not possible as the sample size was too small for appropriate analysis. Cronbach's α for all measurement showed good reliabilities, ranging from acceptable (Illness perception questionnaire α= .65) to excellent (Group Identification scale for Family and Drug Network α values over .9).

Table 5.2: Variables' descriptives and reliability testing

Characteristics (Range)	M	SD	Cronbach's α
Injecting Risk Behaviour (1-4)	1.22	.59	.89
Number Shared with (reported at start)	0.16	0.42	
Number Shared with (reported at end)	0.56	1.05	
Identification Family (1-7)	4.3	2.35	.93
Identification Drug Network (1-7)	3.9	2.42	.94
Depression (0-27)	17.36	7.86	.86
Anxiety (0-21)	14.32	6.39	.86
Post traumatic stress disorder symptomatology (1-5)	3.22	1.69	.76
Illness Perception (8-80)	31.44	13.49	.65

5.4.3 Normality testing

The distribution of the sample was tested using Shapiro-Wilk tests for continuous and discrete variables, given its better suitability to test smaller samples (n<50) (Field, 2018). Normal Q-Q Plots and Box plots were visually inspected to assess distribution. Most variables violated the assumption of normal distribution (Table 5.3); age was the only variable which did not deviate significantly from normal, W(50) = .96, p= .056.

Table 5.3: Test of normality

Tests of Normality		
	Shapiro-Wilk	
	Statistic - df (50)	Sig.
Age	.96	**.056**
Injecting Frequency 1	.78	**.000**
Injecting risk	.61	**.000**
Identification - Family	.84	**.000**
ID – Drug Network	.84	**.000**
Depression	.93	**.005**
Anxiety	.88	**.000**
PTSD	.85	**.000**
Illness Perception	.95	**.042**

*. Lower bound of the true significance.

a. Lilliefors Significance Correction

5.4.4 Correlations

An exploration of the correlations between the primary outcome and all the baseline predictors was carried out to minimise the number of predictors included in the regression model (Table 5.4). Scatterplots of all the variables were visually inspected to check the linearity of the relationship between injecting risk behaviour and all psychosocial factors measured. Given linearity was violated among all pairwise combinations, Spearman's correlation was carried out to test the relationship between factors.

Table 5.4: Spearman's correlations between factors (n=50)

Spearman's Correlations										
		Injecting Risk	Age	Injecting Frequency 1	ID - Family	ID – Drug Network	Depression	Anxiety	PTSD	Illness Perception
Injecting Risk	ρ (rho)	1.000	-.107	**.565****	**-.307***	**.459****	.109	.222	.228	.128
	p-value	.	.458	.000	.030	.001	.452	.121	.112	.377
Age	ρ (rho)		1.000	-.129	-.025	-.169	-.275	-.236	-.150	-.027
	p-value		.	.370	.865	.240	.053	.100	.299	.851
Injecting Frequency 1	ρ (rho)			1.000	-.089	**.344***	-.104	.053	.051	-.243
	p-value			.	.539	.014	.473	.712	.726	.089
Identification - Family	ρ (rho)				1.000	.008	-.246	**-.287***	-.242	.002
	p-value				.	.954	.084	.043	.091	.986
Identification – Drug Network	ρ (rho)					1.000	-.120	-.155	-.214	.056
	p-value					.	.408	.282	.136	.701
Depression	ρ (rho)						1.000	**.824****	**.691****	**.482****
	p-value						.	.000	.000	.000
Anxiety	ρ (rho)							1.000	**.669****	**.392****
	p-value							.	.000	.005
PTSD	ρ (rho)								1.000	**.392****
	p-value								.	.005
Illness Perception	ρ (rho)									1.000
	p-value									.

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Bivariate correlations (Table 5.4) showed that Injecting risk behaviour was significantly correlated to injecting frequency, ρ= .57 with p< .001, identification with family, ρ= -.31 with p= .03, and identification with drug network, ρ= .46 with p= .001. Additional correlations were observed between secondary variables: injecting frequency was significantly correlated with group identification with drug network (ρ= .34, p= .014); group identification with family was significantly negatively correlated with anxiety (ρ= -.29, p= .043).

The three mental health variables (depression, anxiety and PTSD) were intercorrelated with coefficients ranging from ρ= .67 to ρ= .82. These variables were also correlated with illness perception, with all coefficients ranging between ρ= .39 to ρ= .48 (Table 5.4).

Chi square tests of associations were used to check correlations between categorical baseline variables (Sex; Recruitment site; Intervention group; HCV genotype; Partner; Treatment pathway; SVR12 achieved; Drugs injected) and injecting risk behaviour and no correlations were found.

5.4.5 Multiple regression (and bootstrap)

A multiple linear regression was run to predict injecting risk behaviour from injecting frequency, identification with family and identification with drug network. The regression model explained 27% (R^2) of the variance in injecting risk behaviour. The model was statistically significant, F(3,46)= 5.67, p= .002. Two of the variables had a substantial and statistically significant impact on injecting risk behaviour: Injecting frequency (B= .01, p= .035), and group identification with drug network (B= .05; p= .027) (Table 5.5).

The assumptions for linear regression were checked to assess bias within the model. Independence of error was inspected with the Durbin-Watson test (value of 1.71), which showed no cause for concern. Multicollinearity was checked via the Tolerance (above 0.2) (Menard, 1995), the VIF statistic (well below 10) (Myers, 1990) (Table 5.5) and the correlation coefficients among independent variables (all below |.4|).

Table 5.5: Regression coefficients table

Coefficients[a]					
	B	SE	β	Lower 95% CI for B	Upper 95% CI for B
(Constant)	1.051	.138		.774	1.328
Injecting Frequency 1	.013	.006	.291*	.001	.026
ID - Family	-.029	.022	-.167	-.075	.016
ID - Drug Network	.052	.023	.306*	.006	.099

Note: *p< .05.

The eigenvalues also confirmed multicollinearity was not an issue, as each of the 3 predictors showed most of their variance loading onto respectively different dimensions.

However, casewise diagnostics showed that 8% of cases had a standardised residual of over +/- 2 (Table 5.6). More than 5% of the sample with standardised residuals over +/- 2 is usually cause for concern.

Table 5.6: Regression casewise diagnostics

Casewise Diagnostics[a]				
Case Number	Std. Residual	Injecting risk	Predicted Value	Residual
2	**2.96**	2.60	1.52	1.08
9	**2.40**	2.33	1.46	.88
10	**2.04**	2.33	1.59	.75
38	**2.33**	2.13	1.28	.85

a. Dependent Variable: Injecting Risk

Case 36 seemed to be problematic. Its Mahalanobis distance value was greater than 15 and the leverage value was over 3 times the average leverage of 0.08 (Table 5.7). The DFBeta value for inject frequency was over 1 (1.21) (Table 5.8). The covariance ratio also showed deviation from its boundaries: .76-1.24 (calculated as upper= 1+ [3(k+1)/n] and lower= 1-[3(k+1)/n] where k is the number of predictors and n the sample size (Field, 2018)). Cases 2, 9 and 38 were all also outwith these boundaries.

Yet Cook's distance was adequate in all of them, so none of these cases seemed to have an undue influence on the model.

Table 5.7: Regression case summaries A

Case Summaries[a]				
	Case Number	Mahalanobis Distance	Cook's Distance	Centered Leverage Value
36	36	**15.96**	.42	.33

a. Limited to first 100 cases.

Table 5.8: Regression case summaries B

Case Summaries[a]							
	Case #	COV-RATIO	Standardized DFFIT	Standardized DFBETA Intercept	Standardized DFBETA Injecting Frequency.1	Standardized DFBETA ID - Family	Standardized DFBETA ID – Drug Network
2	2	**.46934**	.96999	-.29142	.66338	.16294	.24157
9	9	**.65622**	.68817	-.31981	.21047	.20359	.39351
36	36	**1.24929**	-1.33557	.51158	**-1.20848**	-.37503	.01739
38	38	**.68616**	.74190	-.20159	-.37299	.12258	.57713

a. Limited to first 100 cases.

Case 36 was consented and seen for visit 1 the same day. He was known to the researcher because he used to beg between the university and the needle-exchange. He seems to be influencing the model because he had, by far, the highest weekly injecting frequency score of anyone in the sample. The range usually ranged between 0 and 28 injections a week, but case 36 reported injecting 6 times a day (weekly score= 42). He reported sharing with 1 other person both at the start and at the end of the IRQ. He was consented and the first visit was completed before he had been randomised onto the hepatitis C treatment trial (ADVANCE). His full bloods (which had been taken the day he completed visit 1) came back 2 weeks later as problematic and he was also incarcerated at the same time so he was lost to follow-up (and not treated on ADVANCE). Therefore, there is no follow-up data to check validity of answer; the

researcher double checked during the visit, when he reported injecting so often, if the self-report was correct and he was adamant that it was an average amount for him. By visually inspecting the scatterplot of predicted standardised values against standardized residuals, it is clear that the assumption of homoscedasticity was violated and minor violations of linearity and normality were also observed.

Given these considerations, the model was re-run with the bootstrap option (Table 5.9). Bias corrected and accelerated (BCa) bootstrapping estimates of the regression coefficients were calculated using 95% confidence intervals. The standard errors for the Beta values remained virtually the same for all three predictors. The analysis confirmed the statistically significant effect of group identification with drug network on injecting risk behaviour (B= .05; p= .033 [95% CI: .01, .11). However, both injecting frequency and group identification with family lost significance in predicting the dependent variable.

Table 5.9: Regression with bootstrapping

Bootstrap for Coefficients					
	B	Bootstrap[a]			
		SE	p-value	Lower 95% CI	Upper 95% CI
(Constant)	1.051	.123	.001	.781	1.286
Injecting Frequency 1	.013	.009	.117	.002	.040
ID - Family	-.029	.023	.204	-.071	.018
ID - Drug Network	.052	.023	**.033**	.012	.101

a. Bootstrap results are based on 1000 bootstrap samples;

5.5 Discussion

Injecting risk behaviour, defined in this study as sharing of injecting equipment, is a complex behaviour. The results of this study suggest that injecting risk is significantly associated with injecting frequency and group identifications. Further, although added to the tested model, the main effects of injecting frequency and group identification with family did not significantly add to the predicting model. However, group

identification with drug network was identified as a strong, significant predictor of sharing behaviour.

The relationship between social factors and injecting risk behaviour has been widely documented (Day et al. 2005; Fraser et al. 2016; Latkin et al. 2011; Nasir & Rosenthal, 2009; Shaw et al 2007). Social networks involving drug use can consist of close friends, family, romantic and sexual partner, or simply of acquaintances. The general characteristics of these networks can be associated with risk-taking behaviour. Sharing of equipment is more common in larger networks (De et al. 2007; Heimer et al. 2014; Smith et al. 2017) and in environments with high acceptability of sharing behaviour (Bailey et al. 2007; McGowan et al. 2013; Neaigus et al. 2006). Other studies have found that the presence of multiplex relationships such as drug using sexual partners increases the likelihood of engaging in high-risk behaviours (Cox et al. 2008; Fraser et al. 2016; Gossop et al. 2002; Lakon et al. 2006; Medic et al. 2008; Roux et al. 2014; Unger et al. 2006; Zapka et al. 1993). This might be due to heightened social and instrumental support, e.g. pooling of money for drugs (Shahesmaeili et al. 2018), emotional or injecting support (Unger et al. 2006), or at times to increases in psychological and physical abuse, associated with receptive syringe sharing (Stoicescu et al. 2019).

The results of this study are consistent with previous research that suggests social networks can negatively influence injecting risk taking (De et al. 2007; Dunn et al. 2010; Shaw et al. 2007) yet they present new findings in regards to injecting drug use and group identification. Group identification is characterised by the subjective dimension of an individual's sense of communal experience and psychological connection with fellow group members (Sani et al. 2015b; Tajfel & Turner, 1979). Some research has been carried out on the influence of group identification on substance use in adolescents and young adults (Savolainen et al. 2018; Sussman et al. 2000), yielding conflicting results. The current study, on adult injecting drug users, found that group identification with a drug network was a strong predictor of injecting risk behaviour, revealing that the stronger the sense of identification, the higher the likelihood that an individual was sharing injecting equipment.

Yet the association between social factors and engagement in risk behaviours has potential to be a positive one. Some social associations, such as romantic partnerships, can become sources of social care and protection. They have the capacity to reduce risk behaviour, such as reducing injecting frequency (Chapter 3[1]), and increasing a sense of acceptance, belonging and self-worth (Rance et al. 2017). Identification with a family nucleus can also promote healthy behaviour (Sani et al. 2015a). A positive type of social capita can therefore improve risk-avoidant injecting behaviours (Kumar et al. 2016; Neaigus et al. 1996). Unfortunately the model tested in this study was unable to find a significant main effect of group identification with family on sharing behaviour. Nonetheless, the findings of this study uncover the potential negative impact of an individual's identification with a social group such as a drug network.

The current study did not find any significant associations between psychological factors and sharing of injecting equipment, which have been widely reported in the literature (Bailey et al. 2007; Broz et al. 2010; Cepeda et al. 2012; Gossop et al. 2002; Heimer et al. 2014b; von Hippel et al. 2018; Mackesy-Amiti et al. 2014; Neaigus et al. 2006; Perdue et al. 2003; Roux et al. 2014). Perception of HCV also did not show a significant correlation with injecting risk behaviour. Perception of HCV, in a HCV-positive population, emerged from the literature review as an important factor influencing HCV treatment and risk behaviour (Bailey et al. 2007; Fairnbairn et al. 2010; Langston et al 2016; Langston et al. 2017; Langston et al. 2018; McGowan et al. 2013; Wagner et al. 2010b; Zalai et al. 2015). There was, however, a significant association between mental health variables and the illness perception measure. A larger sample might have enabled an exploration of these variables in the regression model predicting injecting risk behaviour.

[1] Published in *Journal of Viral Hepatitis*: Malaguti et al. (2019): Doi: 10.1111/jvh.13009

5.5.1 Limitations

The sample of this study was small. Green (1991) suggests that for a multiple regression the minimum sample required is 50+8k, where k is the number of predictors. The sample in this study did not reach this threshold. This might have influenced the assumptions of the regression test not being met. To overcome this, a bootstrap analysis was performed. A bootstrap analysis is a robust method of analysis that deals with tests assumptions not being met (Field, 2018). Given its ability to derive a sampling distribution from the sample itself, a core-principle of bootstrapping is that the sample needs to be large enough for this empirically derived hypothetical sample of 1000 to draw information from the original sample (Rousselet et al 2019). An original sample of 50 was considered a respectably sized sample for this function to be performed.

A further limitation of the study is that, in order not to overload participants with questionnaires at visit 1 in the RCT, baseline questionnaires were split into two visits. The results presented in this analysis are measures taken on visit 1 only. Visit 2 saw a dropout rate of 36%, with a sample size of 32. A sample of 32 was considered too small to be able to result in reliable inferences about the data even with bootstrapping, given the skewed sampling distribution (Rousselet et al. 2019). This was unfortunate, as visit 2 included the second primary outcome of ADAPT, self-efficacy, in addition to a further 2 secondary measures of social influence, social connectedness and social norms. Some aspects of social influence were captured via group identification scales. Yet, self-efficacy was not. This is a limitation to the findings of this study as published literature evidences the association and predicting role of self-efficacy with/on injecting sharing behaviour (Bonar & Rosenberg, 2011; Cox et al. 2008; Gagnon & Godin, 2009; Gibson et al. 1993; Nasir et al 2009; Thiede et al. 2007; Wagner et al. 2010a). On reflection, this construct should have been captured on visit 1.

Future research should consider including a self-efficacy measure in the baseline visit. Given the highly correlated nature of the mental health scales, considerations should be made about the need to measure all variables as separate constructs. Interventions on social network identification to reduce sharing of injecting equipment should be designed and piloted with the PWID population.

5.5.2 Conclusions

In conclusion, baseline data shows injecting risk behaviour to be associated with both individual-level and social-level factors. Mental health variables and HCV illness perception, although inter-correlated, showed no significant association with sharing behaviour. A significant effect of group identification with drug network on sharing behaviour was observed in the tested model. Although the study was not able to support findings from previously published literature on the relationship between mental health and risk-taking in PWID, the finding showcase the importance of one's social network when sharing of injecting equipment occurs, in particular the identification of an individual with peers from a drug network. Identification with a social group, usually associated with improved health, may pose health risks depending on the type of group identification. Interventions on social networks are recommended to reduce sharing of injecting equipment.

CHAPTER SIX: Study 3 – ADAPT Results 2

A pilot randomised controlled trial to test a psychosocial intervention on self-efficacy to reduce injecting risk behaviour.

This chapter reports the main findings of ADAPT. After exploration of the data, it focuses on presenting and describing such data in detail, using simple inferential statistics to investigate the effects on the use of implementation intentions with the specified population on self-efficacy and sharing of injecting equipment.

6.1 Abstract

Background: Injecting behaviour in people who inject drugs is the main risk factor for hepatitis C virus (HCV) infection. Self-efficacy has been shown to be associated with injecting risk behaviour. The risk of HCV reinfection in people who inject drugs (PWID) treated for HCV remains high when sharing of injecting equipment continues post-treatment. This study explores the use of implementation intentions on self-efficacy and injecting risk behaviour among PWID on HCV treatment.

Methods: This randomised controlled trial comprised 50 participants on treatment for HCV. Active randomisation tasks were performed on 32 participants so a modified Intention to Treat analysis was carried out with the strategy of last observation carried forward applied for one follow-up point (visit 3). Data were explored in detail. Randomisation and attrition checks were carried out. Correlational analysis was performed as well as simple inferential statistics to observe time differences within-subjects and intervention effects on the two main outcomes (self-efficacy and injecting risk behaviour).

Results: Correlation analyses showed strong correlations between self-efficacy, injecting risk behaviour, injecting frequency and group identification with drug network. Mann Whitney U tests showed no significant differences between control and intervention groups on the two main outcomes. Wilcoxon Signed Ranks showed no significant differences within subjects between Time 1 and Time 2 on the two main outcomes. Analysis of secondary outcomes revealed a significant difference in HCV perception between start and end of treatment.

Conclusions: Despite the large attrition rate and the small sample size, the data exploration highlighted some interesting relationships between the main outcomes (self-efficacy and injecting risk behaviour) and two secondary outcomes (injecting frequency and group identification with drug network). The intervention did not show significant effects on behaviour, but several limitations did not allow a full analysis of the dataset. The results highlighted the importance for harm reduction strategies to emphasise each piece of injecting equipment as a potential source of HCV. Additionally, the change in illness perception should be explored in future research as a potential predictor of HCV reinfection.

6.2 Introduction

As explored in previous chapters, hepatitis C (HCV) is a blood-borne virus that is estimated to chronically affect around 1% of the global population (World Health Organization - WHO, 2017a). Around 57% of people who inject drugs (PWID) in Scotland show antibody positivity, and an estimated 31% present an active infection (Needle Exchange Surveillance Initiative – HPS, 2019; Public Health England - PHE, 2019). Injecting behaviour in PWID is the main risk factor for hepatitis C virus (HCV) infection (PHE, 2019). Spontaneous clearance of HCV infection and successful treatment of HCV infection do not seem to provide protective immunity against future infections (Falade-Nwulia et al. 2018). As PWID continue to engage in injecting risk behaviour after being treated, with one of the highest HCV reinfection rates being reported in Dundee as 21.5 per 100 person years (Schulkind et al. 2019), the National Health Service incurs costs for retreatment. Therefore, it is essential to examine injecting risk behaviours and psychosocial factors that are associated and predict such behaviours in order to intervene on such factors and reduce chances of future HCV reinfection.

Literature suggests a number of psychological and social factors have been associated with injecting risk behaviour (thoroughly explored in chapters 1, 3-5). Of interest to this study, some literature has focused on the association between self-efficacy and injecting behaviour (Bonar & Rosenberg, 2011; Copenhaver & Lee, 2006; Cox et al. 2008; Falck et al. 1995; Gagnon & Godin, 2009; Gibson et al. 1993; Kang et al. 2004;

Latka et al. 2008; Robles et al. 2004). As presented in Chapter 1, the Theory of Planned Behaviour (TPB) (Ajzen, 1991) is a model of behaviour change that highlights the influences of attitudes, societal norms and perceived behavioural control on behavioural intention and subsequently on behaviour itself. Perceived behavioural control is thought to have a direct influence on behaviour, and to consist of controllability and self-efficacy (Ajzen, 2002b), with self-efficacy being a person's belief in their own ability to perform a specific behaviour or succeed at a specific task (Bandura, 1977; 1986). Implementation intentions have been used as an extension of the TPB to intervene on the gap between intention and behavioural action (Higgins & Conner, 2013), and research on implementation intention on behaviours and self-efficacy has produced mixed findings (Chapter 2[2]; Milne & Sheeran, 2002; Murray et al. 2005, Rodgers et al. 2002; Webb & Sheeran, 2008). Using a volitional help sheet can provide participants with a structured approach to creating effective implementation intentions (Arden & Armitage, 2012).

The aim of this chapter is to explore the effect of implementation intentions on self-efficacy and injecting risk behaviour as no published study to date has investigated the use of implementation intentions on injecting drug behaviour with people who inject drugs.

6.3 Methods

The methodology employed in this study was the focus of Chapter 4, reported in accordance with the CONSORT 2010 statement (Schultz et al. 2010) and the TIDieR checklist (Hoffmann et al. 2014) so it will not be repeated here. This section will focus on the participants and the analyses. All regulatory approvals (University of Dundee sponsorship, NHS East of Scotland Research Ethics Committee, Research & Development NHS Tayside) were received in December 2017. Data collection took place between February 2018 and January 2020. The study was longitudinal, divided into visit 1 (start of treatment), visit 2 (mid treatment), visit 3 (end of treatment) and visit 4 (3-months follow-up). The data and results reported in this chapter refer to

[2] Published in *Drug & Alcohol Dependence*: Malaguti et al. (2020). Doi:10.1016/j.drugalcdep.2020.108120

baseline visits 1 and 2 (referred to as Time 1: Baseline) and the 1-month follow-up visit (visit 3, referred to as Time 2: Follow-up) of the pilot RCT. Visit 4 (3-month follow-up) was disregarded given the unreasonably small number (8) of participants who completed it.

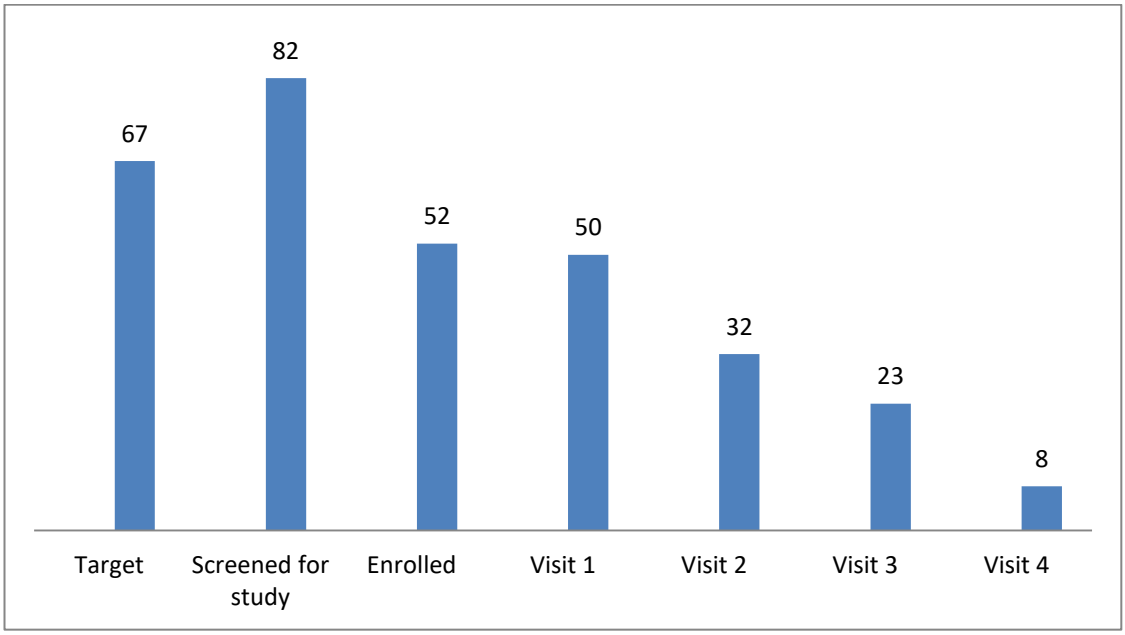
6.3.1 Participants

The trial's target sample size was 67 participants (See chapter 4). A total of 82 people were approached for the study, and 52 participants were consented (See Figure 6.1). Two consented and did not have time to complete Visit 1, but never returned to participate in the study. Therefore, 50 participants were randomised in the study. The intervention and one of the main outcomes (self-efficacy) were completed at visit 2, which was still considered a baseline visit (Time 1) given that baseline measures had been split into 2 visits in the interest of time and to facilitate participants' active engagement. After visit 1, the attrition rate increased at every study visit. Participants were withdrawn for different reasons. Eight participants completed the trial (16%); 22 were lost to follow-up with unknown reason (LTFU= 44%); 9 people were withdrawn from their HCV treatment (18%); 8 people went to prison (16%); 1 participant was withdrawn as cognitively incapacitated due to being under the influence of heroin (2%); 1 participant was hospitalised (2%); 1 participant was in withdrawal and left half way through visit 3 and was then LTFU (2% - Visit 3 data completed as LOCF). The overall attrition rate was 84%. Attrition rate between Time 1 and Time 2 analysed in this chapter was 28.1%.

6.3.2 Analysis

Data was analysed using IBM SPSS Statistics 25. Descriptive analyses showed the characteristics of the sample at Time 1 and mean scores of the 2 main outcomes (injecting risk and self-efficacy).

Figure 6.1: Complete study sample size



A modified intention to treat analysis (mITT) was employed for the analysis of this trial (Fisher et al. 1990; Gupta, 2011; Sabin et al. 2000; Streiner & Geddes, 2001). Given that the intervention was provided on visit 2, only participants who completed visit 2 were considered for the analysis (N=32). Following a Last Observation Carried Forward (LOCF) strategy, the last recorded observation was used in place of the missing data for the 9 participants who did not show for Time 2 (visit 3) (Gupta, 2011; Streiner & Geddes, 2001).

6.3.2.1 Data exploration

All variables were explored to characterise the sample and inspect data visually. Apart from age, social connectedness, depression and illness perception, all other variables showed quite severe levels of skewness and/or kurtosis, as confirmed visually with Q-Q plots and box plots and numerically with skewness and kurtosis values and Shapiro-Wilk test statistics. Three types of data transformations were tried in order to normalise the distribution of the variables and reduce the number of outliers: a log ($\log_{10}x$), a square root ($\sqrt{x}$) and an inverse ($1/x$) transformation. None of these transformations normalised the data distribution.

Non-parametric correlations (Spearman's rho) were carried out to inspect correlations with the two main outcomes (injecting risk – IRQ - and self-efficacy – SES), given the

results in Chapter 5 suggested not all independent variables showed a relation to the dependent variable.

6.3.2.2 Attrition checks

Attrition tests were carried out to compare those who completed Time 2 (23) and those who only completed Time 1 (9). They were also carried out to compare those who completed the full planned 4 visits (8) and those who did not (42), even though the data from visit 4 were not included in the main analysis.

The assumptions for MANOVA were not even approximately met. Univariate tests were used: Mann-Whitney for age, injecting frequency, injecting risk, identification with family and drug network, depression, anxiety and illness perception; and Chi-square for gender, genotype, site, treatment pathway, trial group, partner, SVR12, Post Traumatic Stress Disorder (PTSD) and drugs injected.

The increase in Type I errors when performing multiple tests was not considered here, as almost all tests performed did not approach significance. Relationships among the variables are also ignored in these checks since it was not possible to run MANOVAs.

6.3.2.3 Randomisation checks

Randomisation checks were also carried out on the same variables using the Mann-Whitney U and Chi-square tests to check for differences at baseline between participants in the intervention and control group. Both checks were carried out for a mITT (N=32) and a per-protocol analysis (N=50). In this case too, assumptions for running a MANOVA were not met, leading to multiple univariate tests which did not take into consideration intravariate effects and increased the chance of Type I errors.

6.3.2.4 Main analyses

In the study protocol, the main planned analysis was a MANCOVA, testing self-efficacy and injecting sharing risk as dependent variables, trial group as the grouping variable (intervention or control) and any correlated variables at Time 1 as covariates.

MANOVA and MANCOVA (multivariate analysis of variance or covariance) make a number of assumptions but is generally quite a robust test that can deal with some assumption violation, especially a degree of skewness in data distributions. However, the small sample size, the number of outliers and the ceiling and floor effects of the

two dependent variables (self-efficacy and injecting risk) resulted in severe assumption violations. When all test assumptions were checked, the severe distribution asymmetry (univariate normality being a necessary condition of multivariate normality, which cannot be tested in SPSS IBM Statistics 25), the number of outliers (participants 3 and 40 for both variables, and participant 18 for self-efficacy only), the lack of linear relationship (between IRQ and SES both in the control and intervention groups) and the heterogeneity of variance-covariance matrices (Box's test p=.009), made MANCOVA an unsuitable method.

In order to allow some inferential analyses, a number of other options were considered:

- One option would have been a non-parametric MANOVA or MANCOVA, but this is not available in SPSS 25. Non-parametric MANOVA is available with R packages (e.g. coin package) but given the different software and coding necessary for this analysis, this option was not viable.
- A new score was calculated for the 2 dependent variables as the Difference Score between Time 2 and Time 1 (IRQ_Score_v3 – IRQ_Score_v1= IRQ_Difference & SES_Score_v3-SES_Score_v2= SES_Difference) to check whether the respective scores presented a more normal distribution and fewer outliers. The distributions still had large skew and kurtosis and the number of outliers increased. A log transformation was tried but it did not improve the distributions.
- A Generalised Linear Model (GLM) with a Gamma distribution was considered as it is a type of analysis widely used for continuous, non-negative positively skewed data, able to deal with heteroscedasticity. However, the dependent variable self-efficacy had a strong negative skew (Skewness = -1.57, SE= .41, Shapiro-Wilk test statistic= .66, p<.001) which cannot be used in a GLM with a Gamma distribution.
- A cross-Lagged model was also considered to assess the interplay between Time 1 variables (injecting risk, self-efficacy, injecting frequency and identification with drug network) with the same repeated measures at Time 2. This is a type of structural equation model for information that has not been manipulated and is collected at two or more points in time to assess causality. However, the variables were measured in an experimental setting, and therefore had been manipulated,

and the approximate sample size required for this analysis of 10 cases per variable was 60% greater than the present sample size (Bentler & Chou, 1987; Nunnally, 1967) rendering any results and conclusions unreliable.

- Therefore, due to major obstacles in producing good quality, reliable hypotheses testing analyses, the main analyses on the sample were simple frequencies and descriptives in order to understand and characterise the sample results as well as possible.

  Some Mann-Whitney U and Wilcoxon Signed Rank tests were performed (despite multiple univariate tests not taking into consideration intravariate effects and increasing the chance of Type I errors), with the purpose of exploring effect sizes.

6.4 Results

6.4.1 Descriptive statistics and attrition checks

Exploration of the Time 1 data was carried out to characterise the sample (Table 6.1). Means and standard deviations are presented for the full sample (N=32, Table 6.1) and divided between those who completed (N=23) and those who did not complete Time 2 (N=9). The main attrition checks are also reported in Table 6.1. Secondary outcomes (social norms, social connectedness, identification with family, identification with drug network, depression, anxiety, PTSD, illness perception) were checked for Time 1 differences and are not reported in the table. Table 6.1 shows that the values for completers and non-completers are similar, and no differences approaching statistical significance were found at Time 1 between those who completed and those who dropped out of the study. A full attrition check was also carried out on the whole ADAPT sample (N=50) presenting only 8 participants with a complete dataset and 42 who dropped out before visit 4. No statistically significant differences were found between completers and non-completers at visit 1.

Table 6.1: Characteristics of the full sample and attrition checks

Characteristics	Full sample (N=32)		Completed (N=23)		Dropped out (N=9)		Mann-Whitney U test* p-value
	M	SD	M	SD	M	SD	
Age (years)	38.40	8.10	38.43	8.62	38.22	7.03	.621
Weekly injecting	7.38	9.21	6.22	8.40	10.33	10.98	.212
Injecting Risk Behaviour-IRQ (1-4)	1.22	.39	1.18	.33	1.33	.54	.621
Self-efficacy (1-7)	6.65	.58	6.69	.57	6.54	.63	.592
	N	%	N	%	N	%	Chi-Square* p-value
Sex							.654
Female	8	25	5	21.7	3	33.3	
Male	24	75	18	78.3	6	66.7	
Recruitment site[1]							1
Cairn Centre	28	87.5	20	87	8	88.9	
Drumhar	4	12.5	3	13	1	11.1	
Intervention group							1
Control	18	56.3	13	56.5	5	55.6	
Intervention	14	43.8	10	43.5	4	54.4	
HCV Genotype							.441
Genotype 1	11	34.3	9	39.1	2	22.2	
Genotype 3	21	65.6	14	60.9	7	77.8	
Partner							.681
Yes	11	34.4	7	30.4	4	44.4	
No	21	65.6	16	69.6	5	55.6	
If Yes	**(N=11)**	Valid %	(N=7)	Valid %	(N=4)	Valid %	
1.Partner injects							1
Yes	6	54.5	4	57.1	2	50	
No	5	45.5	3	42.9	2	50	
2. Partner on treatment							.194
Yes	4	36.4	4	57.1	0	0	
No	7	63.6	3	42.9	4	100	
Treatment pathway[2]							.353
DOT	15	46.9	9	39,1	6	66.7	
2/52	10	31.3	8	34.8	2	22.2	
2/52+	7	21.9	6	26.1	1	11.1	
SVR12 Achieved[3]							1
Yes	28	87.5	20	87	8	88.9	
No	4	12.5	3	13	1	11.1	
Drugs Injected							1
Opiates	31	96.9	22	95.7	9	100	
Opiates + Cocaine	1	3.1	1	4.3	0	0	

[1]Sites= Cairn Centre is the main IEP in Dundee; Drumhar is the main IEP in Perth.
[2]Treatment pathways: DOT= Daily Observed Therapy; 2/52= Fortnightly observed therapy; 2/52+ = Fortnightly observed therapy with Psychological intervention (Adherence).
[3]SVR12 Achieved= Sustained Virological Response (HCV undetectable, patient cured).
* Significant at the 0.05 level (2-tailed).

Reliability analyses were carried out for the scales which had not been tested in Chapter 5 (given they were assessed at Visit 2 baseline). An exploratory factor analysis on all the measures was not possible as the sample size was too small for appropriate analysis. Cronbach's α for all measurement showed good scale reliabilities (all above .7) (Table 6.2).

Table 6.2: Visit 2 variable's descriptives and reliability testing

Characteristics (Range)	M	SD	Cronbach's α
Self-efficacy (1-7)	6.65	.58	.76
Social norms (4-28)	7.47	5.47	.77
Social connectedness (8-48)	24.90	11.63	.90

6.4.2 Randomisation checks

Means and standard deviations for those who completed the intervention or control activity are presented in Table 6.3 and are divided by trial group (intervention and control). The randomisation checks on the main outcomes are also reported in Table 6.3. Secondary outcomes (social norms, social connectedness, identification with family, identification with drug network, depression, anxiety, PTSD, illness perception) were also checked for baseline (Time 1) differences but are not reported in the table. No statistically significant differences were found at Time 1 between those who were randomised to the intervention and control groups. A full attrition check was also carried out on the whole ADAPT sample (N=50) which presented 23 participants in the control group and 27 in the intervention arm. This check was run to ensure the randomisation procedure was robust, even though 18 participants completed neither the intervention nor the control task. No statistically significant differences were found between intervention and control participants at visit 1.

Table 6.3 Characteristics of sample by intervention group (N=32)

Characteristics	Intervention (N=14)		Control (N=18)		Mann-Whitney U test* p-value
	M	SD	M	SD	
Age (years)	39.07	6.37	37.83	9.37	.896
Weekly injecting frequency at Time 1	4.93	8.70	9.28	9.38	.125
Injecting Risk Behaviour (Range 1-4)	1.10	.22	1.32	.47	.145
Self-efficacy (Range 1-7)	6.84	.34	6.50	.69	.145
	N	**%**	**N**	**%**	**Chi-Square* p-value**
Sex					.703
Female	4	28.6	4	22.2	
Male	10	71.4	14	77.8	
Recruitment site[1]					.613
Cairn Centre	13	92.9	15	83.3	
Drumhar	1	7.1	3	16.7	
Attrition (Time 1-2)					1
Completed	10	71.4	13	72.2	
Withdrawn	4	28.6	5	27.8	
HCV Genotype					.465
Genotype 1	6	42.9	5	27.8	
Genotype 3	8	57.1	13	72.2	
Partner					.712
Yes	4	28.6	7	38.9	
No	10	71.4	11	61.1	
If Yes	(N=4)	Valid %	(N=7)	Valid %	
1.Partner injects					1
Yes	2	50	4	57.1	
No	2	50	3	42.9	
2. Partner on treatment					.576
Yes	2	50	2	28.6	
No	2	50	5	71.4	
Treatment pathway[2]					.64
DOT	7	50	8	44.4	
2/52	5	35.7	5	27.8	
2/52+	2	14.3	5	27.8	
SVR12 Achieved[3]					1
Yes	12	85.7	16	88.9	
No	2	14.3	2	11.1	
Drugs Injected					.437
Opiates	13	92.9	18	100	
Opiates + Cocaine	1	7.1	0	0	

[1]Sites= Cairn Centre is the main IEP in Dundee; Drumhar is the main IEP in Perth.
[2]Treatment pathways: DOT= Daily Observed Therapy; 2/52= Fortnightly observed therapy; 2/52+ = Fortnightly observed therapy with Psychological intervention (Adherence).

[3]SVR12 Achieved= Sustained Virological Response (HCV undetectable, patient cured).
* Significant at the 0.05 level (2-tailed).

6.4.3 Correlations

An exploration of the correlations between the two main outcome and all the Time 1 predictors was carried out to explore the relation between variables (Table 6.4). Scatterplots of all the variables were visually inspected to check the linearity of the relationship between injecting risk behaviour and self-efficacy with all psychosocial factors measured. Given linearity was violated among all pairwise combinations, Spearman's correlation was carried out to test the relationship between variables.

Table 6.4 shows bivariate correlations between the main outcomes and all Time 1 predictors. In the table, the main outcomes are shown as injecting risk behaviour and self-efficacy.

Significantly correlations were observed between a few variables. A higher level of self-efficacy was associated with lower injecting risk behaviour, lower injecting frequency and a weaker identification with a drug network. A higher injecting risk was associated with a stronger identification with a drug network.

Higher injecting frequency was associated with lower threat of illness perception; higher social connectedness was associated with higher identification with family and fewer PTSD symptoms; interestingly, social norms showed no correlation at all with identification with drug network.

In chapter 5, the 3 mental health variables (depression, anxiety and PTSD) were all correlated using the data from all the 50 participants enrolled. In this analysis, using only the 32 cases that completed visit 2, the 3 mental health variables were all still positively and significantly correlated, as can be seen in the last 3 rows of Table 6.4.

Chi-square tests of associations were used to check correlations between categorical Time 1 variables (sex; recruitment site; intervention group; HCV genotype; partner; treatment pathway; SVR12 achieved; drugs injected) and injecting risk behaviour (computed as a categorical variable), with no significant correlations found.

Table 6.4: Spearman's correlations between factors at Time 1 (n=32)

*. Correlation is significant at the .05 level; **. Correlation is significant at the .01 level (2-tailed).

Spearman's Correlations at Time 1													
		Injecting Risk	Self-efficacy	Age	Injecting Frequency 2	Social Norms	Social Connectedn.	ID - Family	ID – Drug Network	Depression	Anxiety	PTSD	Illness Perception
Injecting Risk	ρ (rho)	1.000	**-.448***	-.003	.268	.306	-.185	-.205	**.517****	.026	.079	.090	.082
	p-value	.	.010	.986	.139	.088	.312	.260	.002	.886	.667	.625	.657
Self-efficacy	ρ (rho)		1.000	-.064	**-.382***	-.142	-.070	-.018	**-.511****	.054	-.148	.108	.040
	p-value		.	.729	.031	.439	.702	.923	.003	.769	.418	.558	.826
Age	ρ (rho)			1.000	-.049	.099	-.325	-.175	-.226	-.228	-.119	-.065	.028
	p-value			.	.790	.590	.070	.338	.215	.210	.517	.724	.878
Injecting Frequency 2	ρ (rho)				1.000	.176	-.038	-.113	.123	-.149	.019	-.108	**-.397***
	p-value				.	.337	.836	.538	.501	.417	.918	.557	.024
Social Norms	ρ (rho)					1.000	-.111	-.328	.036	-.142	-.056	-.002	-.129
	p-value					.	.547	.066	.845	.437	.761	.991	.483
Social Connectedness	ρ (rho)						1.000	**.366***	.151	-.297	-.397*	**-.415***	-.196
	p-value						.	.039	.410	.099	.024	.018	.281
Identification - Family	ρ (rho)							1.000	.279	-.098	-.176	-.202	.039
	p-value							.	.122	.595	.336	.268	.833
Identification - Drug Network	ρ (rho)								1.000	-.095	-.193	-.195	.107
	p-value								.	.605	.290	.285	.561
Depression	ρ (rho)									1.000	**.848****	**.742****	**.455****
	p-value									.	.000	.000	.009
Anxiety	ρ (rho)										1.000	**.747****	**.357***
	p-value										.	.000	.045
PTSD	ρ (rho)											1.000	**.442***
	p-value											.	.011

The correlations between categorical Time 1 variables and self-efficacy could not be checked with a point-biserial correlation, as self-efficacy was not normally distributed and presented outliers. The significance of these relations was therefore checked using a Mann-Whitney U test (Field, 2018) and showed no significant tests.

The correlation between the main outcomes of self-efficacy and injecting risk was checked at Time 2, revealing the strong negative relationship was not sustained at follow-up (Spearman's rho= -0.31, p=0.085).

6.4.4 Exploration of injecting frequency

Given the randomisation checks showed no significant differences between groups at Time 1, the description and exploration of frequencies in the data was carried out on the full sample at Time 1 (N=32).

One third of the sample did not inject in the week preceding the mid-treatment visit 2 (Table 6.5). The sample distribution, however, was very heterogeneous, as injecting frequency for the other two-thirds of the sample was spread between once a week and 28 times a week (or 4 times a day).

Table 6.5 Weekly injecting frequencies

Injecting Frequency 2		
	Frequency	Percent
0	11	34.4
1	2	6.3
2	3	9.4
3	3	9.4
4	1	3.1
6	1	3.1
10	1	3.1
14	2	6.3
18	3	9.4
19	1	3.1
21	2	6.3
28	2	6.3
Total	32	100

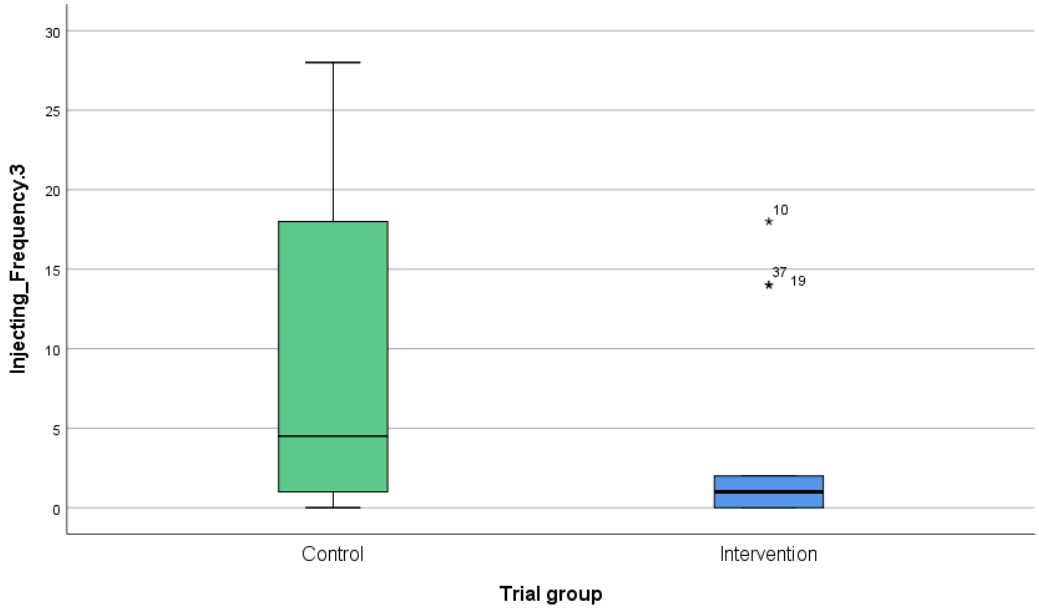
At Time 2 the score spread in the control group remained in the same range, even though fewer participants had not injected in the week prior to the visit, whilst in the intervention arm, the range of scores diminished, with most of the participants featuring at the lower end of the frequency scale (Figure 6.2).

There were 3 measurements of injecting frequency as this was measured at every visit. All participants were current injectors but injecting frequency was quite heterogeneous across the sample. This is quite evident when reporting means and standard deviations for the 3 visits: injecting frequency at start of treatment visit 1 M= 6.69 (SD= 8.42); injecting frequency at mid-treatment visit 2 M=7.37 (SD= 9.21), injecting frequency at end of treatment visit 3 M=6.5 (SD= 8.22).

Nonetheless, a Friedman test for differences in injecting frequency within-subjects between the start, middle and end of HCV treatment on the full sample (N=32) showed no significant difference in injecting frequency over time $\chi_F^2(2)= .33$, p= .848). Wilcoxon tests were used to explore these findings and showed no differences in injecting between start and mid treatment (visit 1-visit 2) (T= 122, *r* = .05), between start and end of treatment (visit 1-visit 3) (T= 109, *r* = -.04), nor between mid and end of treatment (visit 2-visit 3) (T= 51.5, *r* = -.01). The effect size *r* was calculated according to Rosenthal's (1991) formula $r = \frac{Z}{\sqrt{N}}$, where Z is the test score and N is the number of observations and *r* is interpreted as: Small = .1, Medium = .3, Large= .5 (Field, 2018).

A Mann-Whitney test for a difference in injecting frequency between the control and intervention arms at Time 2 was not significant (U= 81, z= -1.74, p= .091). Nevertheless, the effect size was *r* = -0.31 (medium, Figure 6.2), functions as a reminder that the test statistic and significance depend on N as well as any difference between the groups compared.

Figure 6.2 Boxplots of control and intervention scores at Time 2 for injecting frequency



6.4.5 Exploration of injecting risk behaviour

The injecting risk questionnaire was completed at Time 1 and Time 2 (See Thesis Appendix for copy of IRQ and see Chapter 4 for measure description and scoring). It measured on a 4-point Likert scale (1= never shared – 4= frequently shared) an overall sharing behaviour score by asking participants if in the past 4 weeks they had shared equipment, how many people they had shared with (repeated at the start of the questionnaire and at the end), and individually asking which singular equipment piece was lent and/or received for sharing.

The exploration of the behaviour will initially be carried out on the overall injecting risk score, followed by the comparison between the self-reported number of people shared with at start and end of questionnaire. Scores on singular injecting paraphernalia are then examined, followed by the comparison between lending and borrowing of equipment. The difference between trial groups is then investigated on injecting risk at Time 2.

6.4.5.1 Number of people shared with & injecting risk score at Time 1

Time 1 scores were investigated on the full sample (N=32) in more detail than the overall IRQ score used as the main outcome. Injecting risk showed a marked floor

effect (Table 6.6) as almost two thirds of participants reported not sharing equipment at visit 1. Tables 6.7a and 6.7b show self-reported number of peers with whom people had shared injecting equipment. The same question was asked at the start of the injecting risk and at the end of the injecting risk, after single item questions about receiving and lending each piece of injecting equipment (syringe, spoon, filter and water) had been asked.

Table 6.6 Injecting risk score Time 1

Injecting risk		
	Frequency	Percent
1.00	20	62.5
1.07	2	6.3
1.20	1	3.1
1.40	2	6.3
1.47	1	3.1
1.60	1	3.1
1.73	3	9.4
2.13	1	3.1
2.60	1	3.1
Total	32	100.0

Table 6.7a Reported number of people shared with at start of questionnaire

Number_Shared_start.1		
	Frequency	Percent
0	29	90.6
1	2	6.3
2	1	3.1
Total	32	100.0

Table 6.7b Reported number of people shared with at end of questionnaire

Number_shared_end.1		
	Frequency	Percent
0	21	65.6
1	5	15.6
2	4	12.5
4	1	3.1
5	1	3.1
Total	32	100.0

The injecting risk score of 0, obtained from 20 participants, was (all but for one person) in line with the self-reported number of people at the end of the questionnaire, in which 21 people reported not sharing with anyone. A Wilcoxon Signed Rank, run to check for a difference between the self-reported number of people shared with at start and end of the injecting risk at visit 1, showed a significant increase (N=32, z =2.55, p=.011). The effect size *r* = .45 was large.

6.4.5.2 Singular injecting paraphernalia

Because this change in self-report occurred after answering individual questions about injecting equipment, Table 6.8 explores the individual equipment items as individual sub-scores of the injecting risk questionnaire.

Table 6.8 Singular injecting paraphernalia sharing

Singular injecting paraphernalia sharing characteristics			
	Number of scale items in sub-score	Score Range	Mean (SD)
Syringe Sharing	9	1-1.67	1.09 (.17)
Spoon Sharing	2	1-4	1.42 (.83)
Filter Sharing	2	1-4	1.47 (.89)
Water Sharing	1	1-4	3.37 (1.13)

The syringe sharing sub-score was the closest to the overall injecting risk score (M= 1.22, SD=.39), and although the range of scores for sharing of spoons and filters was larger, the mean score was also quite similar to the overall injecting risk score. However, these results showed that sharing of water to inject was common, with the mean score of 3.37 (SD=1.13) with water being shared sometimes (=3) and frequently (=4) in a quarter of the sample. A quarter of the sample also scored over 1 (1=never sharing, anything above meaning sharing at varying degrees), and half the scores remaining closer to the lower end of the scale. This was the only injecting item that was measured by one scale item only.

6.4.5.3 Examining lending and borrowing

The injecting risk also allowed for differentiation between a lending-sharing score and a borrowing-sharing score. Most scores were 1(=never) for both lending and borrowing, yet 4 participants delineated a difference between receptive-sharing and lending-sharing and 8 participants engaged in both types of sharing (Table 6.9).

Table 6.9 Crosstabulation (2x2) of paraphernalia lenders and borrowers at Time 1

Time 1: IRQ_lent * IRQ_borrowed			
	Not borrowing	Borrowing	Total
Not lending	20	2	22
Lending	2	8	10
Total	22	10	32

6.4.5.4 Sharing characteristics at Time 2

Exploration of the same injecting risk characteristics at Time 2 showed a similar picture to those at Time 1, with most of the injecting risk scores at the lower end of the scale (Figure 6.3). The two trial groups were tested for any significant differences at end of treatment using a Mann-Whitney U test. No significant difference was found (U= 122.5, z= -.184, p= .896), with *r* = -.03 a negligible effect. No statistically significant increase or decrease in injecting risk behaviour was observed within-subjects in the two trial arms between Time 1 and Time 2, the intervention group showing a small-to-medium effect, whilst the control group approached a significant reduction with large effect (Wilcoxon Signed Rank: z= -1.87, p=.061, *r* = -.44).

Also, at Time 2, the self-reported number of people with whom participants had shared ranged between 0 and 2 both at the start of the questionnaire and at the end. Two participants (one per trial group) switched from 0 to 1 after being asked about the sharing of each singular injecting equipment piece, with no significant difference found in the self-reports in the full sample between start and end of questionnaire (Wilcoxon Signed Rank z= 1.41, p=.157, *r* = -.25).

The same number of people as Time 1 were not lending and not borrowing injecting equipment at Time 2. No participants reported only lending or only borrowing, with 12 reporting doing both at Time 2 (See Table 6.10). No significant changes were observed within the full-sample (N=32) at the two time points (Wilcoxon Signed Rank test results respectively z= -.65, p= .513, *r* = -.12 for lent and z=-1.72, p=.085, *r* = -.3 for received), nor between control and intervention groups at Time 2 (Mann Whitney U test results respectively z= -.21, p= .896, *r* = -.04 for lent, and z= -.56, p= .722, *r* = -.1 for received).

Figure 6.3 Boxplots of control and intervention scores at Time 2 for injecting risk behaviour

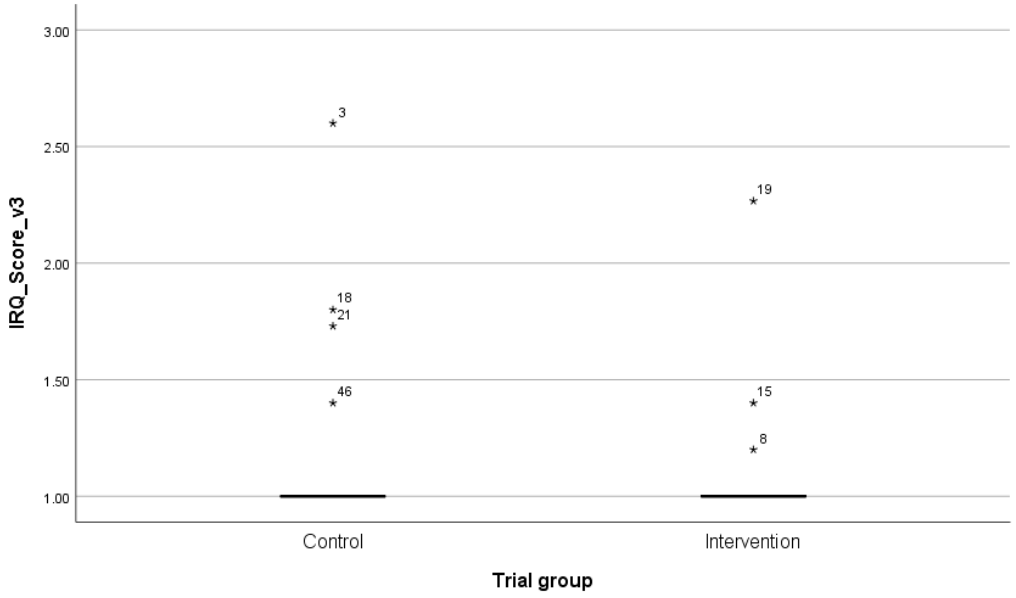


Table 6.10 Crosstabulation (2x2) of paraphernalia lenders and borrowers at Time 2

Time 2: injecting risk lent * injecting risk borrowed			
	Not borrowing	Borrowing	Total
Not lending	20	0	20
Lending	0	12	12
Total	20	12	32

6.4.6 Exploration of self-efficacy to refuse sharing

Self-efficacy to reduce sharing was measured on a 7-point Likert scale (ascending confidence level). It was completed at Time 1 and Time 2 (See Thesis Appendix for copy of self-efficacy scale and see Chapter 4 for measure description and scoring). As presented in Table 6.11, the self-efficacy scores showed a ceiling effect (M=6.65, SD= .58), as two-thirds of the sample at Time 1 reported high levels of confidence in their own ability to refuse and resist sharing of injecting equipment.

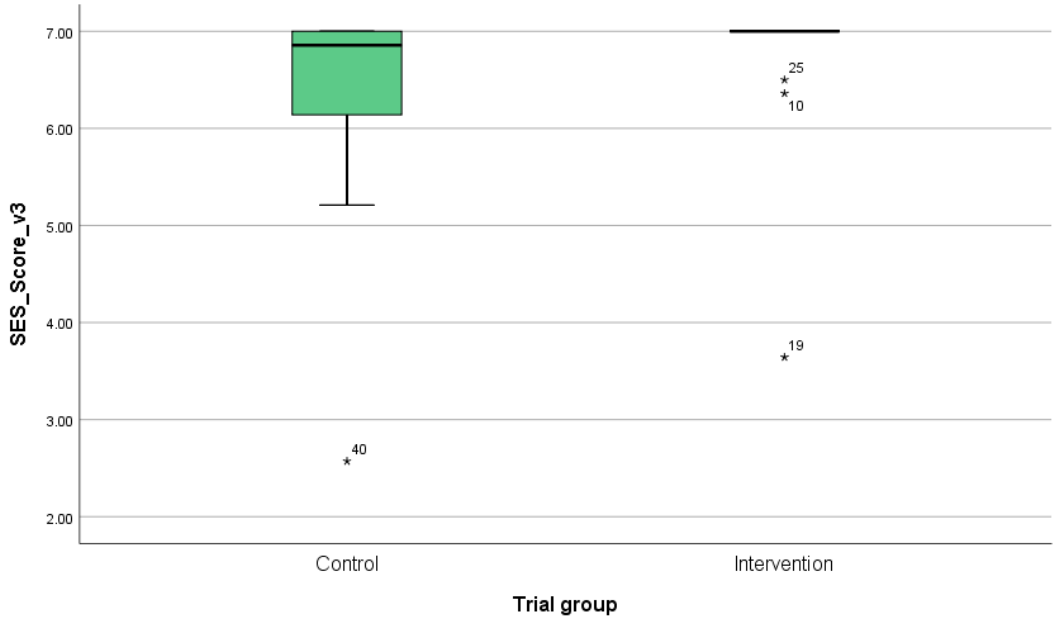
Table 6.11 Self-efficacy score frequencies

Frequency (percentage)			
Self-efficacy (Range 1-7)	Control (valid %)	Intervention (valid %)	Full sample
1 – 4.99	0	0	0
5 – 5.99	4 (22.3)	1 (7.1)	5 (16)
6 – 6.99	5 (27.9)	2 (14.2)	7 (22)
7	9 (50)	11 (78.6)	20 (62)
Total sample	18	14	32 (100)

At Time 2 self-efficacy scores remained very high, with the range increasing only due to two individuals, one in each trial arm (Outliers 19 and 40 in Figure 6.4).

The two groups showed no significant difference at Time 2 (Mann-Whitney U= 161.5, z= 1.55, p= .180). However, the effect *r* = .27 was medium, a reminder that the group sizes were small. No statistical significant increase or decrease in self-efficacy was observed within-subjects in the two trial arms between Time 1 and Time 2. The effect size of the change for the intervention group was *r* = 0, whilst that of the change for the control group was *r* = -.25.

Figure 6.4 Boxplots of control and intervention scores at Time 2 for self-efficacy



6.4.7 Exploration of identification with drug network

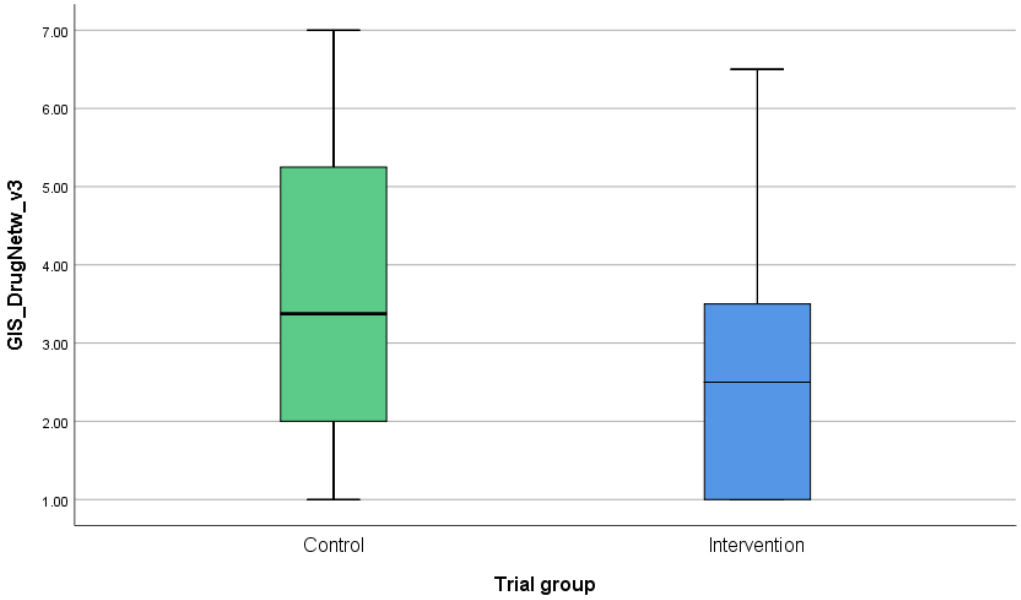
The group identification with drug network scale was completed at Time 1 and Time 2 (See Thesis Appendix for copy of group identification scale (with drug network) and see Chapter 4 for measure description and scoring). The scale measured identification on a 7-point Likert scale (ascending identification level). The drug network group identification scores showed a wide spread throughout the scale, although most frequently scores clustered at the top ends of the range (Table 6.12), thus providing a centrally located mean with wide standard deviation (M=3.39, SD= 2.18).

Table 6.12 Frequency scores for identification with drug network at Time 1

Frequency (percentage)			
Identification with Drug Network (Range 1-7)	Control (valid %)	Intervention (valid %)	Full sample
1 – 1.99	4 (22.2)	6 (42.9)	10 (31.3)
2 – 2.99	4 (22.2)	2 (14.2)	6 (18.8)
3 – 3.99	2 (11.2)	3 (21.4)	5 (15.7)
4 – 4.99	2 (11.2)	0 (0)	2 (6.2)
5 – 5.99	1 (5.5)	1 (7.2)	2 (6.2)
6 – 7	5 (27.8)	2 (14.2)	7 (21.8)
Total sample	18	14	32 (100)

At Time 2 the distribution of scores remained similar in both control and intervention groups (Figure 6.5). A Mann-Whitney U test showed no significant difference between control and intervention (U= 93.5, z= -1.25, p= .22, r = -.22); no difference was observed either within trial groups between Time 1 and Time 2, with Wilcoxon Signed Rank test results respectively: z=.26, p= .798, r = .06 for the control arm, and z= -.51, p= .609, r = -.14 for the intervention arm.

Figure 6.5 Boxplots of control and intervention scores at Time 2 for identification with drug network



6.4.8 Secondary variables measured at Time 2

The secondary outcome variables which were measured at different visits throughout the trial were explored even if no significant correlation between these variables and the two main outcomes (injecting risk behaviour and self-efficacy) were found at Time 1. Differences between Time 1 and Time 2 in the full sample (N=32) were tested for with Wilcoxon Signed Ranks (Table 6.13).

Table 6.13 Full sample Time 1-Time 2 differences in secondary outcomes

Within-subjects Wilcoxon Signed Ranks tests					
	Social Norms	ID - Family	Depression	Anxiety	Illness Perception
Z	-.94	.0	-1.89	-1.61	-3.03
p-value	.345	1.000	.059	.107	.002*
r	-.017	0	-.33	-.29	-.54

* Significant at the 0.05 level (2-tailed).

Illness perception showed a significant decrease in time, whilst depression was not quite significant at 5%. The effect sizes for illness perception and depression were, respectively, large (*r* = -.54) and medium (*r* = -.33).

These two variables were explored in more detail by trial group. Illness perception showed no differences between groups at Time 2 (U= 127.5, z= .06, p= .955, *r* = .01). It remained significantly different for both control and intervention groups from Time 1 to Time 2.

At Time 2, depression did not show any between-group differences either (U= 109, z= -.65, p= .536, *r* = -.12). Within-group differences were checked with Wilcoxon Signed Ranks test which revealed no differences in time in the control group (z= -.8, p=.423, *r* = -.19), and a large significant difference in the intervention group by time (z= -1.96, p= .05, *r* = -.52). This result was unexpected. The intervention was not targeting mental health variables. The time participants spent with the researcher was controlled for, as a time perspective inventory was explained and filled in with participants in the control group. The Time 2 between-group tests would suggest the time-control task was effective. Therefore this finding is considered accidental.

No other variables showed between-group differences at Time 2.

6.5 Discussion

The results of this pilot RCT are exploratory in nature and allow the reader to gain a better understanding of the HCV-positive injecting population. The use of a volitional help sheet to create implementation intentions had not been tested in this population before (Chapter 2). The feasibility and fidelity of carrying out this intervention with this population will be discussed in chapter 8. Nevertheless, the intervention did not result in any detectable effect on self-efficacy nor sharing behaviour.

In chapter 2, the effect of creating implementation intentions for substance use reduction on self-efficacy was explored and a pooled effect size of g=.16, p=.087 was reported. This result was pooled from studies on alcohol and tobacco smoking. The results of this trial are in line with those reported in chapter 2, as no significant effect was found on self-efficacy between- nor within-groups. The negative association between self-efficacy and sharing of injecting equipment has previously been explored in research with PWID, with literature highlighting the need for interventions to target risk reduction motivation and behavioural skills rather than using passive harm reduction education (Bonar & Rosenberg, 2011; Copenhaver & Lee, 2006; Cox et al.

2008; Falck et al. 1995; Gagnon & Godin, 2009; Gibson et al. 1993; Kang et al. 2004; Latka et al. 2008; Robles et al. 2004). Other behavioural interventions have reported promising results, such as a behavioural intervention improving harm reduction self-efficacy in PWID (Pawa & Areesantichai, 2016) and motivational interviewing showing an increase in self-efficacy associated with a decrease in sharing of needles (Robles et al. 2004). In the current study, the measure of self-efficacy to reduce all equipment sharing suffered from a ceiling effect, with all participants reporting high levels of self-efficacy to avoid sharing of all injecting equipment at Time 1. An improvement on the reported self-efficacy scores would have been quite difficult to detect, especially with such a small sample size. In addition, the inclusion of all injecting equipment in the study's definition of sharing compared to sharing of needles only (Robles et al. 2004), might have impacted on people's reporting of sharing as discussed below.

6.5.1 Sharing of injecting equipment

The results of the trial present a detailed picture of injecting behaviour, as a relatively stable and habitual behaviour, even throughout HCV treatment. Unlike results reported in Chapter 3[3] and other published literature (Caven et al. 2019), no change in injecting frequency was observed between start (visit 1), mid (visit 2) and end of treatment (visit 3). Previous studies have mostly been carried out on patients on treatment during the Interferon-era (Chapter 3; Alavi et al. 2015; Artenie et al. 2017; Midgard et al. 2017) with only one study reporting small reductions in injecting and sharing behaviour during DAA treatment (Artenie et al. 2020). The near-to-none side effects associated with DAA treatment might be resulting in no influence on patients' ability to continue injecting.

Sharing behaviour did not change over the course of the HCV treatment in this study. As one of the main outcomes of the trial, change was explored between intervention and control groups at Time 2, with no difference detected between the two groups. The reported scores of injecting risk behaviour suffered from a floor effect, with all participants reporting low levels of sharing of injecting equipment at Time 1. An improvement on the reported injecting risk behaviour scores (i.e. a reduction in

[3] Published in *Journal of Viral Hepatitis*: Malaguti et al. (2019): Doi: 10.1111/jvh.13009

scores) would have been quite difficult to detect, especially with such a small sample size.

By dissecting the overall injecting risk behaviour score, a differentiation among injecting paraphernalia started to emerge. By asking about individual injecting equipment pieces, participants would be reminded that sharing of other paraphernalia other than syringes (such as water, pots and filters) also contributed to HCV risk (Mathei et al. 2006). This allowed them to adjust the self-reported number of people with which they had shared equipment in the previous 4 weeks, resulting in a significantly increased number of 'sharers' between start and end of questionnaire.

Unsurprisingly, linked to these results were the reported sharing behaviour sub-scores according to each piece of equipment, which showed water was the most shared and syringes by far the least shared pieces of equipment. These findings are supported by previous research, which shows spoons and water to be significantly more frequently shared than needles and syringes (Gaskin et al. 2000; Gossop et al. 1997), with as little as 10% of interviewed samples reporting not sharing water or filters during the previous year (Gaskin et al. 2000). Needle sharing has been associated by people to intimate partnerships, as it can be perceived as more intimate and intrusive than spoon or water sharing (Gossop et al. 1997; Unger et al. 2006).

This study explored sharing of injecting equipment in the previous 4 weeks, with participants reporting some instances of sharing (one-third at Time 1 and one-fifth at Time 2). These findings and previous research show that PWID are aware of the health risks associated to sharing, in particular in this study's sample which has been negatively affected by such risk behaviour (HCV infection), yet sharing continues to occur (Gaskin et al. 2000; Gossop et al. 1997). This might suggest that PWID hold a non-threatening perception of these negative consequences, such as HCV.

6.5.2 Change in illness perception

The results of the study do indeed show that PWID hold mostly non-threatening perceptions of HCV. The findings show that between Time 1 and Time 2, irrespective of trial group, the perception of HCV became even slightly less threatening. This decrease in illness perception score suggests HCV becomes less threatening after having been through treatment. Literature suggests HCV diagnosis can be perceived as frightening whether or not people perceive a high degree of susceptibility to the infection (Dowsett et al. 2017; Fraser & Treloar, 2013). The common sense model (CSM) of self-regulation of health and illness can be useful in order to understand this change in HCV perception (Leventhal et al. 1980; Leventhal et al. 1984; Safo et al. 2015). The CSM suggests that patients create an abstract representation of their illness, by interpreting factors such as the severity of symptoms and the socio-cultural context linked to the illness. These illness representations are both cognitive and emotional and inform the personal health threat and emotional response to the diagnosis and the illness itself. The illness is a change in the individual's status quo, which drives forward a self-regulatory process in order to return to such status. This self-regulatory process includes engaging in behaviours, such as seeking treatment, which will aid the individual to return to their original status. This is the coping stage, which is usually shaped by two types of coping strategies: approach and avoidance. The final stage involves the appraisal of the chosen coping strategy, with return to the status quo or identification for the need to re-create an illness representation and/or coping strategy (Leventhal et al. 1980; Leventhal et al. 1984; Ogden, 2012). By undergoing HCV treatment, participants' appraisals of their coping strategies at the end of their treatment would have been positive, considering the selected strategy as effective and rendering the illness less threatening given their experience of successful, and virtually side-effect-free, cure.

6.5.3 Attrition

Recruiting to a full sample size and retaining the full sample are very common issues in RCTs. A review of trials funded by the UK Medical Research Council and the Health Technology Assessment Programme, showed that only 55% recruited to target, with 45% of trials being awarded an extension, 44% failing to meet recruitment target and 22% achieving less than 80% of their required sample size (Duley et al. 2018; Sully et al. 2013). Another review of funded RCTs showed a mean attrition rate in RCT of 21.1% (Cooper et al. 2018). This study managed to recruit 74.6% of the required sample, though only 47.8% completed the randomisation tasks. This impacted heavily on the analysis presented in this Chapter, allowing mostly just descriptive analysis with inferential statistics which suffer from a high probability of Type I errors. Attrition rates also influenced the results, with a total attrition rate of 85% being well above the average for RCTs. If considering only those actually randomised to the conditions (visit 2), the attrition rate fell to 28.1% for 1-month follow-up (visit 3/Time 2), and 75% for 4-month follow-up (visit 4). The results reported in this chapter refer to visits 1 and 2 (Time 1) and visit 3 (Time 2) with an attrition rate of 28.1%, average for longitudinal trials, behavioural trials, and trials that involve PWID. Mean attrition rates vary widely, with studies reporting 66% as a typical attrition rate for self-reported studies (Gratton et al. 2007; Manstead & Semin, 1999), 22.5% (Samo et al. 2016), 29% (Horyniak et al. 2013) and 40% (Gindi et al. 2009) for longitudinal studies with PWID, 22.4% for behaviour change trials (Rigotti et al. 1997), and others (Crutzen et al. 2015) reporting a review of behavioural trials with pooled dropout rates of 18% in intervention conditions and 17% control conditions.

In order to allow an intention-to-treat analysis, missing data was dealt with using a last observation carried forward (LOCF) strategy. LOCF is widely used in trial analysis plans although it presents both positive and negative aspects. LOCF can introduce bias ,as it implies no change (positive or negative) has occurred over the time of the trial and ignores the trend of the data prior to the final value (Streiner, 2008; Streiner & Geddes, 2001). However, it allows the assessment of effects of interventions on slightly larger samples by minimising the number of participants excluded from the analysis (Conroy et al. 2015; Streiner, 2008). Overall, the bias introduced by using LOCF

is considered acceptable in order not to exclude participants from the trial analysis (Streiner & Geddes, 2001).

6.5.4 Limitations

The sample size was a large limitation of this study. A small sample size reveals an underpowered study which in turn is subject to an increase in Type II errors. Therefore, multiple univariate tests (which are associated with increase in Type I errors) were not considered a problem as the analysis was severely underpowered and the two types of errors are inversely proportional. The main MANCOVA test, which could not be carried out due to violation of assumptions, would also have been underpowered and would likely not have resulted in any meaningful results.

Although the design of the trial was adapted at the start of the recruitment to try to minimise drop-out rates (reduction of questionnaire repetitions between visits and reduction of visits from 5 to 4 with longest follow-up reduced from 6 months to 3 months), attrition rates remained high.

As a pilot study, the results reported in this chapter are informative for future research. They highlight different practical aspects which need to be considered for future research planning with this population. The physical difficulty of one person running an RCT individually was evident specifically when there were two recruitment sites open simultaneously and at times when the researcher was not at the site due to meetings or trainings. A larger research team involving treatment nurses seeing the patients for their routine appointments might reduce the attrition rate.

The number of questionnaires was too high. The results reported in this and in previous chapters will help guide future selection of psychosocial factors to be tested, alongside appropriate theories and models of behaviour change.

The visits were too long, with participants repeatedly reporting they did not have time to stay when being asked to stay for a visit, until the window in which that visit was meant to take place would close and they would have to be withdrawn as lost to follow-up. This specific issue had been thought of during the planning stages, as, per protocol, participants were given protein drinks at each visit as an incentive to take part in the trial. During the trial, participants always attempted negotiations and

bargaining in order to receive more protein drinks than the usual amount of 4 per visit. This might suggest that the perceived benefits of participating in the trial did not meet the perceived costs (e.g. effort and time).

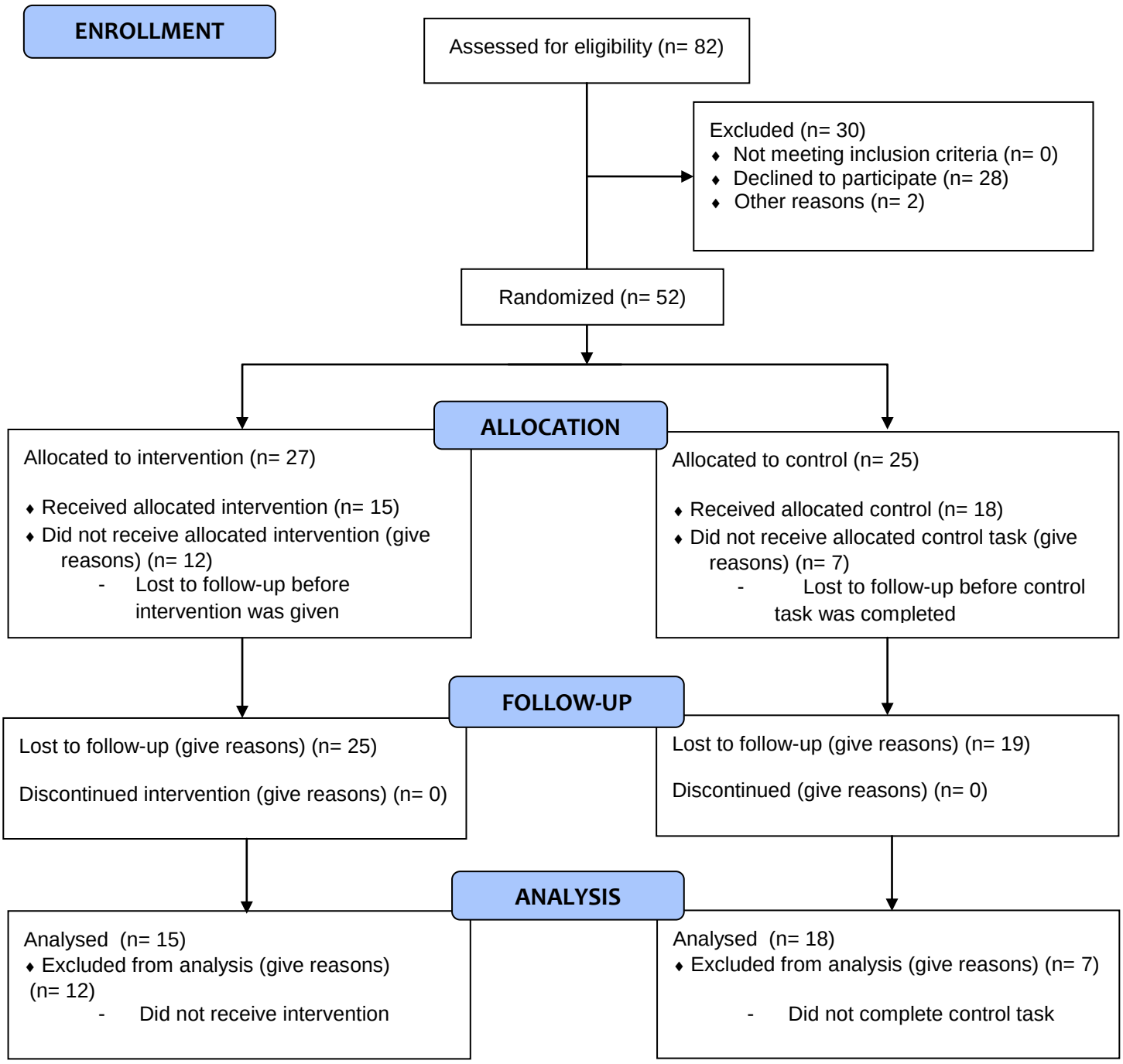
6.5.5 Conclusions

In conclusion, despite the large attrition rate and the small sample size, the data exploration highlighted some strong correlations between self-efficacy, injecting risk behaviour, injecting frequency and identification with drug network. No significant differences between trial groups and between baseline and follow-up were found in self-efficacy and injecting risk. Therefore, the intervention was not able to show significant effects on behaviour, but several limitations did not allow a full analysis of the dataset. The importance for harm reduction strategies to highlight each piece of injecting equipment as a potential source of HCV infection was evidenced by the results on the individual analysis of injecting risk behaviour. Additionally, the change in illness perception should be explored in future research as a potential predictor of HCV reinfection and as a target for intervention.

Supplementary File 6.1

CONSORT
TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram



Chapter Seven: Qualitative study

A qualitative study investigating the lived experience of patients with HCV on DAA treatment.

This chapter presents the small qualitative sub-study to ADAPT that was carried out with 5 participants enrolled on ADAPT whilst concluding or having concluded their HCV treatment. The interviews explored experience of diagnosis, treatment experience, occurrence of stigma, therapeutic alliance and illness perception. Qualitative exploration of the acceptability of use of implementation intentions with the population was not possible as none of the participants of this sub-study had completed the ADAPT intervention.

7.1 Abstract

Background: An estimated 1% of the global population is chronically infected with hepatitis C (HCV). Advances in pharmacological interventions have enhanced sustained virological response (SVR) rates and lowered side effects associated to treatment. These novel therapies have been implemented now for a number of years and this study aimed to provide updated understanding of illness perceptions and the lived experience of HCV treatment amongst people who inject drugs (PWID).

Methods: Semi-structured interviews were conducted with 5 adults who injected drugs on HCV treatment. The interviews took place in two Injecting Equipment Provision (IEP) sites in Tayside, Scotland. Data was analysed using thematic analysis, applying an inductive approach with experiential and essentialist orientation, as it aimed to understand and voice the experiences and perspectives of participants.

Results: Three overarching themes were identified in the interview transcripts: 1. “Changing illness perception”, which provided an insight into the journey that participants embarked on from diagnosis to end of treatment. It explored how their perception of HCV changed throughout treatment, from a dichotomy of ‘the great scare vs the great indifference’ to the ‘acceptance of individual and societal coexistence’ with the virus, to the view of a ‘de-stigmatised illness’; 2. “Shifting

agency", presenting an internalised conflict of accepting and rejecting a sense of agency for individual behaviours, such as: a 'socially responsible injector'; 'powerlessness in drug use', as one is overcome by temptations; and 'locus of control in treatment' with healthcare staff actively providing choice and agency to patients; 3. And lastly, "Treatment adherence" which allowed participants to share what aided and hindered their treatment.

Conclusion: Enhanced effectiveness and availability of HCV treatment is changing illness perception and social norms on treatment among people who inject drugs. Behavioural insights into sense of responsibility associated with diagnosis, sense of agency associated with treatment, and powerlessness associated with substance temptation and HCV ubiquity will help inform treatment adherence and harm reduction strategies.

7.2 Introduction

Hepatitis C (HCV) is a blood-borne virus that primarily affects the liver. Globally, the World Health Organization (WHO) estimates that 71 million people are chronically infected with HCV, which translates to around 1% of the global population (WHO, 2017a). In the UK, approximately 214 000 people are infected with HCV (Public Health England - PHE, 2017a), with an estimated 1% of the Scottish population being affected (Health Improvement Scotland, 2017a). In Tayside, estimates posit that between 0.5-0.6% of the resident population are affected by HCV. The most common transmission risk factor for HCV infection, in high-income countries such as Scotland, is injecting drug use, with around a half of all people who inject drugs (PWID) infected with HCV (PHE, 2019). The Needle Exchange Surveillance Initiative (Health Protection Scotland - HPS, 2019) in Scotland reports 57% HCV antibody positivity in people who inject drugs and attend needle-exchange services. This association between injecting drug use and HCV infection has produced a social stigmatisation of the condition and discrimination of those infected on multiple levels (Contreras & Jason, 2013; Treloar & Rhodes, 2009).

The way in which the illness is perceived can have a variety of consequences on the experience of patients living with HCV (Jordan et al. 2013; Langston et al. 2016). Studies on the perception of HCV have focused on awareness and knowledge of the

virus (Cruz et al. 2018; El-Sayed et al. 2019; Owiti et al. 2015; Saleh et al. 2014), on effects of diagnosis (Fraser & Treloar, 2006), on treatment uptake (Mehta et al. 2008; Skolnik et al. 2019; Sublette et al. 2015) and on treatment outcome (Langston et al. 2016), coping and adjustments (Langston et al. 2017; Langston et al. 2018; Zalai et al. 2015).

Most of the qualitative studies investigating the experience of patients living with HCV have been carried out in the Interferon era of treatment, which was associated with severe side effects and low treatment uptake (Butler, 2017; Grebely et al. 2011; Sublette et al. 2015; Treloar & Rhodes, 2009). The continuously changing landscape of available HCV treatments has improved not only sustained virological response (SVR) rates, but also diminished side effects associated with therapies (Pawlotsky et al. 2015). More recent studies about the lived experience of patients engaging in the new direct acting antiviral treatments (DAA) revealed that societal and cultural understanding of the new therapies was not up to date (Whiteley et al. 2016; Whiteley et al. 2017). The interferon-free DAA regimens were introduced in 2015 with restricted use in clinical practice because of financial constraints (Whiteley et al. 2017). PWID, who represent the majority of HCV+ patients, were often still offered interferon treatments, as they did not clinically qualify for interferon-free treatments, mostly given to being diagnosed during early stages of infection and liver disease. Therefore, despite the start of the DAA-era, constructions and perceptions of the illness were still being influenced among PWID by the personal and peer knowledge and experience from the interferon treatment era (Whiteley et al. 2016; Whiteley et al. 2017). These perceptions continued to produce multiple barriers to treatment uptake and completion (Skolnik et al. 2019).

This study aims to provide an updated understanding of illness perceptions and the lived experience of HCV treatment amongst PWID after access to DAAs had been broadened (Healthcare Improvement Scotland and NHS National Services Scotland, 2018; WHO, 2018d) and implemented in Tayside (Hickman et al. 2019; Inglis et al. 2019; Radley et al. 2018). The findings aim to enrich behavioural insights into therapeutic uptake and retention and to enhance harm reduction strategies.

7.3 Methods

7.3.1 Participants and procedure

This study is the qualitative component of a larger study (ADAPT, See Chapter 4). All regulatory approvals (University of Dundee sponsorship, NHS East of Scotland Research Ethics Committee, Research & Development NHS Tayside) were received at the beginning of August 2019 (in the final stages of the ADAPT trial). All participants on the ADAPT trial that had concluded or were concluding their HCV treatment were asked if they would be interested in being interviewed about their experiences with HCV infection and treatment. All participants received verbal and written (in the form of a patient information leaflet) information about the qualitative study and were offered £10 cash to cover costs for travel and time commitment. After being consented, they were assigned a pseudonym to ensure anonymity. Only 5 participants were consented onto this study, exhausting the available population sample pool. In this paper, no claims are made that this number of participants can be used to generalise results, but there was an attempt to voice and highlight the importance of individual experience and perceptions of HCV infection and treatment.

Recruitment was both planned and opportunistic, yet not biased by targeting any particular participant: all available participants were asked to take part in the interviews and all those approached agreed. Two of the 5 participants were seen for scheduled visits on ADAPT towards the end of their HCV treatment. Another 2 were seen opportunistically as they had concluded the ADAPT study and their HCV treatment but had accessed the IEP service whilst the researcher was on site. One participant had been released from prison and was contacted by one of the nurses, and whilst on the phone was asked if he'd be interested in participating in the interview, so a time and place were arranged.

Semi-structured interviews were conducted between the end of August 2019 and December 2019 by one researcher. All interviews took place in a clinic room at the main IEP service in two different locations, four interviews in Dundee and one in Perth, where participants had received or were receiving HCV treatment and where they had previously been seen by the same researcher for the ADAPT trial visits. Therefore, the researcher conducting the interviews was acquainted will all participants prior to the

interview taking place.

The interviews lasted between 15 and 20 minutes, with an average duration of 17 minutes. They were audio-taped and transcribed Verbatim. The Verbatim transcription reported the same words and sounds produced by participants and the interviewer, including 'ehm' and 'uh' sounds. Where possible, words were spelled phonetically in order to adhere to the participants' Scottish accents, and laughs and long pauses were reported in square brackets. A member of the research team checked the transcripts for accuracy against the recording.

It was not possible to qualitatively explore the acceptability of using implementation intentions during the interviews. Four out of the 5 participants in this qualitative study had been randomised to the control group in the quantitative study component. The only participant randomised to the intervention group never completed the intervention as he was incarcerated after the baseline visit (with the intervention being carried out on visit 2).

7.3.2 Analysis

The data was analysed using thematic analysis. Thematic analysis was chosen because of its relative flexibility allowing for identification of semantic meanings in the data but also for interpretation and exploration of latent meanings and assumptions 'hidden' amongst the data (Braun & Clarke, 2006). A six-phase approach was applied to the thematic analysis (Braun & Clarke, 2006), which was carried out manually, i.e. without analysing software. Firstly, all 5 interview transcripts were individually read and reread by two authors (AM and FS) to get more familiar with the data. Transcripts were annotated during this process. Phase 2 involved the initial generation of codes. Both semantic and latent levels of meaning in the transcripts were coded. Interpretation of the content of the data was deemed effective to delve deeper into the hidden meaning behind participants' narratives. Phase 3 involved the generation of themes. In this phase, it was particularly useful for the two researchers conducting the analysis to discuss the identified codes and potential themes. This discussion led to the generation of themes to make sense of the data, identifying where codes overlapped and when themes were recurring throughout transcripts. The codes and themes were discussed

by the two researchers to improve analysis accuracy and reduce bias. During phase 4, the developing themes were reviewed in the context of the full dataset. Quotes were selected from the individual transcripts and catalogued under themes and sub-themes or simply as standalone codes. The themes were then once again reviewed against the full dataset to ensure the data was fully captured in these findings. Phase 5 involved defining and naming themes, by ensuring they were focused, related to other themes and addressed the research question. Finally, phase 6 involved writing up the findings, which continued to involve analytical, procedural and conceptual thinking. This process continued the exploration of the themes, investigating their relation to each other and to the research question, in order to create a narrative supported by the data.

The data coding and analysis (Phases 2 and 3) was mainly inductive, using a bottom-up approach to allow analysis to be driven by the content of the data. It is, however, important to recognise the inherent bias of the researcher who knew the participants and had carried out the quantitative component of this research, therefore being influenced by concepts and topics which had been or were being concurrently discussed with participants in ADAPT, presenting a degree of deductive influence to the analysis. The analysis orientation was experiential and essentialist as it aimed to understand the experiences and perspectives of participants, with the researcher making sense and giving voice to what the participants reported and trying to understand how the participants themselves made sense of their own experience of living with HCV and being treated (Braun & Clarke, 2006).

An experiential orientation allows the participants' views, meanings, perspective and experiences to be explored by the participant themselves as they use language to reflect internal categories of understanding. It allows the researcher to hear from the participant directly how they see, perceive and understand the world around them (Braun & Clarke 2013; Mcleod 2011; Reicher 2000). The polar aspect to the experiential orientation is the critical one, which interrogates the meanings and experiences voiced by the participants, exploring them through the way narratives are phonetically and semantically constructed, through factors that influence them, and particular meanings and representations hidden behind the data. In this orientation, the interpretation carried out by the analyst is given more weight than the

interpretation carried out by the participants when they voice their experience (Braun & Clarke 2013; Mcleod 2011; Reicher 2000).

An essentialist method of analysis reports the reality lived by the participants, their meaning and experiences, with a belief that these are natural phenomena. The opposing method of analysis, constructionism, seeks to understand the socially constructed reality of events, meanings and experiences and how these are constructed using language as a vessel interpretation (DeLamater & Hyde, 1998).

Although this study was the qualitative component of a larger study, the design of the two studies was concurrent, as both ran at the same time, recruitment took place contemporarily and analysis was run independently. The concurrent design was selected in order to investigate convergence of results yet allowing both datasets and analyses to be independent from one another. The results from the quantitative component and those of this qualitative component will be integrated in the discussion chapter (Chapter 8).

7.4 Results

All 5 participants were white Scottish. One was female and 4 male, which closely represents the female gender split in the quantitative component of the trial (24%). They were all current injecting drug users when consented on ADAPT. Mean age was 33.4 years old (range 23 – 41 years old), slightly younger than the quantitative component of the trial with mean age of 37.4 (range 22-55). Genotype 3 to genotype 1 ratio was 3:2, mirroring the exact genotype ratio in the quantitative component of the trial. All 5 participants achieved a sustained virological response 12-weeks post treatment. Three overarching themes and 8 themes were identified in the interviews and are presented below.

7.4.1 Changing illness perceptions

7.4.1.1 The great scare VS the great indifference

The participants reported dichotomous perceptions of HCV as an illness when they were diagnosed, some frightened by the diagnosis, with the test result being a life defining moment, whilst the others indifferent as if nothing had changed. All participants were clients of the needle-exchange, with harm reduction messages being instilled habitually and most of them being tested regularly for blood-borne viruses (BBVs). Despite this, for some, HCV was an unexpected diagnosis. A sense of unrealistic optimism left participants scared and in disbelief:

> *"Oh I felt, my legs went all jelly, and and, I was upset. Ehm. Gobsmacked. I couldn't believe it." David, 33 (years old)*

> *"I just, I want to come in and get tested because I knew I was injecting [but] I was shocked. [...] Cause like, I wasn't expecting to have it [...] I was kinda thinking like 'Uhhhh!', took aback, a back seat, and was like 'oh no'. And I was, I was scared." Laura, 23*

> *"Yeah, yeah, I was scared. I had a, a horrible feeling all the time, and and I was wondering to myself what, what is it? [...] I was, I was putting it down to anxiety, just putting, putt, Pushing it to the side and that, And then it got real, come on and got tested and everythin'" Jason, 41*

Whilst on the other hand, some participants felt the diagnosis was just confirmation of something they knew already, portraying a sense of indifference to their condition:

> *"Ken what, at the time I wasnae really shocked cause I was daeing stupid things with needles and [...] I think I thought I knew I had it, just cause of stupideh things I waes doing." Peter, 32*

> *"Ken what? Deep down I think I ken I had it anyway, so it wasnae any surprising news." Gordon, 38*

However, the perception of HCV as an illness transformed throughout the participants' experience of living with the illness and treating it. This shift in perception was particularly marked at the end of the treatment, when the perception dichotomy seemed to have swapped: those scared of HCV having dealt with their fears and learning from their treatment experience; whilst those indifferent being wary of the health consequences of having HCV, suggesting a positive influence of being in contact with healthcare staff:

> *"I think..Yeah it could be a lot scarier, it could be a lot scarier. Like you say interferon and that if it was still at that stage it could be a lot scarier. But because the treatment is easy..Ehm I mean I, I, I'm not playing down hep C, I know it's a bad thing. But the treatment that's there for us is excellent, it's excellent " Jason, 41*

> *"Aye. I never even, it never seemed to affect my everyday life hevin' it like, but kennin' that it was, that it was there and it was, doing your liver in. Then at least, at least I could have stopped that, ken what I mean" Gordon, 38*

> *"Means everything to be honest with you [being HCV-free]. Yeah. It was either life or death eh. And sometimes. Cause it's gonna kill you in the end, ken." Peter, 32*

7.4.1.2 Acceptance of individual and societal coexistence

At a personal level, there seemed to be a shift in illness perception in light of an 'easy' treatment experience, and, at times, after a comparison with other BBVs. There was a sense of having HCV as being normal, because it did not have negative effects on everyday life:

> *"I've been injecting, I've been an IV user all my life, well not all my life. But through ma, adult life. Ehm, And I never, never had anything like this before. But it's nothing, nothing eh too bad, it's curable. And with the medication obviously, which is quite, quite amazing. [...] It's...just feel*

normal. Get up in the morning. Take my tablet. Nothing's different." David, 33

"In a, in a way I waes kinda glaed it was hep C [yeah?] nothing else, ken what I mean..oh, God no, HIV or anything." Jason, 41

Yet, a feeling of resignation transpired for the sense of ubiquity of HCV at population level among PWID, which increases the risk of getting infected again as the virus presents itself as unavoidable:

"Ken what it's just normal now. Eh.[...] Eh. You no get rid of it. Ken, It's always gonna be there, is it. [you got rid of it] Eh, it's keeping it staying like that though. Cause too many people got it. People that dinnae ken they got it." Peter, 32

"It's like, mes mes, mest people I think, that, bang up probably got it and dinnae, dinnae know [...] eh. Sometimes is easier just to put the blinders up." Jason, 41

7.4.1.3 De-stigmatised illness

The sense of ubiquity of the virus in the population, which produced negative perceptions on one's own sense of agency and powerlessness against the infection, also seemed to have a positive effect on reducing stigma towards the illness:

"I dinnae think it's as much as a, a deal now as it used to be, cause like, it used to be "ah stay awae from him he's got hep" but it's not like that anymair. Like, every 3 or 4 people that's used drugs have probably had it or have it or have had it before, so..it's not so bad now. Like few years back it was well mair stigmatised than it is now. Now people think right well I can get treatment in 6 weeks and that will be awae.[...]I dinnae think, they still dinnae want it, but they ken that it's an easier treatment. So they're not as

scared of it, but then again hep C is hep C it still ruins your liver so I dinnae think naebody wants it, ken what I mean. That's it." Gordon, 38

"Yeah people could judge, yeah. You don't know who's out there that will judge you. Nah fe, fe I've had it, I've been been alright. Nobody's judged me. Nobody's ehm not been any stigma about it" David, 33

However, one participant reported experiencing stigmatising behaviour among his family members, who did not use drugs. He linked the behaviour to ignorance on the subject:

"I told my mum and my sister. But I was feel, I was getting, eh like, my mum, mum was geein' us a certain cup and I was thinking to myself how come I keep on getting the exact same cup every single time I come in here, ken what I mean. And, And I figured oot, cause..[had hep C] Yeah, But I understand that cause my mum, I think my mum had to look it up on the internet and stuff cause when I first told us she was like 'what's that?'" Jason, 41

7.4.2 Shifting agency

7.4.2.1 Socially responsible injector

The de-stigmatised nature of HCV among PWID in this study made it possible for participants to be open about their diagnosis with their peers. This required a high degree of agency, as participants were taking the responsibility of informing peers and allowing them to make informed decisions (about sharing drugs and injecting equipment). This seemed to create an image of socially responsible injector, but it also allowed the participants themselves to shift the sense of responsibility of having the virus to others, by letting their peers make that informed decision to share injecting equipment (so if they acquired the virus they could not have blamed the participants):

"No I'm honest with people. If I'm having, like [a charge with someone else] Yeah, like, I'll say to them , like look I'm not gonna lie, but hep C. I says, but I'm on treatment for it, so." Laura, 23

"I would tell them. Ken, especially if they were gonna use I was, I'd say to them "look I've got Hep you cannae use wi' me, you gotta get yer ain stuff". So in that respect it put me in position to need to tell certain people, ken? But. And. [they would react like..]"Well at least you telt us" ken, cause I never got told." Gordon, 38

"But eh.. he, heving hep C, jee you get people that go aboot that got it and they won't tell anybody that they got it, ken like I would tell people if I had it. Ken what I mean, I'd say 'listen, listen I've got hep C, so if you're wantin' to ge' a hit, ge' a hit, but if you're no, if you dinnae, you got first I go whatever ken? but I just get people that don't even tell you they got it, in the middle of the treatment and then they tell you they've got it and then you're like 'what, what's the point in that?' it's stupid." Jason, 41

Although the decision to share equipment was bestowed upon their peers (creating the socially responsible injector), the openness about their diagnosis put the participants at increased risk when injecting equipment sharing did occur. There was a sense of duty for sero-sorting, given their own HCV status was known, coupled with a sense of safety because they were not infecting anyone else:

"Like, we used clean needles, like everything is clean. It's just like, soocking up of the pot. I do A's [friend] first and then I do mine. So that it's safe." Laura, 23

"They would go first; they would, they wouldnae go awa' [laughing] they would go first [laugh]. [did you know if they had it? Did they know if they had it?(HCV)] No, they didn't know if they had it.." Jason, 41

7.4.2.2 Powerlessness in drug use

Shifting the sense of responsibility away from the self was also part of the reasoning why participants continued to use drugs and put themselves at risk. This powerlessness was particularly evident for Peter and Jason, who described how difficult it was to fight temptation due to their social environment:

> *"Just need to stay awa' fae the needles. That's my fucking problem eh.[or get clean ones] I do all the time but when you're rattling you're feeling that shite and somebody's got a pin, like my ex girlfriend, I think it was her eh, sharing needles and, not caring. But. Naething to dae. I dinnae want to [share], but It just happens, eh. [...] See what happens when I go into town now. Bump into people and they think you're back into it. And. Nah, I've had enough of it eh. I need to gi' up. Drugs are for mugs eh. {But] Eh, naewhere to stay and, staying wi' fucking idiots, and end up jagging. Stupid eh. [temptation] It's always there, it's always there, it's always gonna be there. [inaudible] the mentality to say no. I cannae do it eh" Peter, 32*

> *"Cause environment is a big thing. Because in S. lane [hostel 1] it was all people just on drugs and there's door here door there, door there and door there. And everybody, 2 different people selling drugs in they 4 doors. So you're like Phf. Just you're facing it awe the time. So when I got moved up there [hostel 2] I was like 'oooh bliss, bliss' [It must be really difficult] Yeah it is. Especially if you have nae money and aeverybody's running around rattling and you're like..ken" Jason, 41*

7.4.2.3 Locus of control in treatment

The nurses providing the HCV treatment, notwithstanding wanting to treat as many people as possible, applied trauma-informed principles to their practice. They built safe, trusting and collaborative relationships with the patients, and facilitated their choices over their own treatments, about whether they wanted to be treated or not, thus empowering the participants and handing them the responsibility for their own

treatment. This helped shift the participants' locus of control from external to internal. In a social environment where often these participants have little agency, due to substance use services using negative operant conditioning to control behaviours, they commented on the sense of free will they felt in regards to obtaining HCV treatment:

> *"Yeah. Cause they did say, like, you don't have to take it. We're not forcing you to take it. But if you take it, then, you could get rid of it. And I was like, I want, I want rid of it." Laura, 23*

> *"No it was kinda mair or less saying that if you want the chance there it is, yeah here it is, tak it if you want it, if you dinnae want it then [it's your own decision] yeh yeh yeh. [...] this is your treatment yeah that's it yeah" Jason, 41*

Jason also felt responsible to champion the HCV treatment and reduce his peers' anxieties:

> *"Oh brilliant. It's great. It's brilliant. It's, It's quite funny now you hear people saying ah ah chatting to them 'now I've got hep C' and I'm like 'dinnae worry about it, C. [nurse] will sort you oot, and the rest will sort you oot, 8 weeks done, 12 weeks it'll be gone, it's brilliant'. Say you gotta tell people ken I suppose to help people after they're all like ahhh pure all that worried about it ken." Jason, 41*

7.4.3 Treatment Adherence

7.4.3.1 Facilitators

Facilitated by the internal locus of control experienced in relation to their treatment, participants perceived treatment as being easy to take, with no issues arising in relation to attending for the dispensing of medication and/or adhering to the daily dosage. The sense of freedom of having a choice was present throughout the treatment:

"You knew that when your 2 weeks were up your last 2 pills were gone so you need mair anyway. So if you wanted to continue the treatment you'd, you'd have to come around to take the pills anyway, so it was easy in that aspect." Gordon, 38

Participants spoke about how easy the treatment was and therefore easy to forget one was on any medication at all. It had no effects on day-to-day life and most reported having strategies and forming habits in order to remember to take the tablets:

"Nothing. Nae side effects. Honestly, nothing, noth. I cannae think of..[...] It was just like not being on anything aye, there were nae side effects that I could remember, whatsoever." Jason, 41

"It's easy, easily forgotten, Ehm sometimes if you's no there. I've got them on my bedside cabinet so when I wake up in the morning I'll take it." David, 33

"Aye, aye cause they were always in my top drawer where my socks were so that's was..every time I opened the drawer I would see them so I would remember to take them. [And] you knew that when your 2 weeks were up your last 2 pills were gone so you need mair anyway. So if you wanted to continue the treatment you'd, you'd have to come around to take the pills anyway, so it was easy in that aspect." Gordon, 38

Vicarious experience also facilitated treatment adherence, as knowing what the treatment was like before starting it, or knowing how bad older treatments (Interferon-based) had been in comparison to the newer treatments (DAAs), allowed participants to create outcome expectancies about treatment:

"So obviously because K's [partner] gone through treatment and cleared it up and that. I done it, I'm doing it as well [...] Plus plus I'm quite optimistic it's going to work for myself. Cause I knew it worked, I knew this is gonna, this

is gonna work for myself. Yeah. So, if it doesn't work then it'll be.. Not happy [laugh]" David, 33

"I got the new treatment eh so, I was only, I was only taking the tablets so, so it was fine to me. Didnae really make any difference to my everyday life. Ken like that eh, that other stuff, interferon aye, nothing aye nothing like that ah!" Gordon, 38

Experienced peers, the nurses and the staff of the IEP service all provided a supportive role and facilitated treatment:

"What helped me? My fiancé, yeah, definitely my fiancé. Pushed me. Which was a good thing. [And] Staff at clinic. Always supportive and welcoming. [inaudible] 'Oh I've not seen you here in a while' I says 'yeah', how you doing and things like that, so it's. [...] always chatting to me, and wanting to know how you are, and things like that, yeah" David, 33

The accessibility and familiarity of the IEP service allowed participants to feel at ease about getting treatment, in an environment they knew, with people they had seen before, whilst also providing a level of anonymity given the variety of services offered under one roof:

"[getting treatment in IEP] Oh, it's made it, made it easier here, a lot easier yeah. Cause I know a lot of people in here" David, 33

"Cause I was here for my drug treatment anyway, so...so it was easy just to pop in, and every time I had an appointment I could pop in and check up, ken what I mean. What the score was with the results or that, so aye." Gordon, 38

"Yeh, straight away, nane, nane of this you right you have to go here and dae this and then dae this and dae this. [...] Eh, when I came in here at least I knew people fae coming in here fae needles and that, at least I had a, at least I

knew your faces at least. Yeah I had a relationship with yous at least. So, so it was a lot easier coming in here eh. I think if I'd have to go to a chemist or somethin' I'd be a bit freaked oot. [would you prefer the chemist now that you are on daily methadone pick-up?] No I'd rather it'd still be here [yeah]. Eh. Cause it's quiet, it's out the wae, naebaedy knows kinda thing, ken what I mean." Jason, 41

7.4.3.2 Barriers

For some participants accessibility could be a barrier to treatment, given the service had defined opening hours (Monday-Friday 9am-5pm). Laura (on daily pick-up) reported HCV making her feel fatigued. This affected her sleep and her ability to pick up her medication daily:

"Just slept in [...] Annoying...cause I don't know all the times that yous close at, like, everyday. I ran down, every day I was running down and then it was like, 'closed', [laughs]" Laura, 23

Forgetting to take the tablets was a problem mentioned by the participants who were dispensed with a fortnightly dose. Having little to no effect on daily life, forgetting to take the medication was irregular but common across the sample:

"It was probably just sitting there and seeing the bottle and night and just go and remember. Cause you forget cause it's that easy you know" Peter, 32

The size of the tablets was commented on by most participants, being referred to as "horse tablets" by Gordon, but it did not affect the participants in a negative way. Near to no side effects were reported by participants, with only one participant reporting a headache that didn't last long enough to put him off getting treated:

"A wee bit of a headache, nausea at first, first eh tablets, yeah, but then that went away, died down. And it just levelled down." David, 33

7.5 Discussion

Qualitative approaches have helped to understand the lived experience of HCV throughout the years as HCV treatment was in the process of being optimised (Dowsett et al. 2017; Treloar et al. 2013a; Whiteley et al. 2017). Studies on the lived experience of HCV in patients on treatment have previously been carried out when the DAA treatments were still novel and patients had little experience of them, presenting a general lack of personal and peer knowledge given interferon-based treatments were still at the forefront of patients' minds (Whiteley et al. 2017). This study provides an updated understanding of illness perceptions and the lived experience of HCV treatment amongst PWID a couple of years after access to DAAs was broadened in Scotland (Healthcare Improvement Scotland and NHS National Services Scotland, 2018; WHO, 2018d) and implemented in Tayside (Hickman et al. 2019; Inglis et al. 2019; Radley et al. 2018).

7.3.1 Change in illness perception and de-stigmatisation

The perception of HCV as an illness presented itself as a fluid concept in this study's findings. The changing perception provided an insight into the journey that participants embarked on from diagnosis to end of treatment. Two polar reactions to diagnosis were observed in the data. The reaction of disbelief and shock is present in literature from all therapeutic eras (Dowsett et al. 2017; Fraser & Treloar, 2013; Whiteley, 2017). Those who were shocked and scared by their diagnosis, tended to present a level of unrealistic optimism about their susceptibility to the virus. Although they were aware of some degree of susceptibility, as suggested by them engaging in regular testing arranged annually, they still held the belief that becoming infected was not going to happen to them. Unrealistic optimism is a common trait observed in the general population and published literature suggests that those with unrealistic optimism tend to undermine their actual risk, worrying less about negative consequences and applying fewer risk reduction strategies, which might actually lead

PWID to an increased susceptibility to infection (Harris & Middleton, 1994; Weinstein, 1982). The opposite reaction, that of indifference, is observed in previously published literature even during the interferon-era of treatment (Rhodes & Treloar, 2008; Roy et al. 2007; Wozniak et al. 2007), and is associated with a perception of susceptibility to the infection based on past behaviour and knowledge about the virus. The perceived susceptibility was also linked to the belief that HCV was ubiquitous in the PWID population, creating the perception of HCV being an unavoidable and accepted consequence of injecting (Rhodes et al. 2004; Rhodes & Treloar, 2008; Roy et al. 2007; Wozniak et al. 2007). The ubiquitous nature of the virus coupled with the absence of any symptoms brought on by the virus, led participants to accept the virus as coexistent, both in their body and in their social network, without affecting their will and motivation to be treated and cured. The data suggests that this internal and external coexistence may have produced a de-stigmatisation of HCV as an illness among PWID. Participants' reports of no experiences of stigma was a novel finding compared to the vast amount of literature that focuses on the terrible lived experiences of stigma among HCV-positive PWID (Fraser & Treloar, 2013; Treloar et al. 2013a; Treloar & Rhodes, 2009; Whiteley et al. 2017). When asked about the experience of any stigma, participants in this study mostly focused on the experiences relating to HCV mentions or conversations with their peers. This would suggest there has been a reduction in stigma about HCV infection among PWID. One of the 5 outcomes established by the Scottish Government (2015a) in their updated framework on sexual health and blood borne viruses (BBV) specified a need for a societal attitude change towards sexual health and BBV to become more positive, non-stigmatising and supportive. The results of this study would seem promising in this respect, yet no firm conclusions on improvements on stigma and attitudes towards HCV can be drawn at a societal level given these were not mentioned by participants, because absent, forgotten or not considered worth mentioning. The de-stigmatising theme presented referred to attitudes and stigma among PWID only. De-stigmatisation among PWID might be the result of more effective treatment with fewer side-effects and of the relative widespread nature of HCV within the PWID population in Scotland with reports of 57% HCV antibody positivity in PWID who attend needle-exchange services (HPS, 2019; Rhodes & Treloar, 2008). Participants did not feel shame associated with

their HCV status, possibly because they believed most of their peers either had or had previously had it, in addition to the fact that they were on treatment and efficiently coping with it (Langston et al. 2017; Langston et al. 2018; Zalai et al. 2015).

7.3.2 Shifting agency

The process of de-stigmatisation encouraged participants to be open about their condition with their peers. The findings on shifting agency presented an internalised conflict of accepting and rejecting responsibility for individual behaviours. Agency is the capability to make free choices and act independently (Barker, 2002). The 'socially responsible injector' presented in Plumridge and Chetwynd (1998) discourse analysis revealed the moral intricacies of lending and borrowing injecting equipment among peers and the concept of shifting agency. A discourse of moral exoneration for lenders, who were altruistically lending because of the need of peers, meant borrowing came with the duty to accept the consequences of one's own decisions; yet borrowing was exonerated from moral culpability too because of the individual's powerlessness in front of the need to consume drugs to annul withdrawal symptoms (Plumridge & Chetwynd, 1998). The interesting aspect of the findings in this study's cohort is that participants introduced the concept of the 'socially responsible injector' as the actor, the lender of the transaction. However, in reality the 'socially responsible injector' came to signify the openness about one's infection status, the lending of equipment and drugs but also the social responsibility about letting the 'borrower' use first, putting the lender at risk of further infection: a sort of 'ultimate socially responsible injector'. The sense of powerlessness described by Plumridge and Chetwynd (1998) was also voiced in this study's findings, with a shift in responsibility and perceived behavioural control. Temptation was too hard to fight and social environment was the primary culprit, shifting away the moral culpability from the self and assigning it to the social environment, with temptation becoming a social production (Gyarmathy et al. 2009; Muñoz et al. 2015; Rhodes et al. 2005; Rhodes & Treloar, 2008, Sherman et al. 2001).

Even though for drug use the sense of agency was rejected through a loss of willpower in front of temptation and locus of control being placed externally, this was not the

case for HCV treatment. This was perceived differently due to the healthcare staff providing it. The nurses providing treatment for participants applied trauma-informed principles to their practice (NHS Education for Scotland, 2017). They built safe, trusting and collaborative relationships with the patients, and allowed them to choose freely whether to get treatment or not, allowing participants to build agency. This helped shift the participants' locus of control from external to internal. In healthcare settings, PWID are often custom to having very little agency, due to substance use services using negative operant conditioning to control behaviours. Opiate Substitution Therapy (OST), for example, is supervised, controlled, restrictive and part of a system that allows the provider to control the individual by the means of punishing strategies (Duff, 2013; Earnshaw et al. 2013; Fraser, 2006). This type of power dynamic between provider and patient offers little chance for patients to increase their agency and internalise the locus of control. The approach that the nurses applied when offering treatment allowed participants to experience a sense of free will and choice, and allowed them to act independently, welcoming a sense of ownership over the desire to be cured and a sense of agency over their treatment (Braun et al. 2018). Involving individuals in their own treatment has been shown to improve outcomes and experience (NHS England, 2014; Vahdat, 2014). This study's findings suggest that National Health Services' recommendations of involving patients in their own care (NHS England, 2014) and utilising a trauma-informed approach (NHS Education for Scotland, 2017) ought to be implemented as they could improve PWID's experience of general and specialist health services.

7.3.3 Treatment barriers and facilitators

On the topic of health service improvement, participants also shared the factors that facilitated or hindered their treatment. Previous research has widely reported on barriers and facilitators of HCV treatment (Dowsett et al. 2017; Mehta et al. 2008; Skolnik et al. 2019; Treloar et al. 2013a), as understanding these factors is indispensable to improving experience of treatment for patients and increasing treatments delivered to the population. The perspectives of people living with, and getting treated for, HCV are key to developing evidence-based clinical and policy

decision and better patient-centred healthcare (Dowsett et al. 2017). The findings of this study indicated a tendency for participants to report facilitators to their treatment more often than barriers, as generally the treatment was perceived as easy and immediately available. They perceived facilitators of treatment to be mostly of social nature. Patient-provider relationship, linked to the previously discussed trauma-informed approach used by the nurses to build safe, trusting and collaborative relationships with the patients, allowed participants to have choice, control and a sense of agency over their treatment. This helped them to be confident in forming personalised habits in order to remember to take tablets daily. They built knowledge of their treatment and experienced virtually no side-effects, generating the belief of an easy treatment, especially in those whose peers experienced HCV treatment using Interferon and socially shared such an experience. This exchange of experiences relating to previous treatment led to vicarious experience becoming an important facilitator. In Bandura's (1977) work on self-efficacy, vicarious experience is one of the most important factors involved in building confidence in one's own ability to perform a behaviour, together with mastery experience, persuasion and affective/physiological feedback. Knowing a peer who had gone through the same treatment and had been cured built the positive belief in the participants that they would also have been able to experience a successful treatment. In addition, the familiarity of the location where the treatment was provided was reported in the findings as a major facilitator, with co-location of services, familiarity of setting and familiarity with staff (admin, healthcare and IEP) playing an important role in facilitating treatment. Co-location of substance use and HCV treatment services has previously been reported in the literature as an important factor in facilitating HCV treatment. It helps patients to avoid stigmatising and discriminatory experiences in unfamiliar healthcare facilities (in particular hospital settings) and patients' familiarity with the environment and the staff reduces potential anxiety and discrimination since trusting and positive relationships are already established (Harris et al. 2013; Treloar et al. 2013b).

Findings on barriers to treatment were scarce in this study and they focused on more logistic factors (compared to the more social nature of facilitating factors). Accessibility of the service, although reported mostly as a facilitator because it was a known

physical and social environment, could also act as a barrier because of its defined opening hours (9am to 5pm), which were perceived by some as restrictive. The ease of the therapy, also a facilitator, could work against patients as they would forget they were on any medication at all and therefore forget to take the tablets. To combat this, all participants had strategically stored tablets in places (contextual cues) that would automatically function as daily reminders (such as bed side tables or sock drawers) in order to facilitate forming a daily habit. Habit formation allows actions to become automatic, with automaticity in turn reducing the cognitive load and the need for motivation or conscious action (Gardner et al. 2012; Lally & Gardner, 2011). All participants in the study achieved an SVR, which would suggest the strategic reminders and habits that they formed facilitated adherence and cure.

The lack, or very mild presence, of side effects and the ease of the DAA therapy influenced participants' change in illness perception throughout the course of treatment. Perceptions and knowledge of Interferon treatment, which heavily influenced illness perception and treatment uptake in previous literature (Skolnik et al. 2019; Whiteley et al. 2016; Whiteley et al. 2017), has remarkably reduced in this population, with knowledge and perception prior to HCV diagnosis and treatment now influenced by social norms of HCV ubiquity and relative ease and availability of treatment.

7.3.4 Future research and limitations of the current study

Further research should focus on whether this perception of HCV and HCV treatment influences HCV reinfection rates, as the illness continues to be considered ubiquitous yet non-threatening. An update on societal attitudes toward HCV in the established DAA era should also be the focus of further research, as stigma and attitudes were only mentioned at peer-level in the current study.

The study presents a number of limitations. The study sample was very small, yet sufficient for the methodology applied. Thematic analysis was chosen because of its relative flexibility allowing for identification of semantic meanings and interpretation of latent meanings and it does not require a large sample size as its aim is to give voice to people's lived experiences. In addition, the 5 participants were considered to be

closely representative of the PWID population accessing treatment and IEP services, as presented in the demographic characteristics result section. Participants were from two Scottish cities in the Tayside region, which has an estimated lower prevalence of HCV compared to the rest of Scotland and in which interferon-free DAA treatment has been available for several years to the PWID population through clinical trials and standard care. The two Scottish cities are relatively small in size (of between 50 thousand and 150 thousand inhabitants). The networks of people who use drugs are therefore geographically and socially restricted, which facilitates communication and shared knowledge among peers, which might have impacted on the shift of HCV perception, given vicarious experience of DAA treatments would have been quite common amongst the sample. In addition, as stated in the methods section, the interviewer was acquainted with all 5 participants as they had taken part in the quantitative component of the trial. This prior established relationship might have influenced answers to questions of experience of treatment, such as all participants reporting more facilitators than barriers to their treatment.

7.3.5 Conclusions

In conclusion, the findings enhance the available understanding and knowledge surrounding the perception of HCV as an illness in PWID and their lived experience of treatment. The rapidly improving treatment effectiveness and availability in Scotland has, for the first time with this study's findings, shown that illness perception and social norms on HCV treatment are changing accordingly among PWID. Behavioural insights into sense of responsibility associated with diagnosis, sense of agency associated with treatment but powerlessness associated with substance temptation and HCV ubiquity will aid therapeutic uptake and retention for people who inject drugs and could enhance harm reduction strategies.

Supplementary File 7.1

Interview schedule for ADAPT sub-study

1) Tell me a bit about what it's like for you to have hepatitis C.
2) What was your experience of hepatitis C diagnosis?
3) What led you to seek treatment?
4) Tell me about the barriers you have encountered to get treatment.
5) What has facilitated getting you onto treatment?
6) What does getting treatment mean to you?
7) What has been your experience of treatment?
8) What was your relationship like with the nurses who gave you treatment?
9) Tell me about the barriers you have encountered whilst on treatment.
10) What has facilitated your adherence to treatment? /taking your tablets?
11) What would it mean for you to be hep C - free?
12) Has there been any change in your injecting sharing behaviour since starting on treatment?

HINTS
Interferon vs DAA if experienced both + reinfection
Illness perception – feeling during diagnosis
Stigma (from self or others)

Chapter Eight: Discussion

This chapter presents an overall discussion of the results presented in the thesis. It aims to integrate the findings of studies 3 and 4 into one final discussion. The concurrent design of these two studies allows the analysis of the convergence, divergence or contradiction of the findings of the two datasets in an overall discussion, presenting the implications of these findings, the limitations of the studies and suggestions for future research. The chapter also aims to provide narrative reflections on lessons learnt from planning and carrying out the study with a population which is traditionally considered to be 'hard-to-reach', people who inject drugs (PWID) (van Baelen et al. 2020).

8.1 Primary study findings: creating implementation intentions with PWID

Models of behaviour change such as the Theory of Planned Behaviour (Ajzen, 1991) highlight the importance of intention to perform a behaviour as a direct predictor of the behaviour itself. However, intentions do not always translate into actions (Prestwich et al. 2006; Sheeran, 2002). Implementation intentions are used to change behaviour by enabling individuals to recognise a high risk situation, committing to an action and automatically and unconsciously implementing their intention when the specified environmental cues are encountered (Aarts et al. 1999; Brandstätter et al. 2001; Prestwich et al. 2006). Cognitive models of addiction, such as that described by Tiffany (1990), propose that drug use is triggered by cues of automatic action. Implementation intentions could therefore be used to redeploy these attentional triggers to automatically activate a counter behaviour (Prestwich et al. 2006). In this study, the behaviour being countered was sharing of injecting equipment. Higher levels of polydrug use, in particular using heroin on top of benzodiazepines and amphetamines, predicts more recent and frequent needle sharing with a greater number of people (Darke & Hall, 1995; Darke et al. 1992; Darke et al. 1995).

8.1.1 Using a volitional help sheet

The volitional help sheet (VHS) was introduced to the participants by the researcher, who explained what the exercise involved and offered the pen to the participant. The researcher explained that detailed on the VHS are some situations in which people can find themselves when they end up sharing equipment. Some situations may be applicable and some may not, and participants could skip those that did not apply. In addition, if they were able to think of a situation in which they shared equipment that was not on the list, they were asked to add it at the end of the situation list. Similarly, the solutions were presented as an assortment of solutions which people might devise to avoid sharing of injecting equipment. Some solutions might not be applicable personally and, if so, they were not to use them. If they could think of any of their own personal solutions which were not on the list, they should add them to the end of the solution list. The researcher read the solution list to give participants an idea of what was listed and then the situations were presented one by one. No participants added any situations or solutions to the lists. A number of the stated situations and solutions did not apply to all participants.

The VHS was used as an intervention tool rather than a data collection device, so every participant that completed the VHS was offered the opportunity to take it away with them. A handful of participants did so, but most of them just asked for the VHS to be kept in their case report form.

On two occasions the participant did not wish to carry out the intervention. One did not understand the exercise and felt overwhelmed. Limited engagement is sometimes associated with fear of disclosure of low literacy (Easton et al. 2013) and literacy cannot be assumed with patients from any background and patients are often reluctant to disclose any difficulties. Therefore, the researcher offered to go through the VHS with the participant and complete it together. The participant agreed to continue but the links between the situations and the solutions were drawn by the researcher. The other participant simply refuted they would ever be in a position in which they would need to share equipment and stated the exercise did not apply to them. Interestingly, this participant was the only one to become reinfected with

hepatitis C (HCV) (with a different genotype) out of the whole sample during the full follow-up period, up until the database was locked (28th April 2020).

Several participants found one solution fitted most situations: “Then I will do something else instead of injecting”. Being flexible and using alternatives to injecting when consuming drugs is regarded as a protective harm reduction strategy. When injecting can only occur via sharing of paraphernalia, temporary smoking or snorting of heroin can help to avoid blood-borne virus (BBV) infections (McGowan et al. 2013).

A few participants also found that some situations did not apply to them, as in they would not feel the need to share equipment if they were in that situation. Yet a lot of them described one situational example of a time in which they were most likely to share: “If I am tempted to share equipment when I am under the influence of other drugs”.

8.1.2 Effects of the intervention on self-efficacy to refuse injecting sharing and on sharing behaviour

In chapter 2 the use of implementation intentions on use of substances and self-efficacy showed statistically significant small-to-medium effects of the intervention on alcohol use and cigarette smoking and a small effect on self-efficacy that did not reach significance. The significance of effect sizes provides information about how precise the sample-based estimates are (Ellis, 2010). These results were helpful to estimate the ADAPT sample size, but did not eliminate the risk of Type I error. There were no published studies on the use of implementation intentions with people who inject drugs on sharing behaviour so there was still a risk of finding a false positive effect of the intervention. When it came to analysing the results, however, the main issue faced was the lack of statistical power as a consequence of the small sample size and its associated risk of finding a false negative effect of the intervention (Type II error). Carrying out multiple univariate analyses, which is associated with an increase in Type I error, was therefore not considered a problem, as the risk of a false negative effect was still more substantial than that of a false positive one. The results confirmed these suspicions, as for both self-efficacy and sharing behaviour the null hypotheses of no difference between control and intervention groups were retained.

The results of the self-efficacy outcome highlighted the importance of the group sizes. Self-efficacy was not significantly different in the two groups at follow-up, but it did show a substantial effect size. When analysing this further for time differences in the two groups, it was clear the intervention group showed no change in self-efficacy over time, whilst the control group showed a small-to-medium decrease in self-efficacy scores between baseline and follow-up. Therefore, although implementation intentions did not increase self-reported levels of self-efficacy, it is unclear whether the intervention helped maintain participants' level of self-efficacy to refuse sharing throughout a 4-week period. A complete sample size in this trial would have allowed the analysis of this hypothesis.

Other behavioural interventions have reported positive results on self-efficacy and PWID (Pawa & Areesantichai, 2016; Robles et al. 2004), yet the current study would suggest that the behavioural intervention functioned as risk limitation rather than as active instrument producing positive change.

The results for sharing behaviour showed a negligible effect size, regardless of the small sample. When delving deeper, the control group was approaching a significant large reduction in sharing, whilst the intervention group showed a non-significant small-to-medium increase. A full sample and its retention in the study would have help to better understand the differences in sharing behaviour between groups and time. Previous literature does not present the use of implementation intentions to reduce sharing of injecting equipment so no comparison can be drawn; however, literature would suggest that participants that receive HCV treatment without the addition of a behavioural intervention, show changes in injecting behaviour, supporting the reported effect size in the current study (Chapter 3; Alavi et al. 2015; Artenie et al. 2017; Artenie et al. 2020; Midgard et al. 2017). Although most literature produced evidence of a change in injecting behaviour during the interferon-era of HCV treatment without the use of a purposely designed behavioural intervention (Chapter 3; Alavi et al. 2015; Artenie et al. 2017; Midgard et al. 2017), one study reported small reductions in injecting and sharing behaviour during DAA treatment (Artenie et al. 2020).

These findings stand in contrast to the results reported in the meta-analysis in chapter 2, which suggested a medium effect of implementation intentions on substance use

behaviour and a small and non-significant effect on self-efficacy in non-clinical populations (i.e. general population and students). Additionally, at baseline self-efficacy and injecting risk were highly negatively correlated (an inversely proportional relationship), the higher the self-efficacy, the lower the self-reported sharing frequency. The results of the univariate analyses would suggest the strength of this correlation not to be sustained at follow-up, with the control group showing a reduction in self-efficacy but also a reduction in sharing behaviour, whilst the intervention group showed a very slight increase in sharing whilst maintaining a constant self-efficacy level. These results were confirmed by testing the relationship between self-efficacy and injecting risk at Time 2 (follow-up).

The results of the quantitative study would benefit from clarification via a larger study, to more confidently report the intervention effects. However, the results that were found were convergent to those of the qualitative study for the injecting risk outcome. No difference was observed in the quantitative study between baseline and follow-up and participants in the qualitative study reported their injecting behaviour not to have changed during treatment. There was no or weak evidence for injecting frequency and sharing of injecting equipment changing over time during HCV treatment, both in the presence or absence of creating implementation intentions.

Self-efficacy, however, was not described as such by participants in the qualitative study. What the study did find was that participants spoke about a sense of powerlessness in front of temptation, especially when under the influence of other drugs. This qualitative theme converged with the quantitative study when participants anecdotally recognised their highest-risk situation for sharing in the volitional help sheet as that of being under the influence of other substances. But the theme also completely contradicts the participants' self-efficacy scores. A sense of powerlessness can be conceptualised as a complete lack of the belief in one's own capability to perform a behaviour or control internal states (Lim et al. 2018; Wallston et al. 1987) and can present a link to low self-efficacy. These contradicting results are explored in the proceeding section.

8.1.3 Temptation, powerlessness and impulsivity

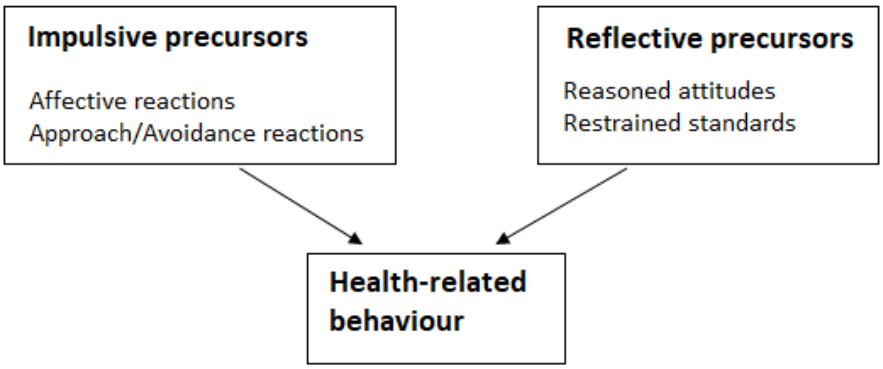
The common recognition of participants for being under the influence of other substances as the highest risk situation for sharing injecting equipment could help explain the main study findings. Albeit reporting low levels of sharing behaviour and high levels of self-efficacy to refuse sharing, being under the influence of other substances could be moderating the strong negative correlation between self-efficacy and sharing behaviour. As seen previously, polydrug use predicts needle sharing with a greater number of people (Darke & Hall, 1995; Darke et al. 1992; Darke et al. 1995). Previous research also shows that PWID are aware of the health risks of sharing equipment, yet sharing continues to occur irregularly for the majority of people (Gaskin et al. 2000; Gossop et al. 1997). This might suggest that sharing of injecting equipment could be characterised as sporadic, impulsive and non-rationalised. The reported sense of powerlessness of participants in front of temptation supports this view of the behaviour. A high self-efficacy to refuse, instead, requires conscious and non-impulsive processing of situational information coupled with conscious volition (Hofman et al. 2008).

Many health promotion campaigns and harm reduction messages seem to portray people who inject drugs as rational and health-conscious beings who are autonomously responsible for their risk-taking actions (Fraser, 2004; Miller, 2005; Rhodes & Treloar, 2008). These assumptions of reflective processing capabilities are a common element of many models of behaviour change. They tend to assume cognitive appraisals and cost-benefit analyses to be associated with volitional control and willpower over reasoned goal-directed behavioural decisions (Hofman et al. 2008). Yet the results discussed so far paint the picture of a behaviour (sharing of injecting equipment to consume illicit drugs) which is unplanned, impulsive, subject to the individual's cognitive capacity in the moment, physical capacity if/when in opiate withdrawal, coupled with a sense of powerlessness in front of temptation and the complete loss of willpower due to an absolute need to consume substances.

Dual-system models, such as the framework presented in Figure 8.1, attempt to integrate the orbitofrontal reflective predictors of behaviour (those reasoned goal-directed behavioural decisions) with the amygdala-dependent impulsive influences

(Bechara et al. 2006; Strack & Deutsch, 2004). They assume there are two different systems which process information and produce either impulsive or reflective forms of behaviour (Bechara et al. 2006; Hofman et al. 2008; Strack & Deutsch, 2004).

Figure 8.1 Dual-system framework of behaviour change prediction



Source: Hoffman et al. 2008

Chronic drug use reduces neural processing of the frontal regions of the brain, involved in executive functioning, decision making and appraisal of future consequences (Jentsch & Taylor, 1999). The dysfunction in the frontal lobes is also associated with an increase in impulsivity. Impulsivity, however, has also been identified as a pre-existing vulnerability marker for substance use disorders (Verdejo-García et al. 2008), confirming a correlation between impulsivity and drug use but rendering unclear the direction of the relationship and making it difficult to infer causality. Nevertheless, published literature has shown moderating effects of impulsivity on implementation intentions effectiveness (Churchill & Jessop, 2010; Hofman et al. 2008). Evidence shows that implementation intentions can be effective in patients with frontal lobe dysfunction (Lengfelder & Gollwitzer, 2000) and in patients in opiate withdrawals (Brandstätter et al. 2001) when they are creating intentions to perform everyday activities. This evidence presented a good rationale for the present study, to test implementation intentions in a drug-using population.

Implementation intentions were specifically used in the current study because of their automatic activation of goal-directed responses as a result of unconscious

environmental cues (Gollwitzer & Sheeran, 2006; Hofman et al. 2008; Webb & Sheeran, 2007). If sharing of injecting equipment is also considered an impulsive, non-reflective behavioural process, then it might be the case that implementation intentions are 'fighting' for a space in the 'Impulsive Precursors' system with the well-established automatic impulsive reactions associated with illicit drug attentional cues. Although implementation intentions are automatically triggered by environmental cues, those same environmental cues are also triggering an effortless associative cluster for drug consumption, which has a positive 'hedonic' value associated to it (the hedonic value will be discussed in the subsequent paragraphs).

Furthermore, in chapter 2, implementation intentions were defined as self-regulatory processes which take the form of 'if-then' plans and facilitate the attainment of goals and behaviour change (Gollwitzer, 1993). The automatic and unconscious nature of implementation intentions might be reduced by the self-regulatory nature of the plans themselves. Evidence shows that effective self-regulation requires willpower and control over thoughts emotions impulses and behaviour (Baumeister et al. 1994), yet conflicting goals such as a desire to abstain from injecting risk behaviour coupled with a physical need to use an illicit substance to reduce withdrawals symptoms, result in self-regulatory failures (Prestwich et al. 2006). Self-regulation is a limited resource. When self-regulatory failures occur, there is an ego-depletion and an increase in the vulnerability of an individual to act impulsively (Baumeister et al. 1994; Prestwich et al. 2006). Additionally, further factors such as cognitive load, emotional distress and substance intoxication, all commonly observed among people who inject drugs, have been associated with self-regulatory disruption (Hoffman et al. 2008).

An observation not currently stated in theories and evidence is that drug-taking is, in itself, a form of self-regulation. Deficits in the ability to self-regulate emotions, thought and behaviour have been shown to be associated with the initiation and escalation of illicit drug use (Kober, 2014; Wong et al. 2013). Drug taking can be perceived as a positive hedonic associative cluster (Hofman et al. 2008). However, the body's tolerance to substances, emotional dysregulation and the nature of addiction itself, can transform chronic drug taking from a pleasure-seeking activity to a pain-avoidant one (Kober, 2014; National Institute on Drug Abuse, 2020). This is highlighted

by the incentive-sensitisation theory, which posits the existence of two different brain circuits associated with 'wanting' and 'liking' (Berridge & Robinson, 2016). People's first experiences of drug taking could be argued as being hedonistic, with the reward (drug) being both wanted and liked (although difficulties with emotional regulation skills could also suggest that the first instances of drug taking are a form of self-regulatory strategy in itself). Long-term drug-taking quickly transforms into a need to self-regulate and return to the status quo. Incentive salience ('wanting') is a form of motivation generated by robust neural systems which include mesolimbic dopamine. The actual pleasurable reward consumption ('liking') is controlled by smaller and more fragile neural systems which are not dependent on dopamine (Berridge & Robinson, 2016). According to incentive-sensitisation theory, drug addiction is a result of the amplification of incentive salience as a result of triggering cues which do not amplify the 'liking' system. This amplification is, in turn, a result of neural sensitisation of dopamine-related motivation systems (Berridge & Robinson, 2016).

These motivational processes produce hypersensitivity to substance-related cues, i.e. attentional bias, which both implicitly and explicitly influence an individual's decision-making process (Cox et al. 2006; Field et al. 2006; Robinson & Berridge, 2003). The environmental stimuli which arouse incentive salience, are the same which implementation intentions try to engage to automatise a self-regulatory response which is in direct opposition to the dominant tendency of the consumption of a substance (Palfai, 2006; Rachlin, 2000). Self-regulatory abilities can be increased, and automaticity of selected self-regulatory processes can be enhanced, through practice and planning (Fitzsimons & Bargh, 2004; Palfai, 2006). Practice and planning require effortful, conscious decision-making to support the repeated use of skills (such as the VHS 'solutions'). However, creating plans such as those when forming implementation intentions, allows individuals to mentally simulate practice and enables the automatic execution of goal-directed behaviours (Gollwitzer, 1999; Palfai, 2006; Prestwich et al. 2006). The findings of the current study did not provide evidence for the successful use of implementation intentions to reduce sharing of injecting equipment and to increase self-efficacy for refusing sharing of injecting equipment. A one-off session creating implementation intentions in this study was not enough to provide the necessary

repeated practice to replace the dominant automatised 'solution' (sharing and drug consumption) with the desired non-sharing 'solutions'.

8.2 Other study findings

8.2.1 Group identification

Identification with a drug network was explored in Chapter 5 as a strong predictor of sharing behaviour. Chapter 6 showed that no change in group identification was found in the trial groups at follow-up. Levels of sharing also remained similar suggesting the trend of the correlation was stable over time. Evidence shows that social networks can have negative influences on injecting risk taking (De et al. 2007; Dunn et al. 2010; Shaw et al. 2007). The qualitative results slightly diverged from those of the quantitative as group identification with drug network did not feature heavily. When discussing the sense of powerlessness in drug use the influence of social networks was clear, though there was no explicit mention of identification with a group of peers using drugs. The sense of communal experience was present in the participants' descriptions of why they would share equipment or give into temptation to use drugs, but there did not seem to be an overt psychological connection with peers.

Social Identity Theory suggests that an individual's sense of self is the product of the membership to various social groups (Tajfel & Turner, 1979). This produces social identities which influence people's behaviours, perceptions, values, norms, goals and relationships (Haslam, 2014; Tajfel & Turner, 1979). Typically a social identity approach would propose group identification as a social cure (Jetten et al. 2017). This was evidenced in previous literature on injecting drug users and the general population (Chapter 3; Kumar et al. 2016; Neaigus et al. 1996; Rance et al. 2017; Sani et al. 2015a). It is also evidenced by the importance of social groups and social connectedness for substance recovery, particularly in social groups that do not support substance use and are able to support a social identity change (Best et al. 2010, Zwiayk et al. 2009).

However, the results of the present quantitative study, in which group identification with drug network became a social curse, contradict those of the social identity approach that suggest group identity as a social cure (Jetten et al. 2017). Strong

identification with a group which is considered socially deviant, such an injecting drug users, has been evidenced to increase general social exclusion and stigma coupled with reduced self-esteem, health and wellbeing (Best et al. 2016; Savolainen et al. 2018; Schofield et al. 2001; Sussman et al. 2000). By identifying more strongly with a group, members internalise group norms (Best et al. 2016) and the group norms of drug networks might be a negative influence. However, the social norms regarding sharing of injecting equipment reported by participants (Chapter 6) were mostly critical of sharing of injecting equipment and were not correlated with identification with drug network, with no differences found by group or in time.

The findings on group identification in the quantitative study and peer facilitation of drug use in the qualitative study suggest a potential negative impact of a social identity on health behaviour. These findings coupled with the evidence discussed above, present the picture of social groups and identification as a bipolar force which can influence individuals both positively and negatively. This suggests integration of health and social psychological intervention should be explored to facilitate social identity change and improve health behaviours associated to sharing of injecting paraphernalia.

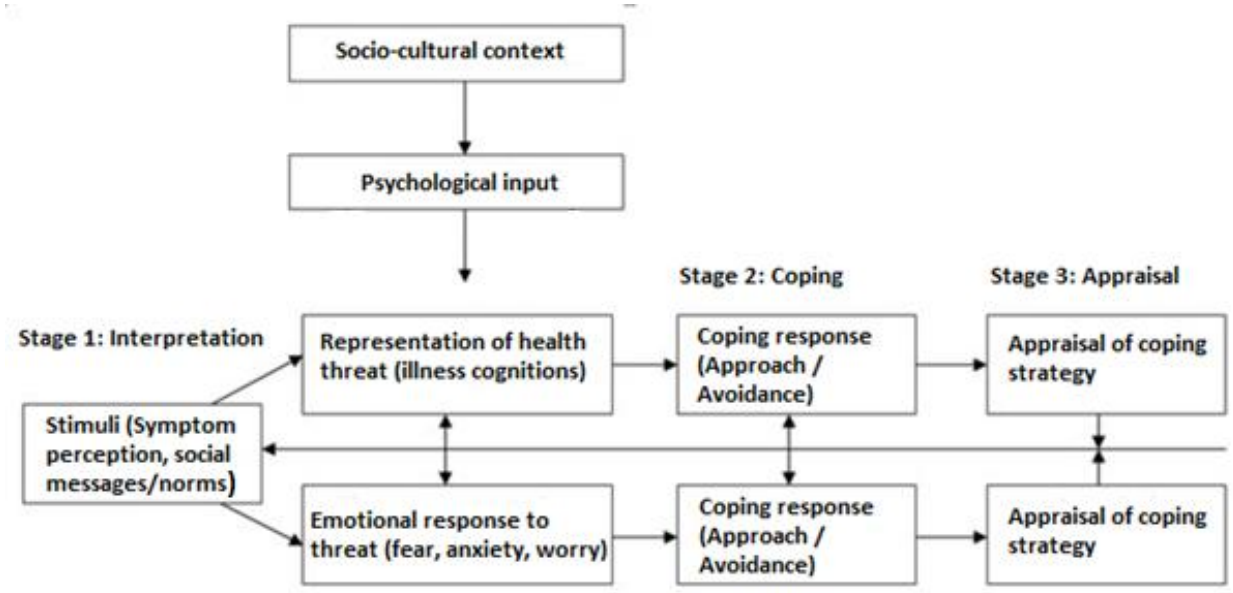
8.2.2 Changing illness perception

Perception of HCV as an illness was explored in both the quantitative and qualitative studies; the perception of the illness presented as a fluid and changeable concept in both the quantitative and qualitative studies, suggesting a degree of convergence of results. At Time 1, participants overall did not hold threatening perceptions of HCV. Some aspects of illness perception, such as concern and emotional impact, scored as mildly threatening. The wide standard deviation of the illness perception score was obvious in the qualitative study which showed two polar reactions to diagnosis and perception of illness threat at baseline. Similar reactions have been observed and evidenced in published literature. Some patients displayed disbelief and shock to their diagnosis (Dowsett et al. 2017; Fraser & Treloar, 2013a; Whiteley, 2017); whilst other patients were aware of their susceptibility and displayed indifference and a degree of

expectation to an eventual and inevitable diagnosis (Rhodes & Treloar, 2008; Roy et al. 2007; Wozniak et al. 2007).

In both the quantitative and qualitative studies, however, no matter the degree of threat participants had assigned to HCV at baseline, at follow-up they reported a decrease in perceived threat of the illness. These results were confirmed in Chapter 6 with significant differences found in illness perception scores between Time 1 and Time 2 irrespective of the trial group. This decrease in illness perception suggests HCV becomes less threatening after undergoing treatment. As explored in Chapter 6, the common sense model (CSM) of self-regulation of health and illness (Figure 8.2) was useful to understand this change in HCV perception (Leventhal et al. 1980; Leventhal et al. 1984; Samo et al. 2015).

Figure 8.2 Leventhal's Common sense model of self-regulation



Adapted from Ogden 2012

When asked about HCV symptoms, participants generally reported very few if any. Some would report not knowing they were ill; others reported feeling tired or 'having a feeling' something was wrong. For those who were shocked at their diagnosis and worried about the infection, basic knowledge of the virus was slightly lacking; they

knew the causes of the infection, but could not relate that to their own behaviour. They also presented a degree of unrealistic optimism (Harris & Middleton, 1994; Weinstein, 1982), believing they were taking good precautions against infections. In other participants, the ubiquitous nature of the virus, coupled with the absence of any symptoms, led participants to be acceptant and indifferent towards the virus, with an acknowledgement of the perceived susceptibility and causes of the virus (Rhodes et al. 2004; Rhodes & Treloar, 2008; Roy et al. 2007; Wozniak et al. 2007).

All participants had started on HCV treatment by the time they were enrolled onto the study, so they were aware of DAA treatments, of the successful cure rate of the treatment, the timeline of the illness/treatment and any consequences of the virus if left untreated, as all this information had been provided to them by the nurses before commencing on treatment.

The second stage of the CSM model comprises the self-regulatory coping strategies that drive the individual to seek a return to their status quo, their un-infected self. In the present studies, this stage was uniformly an approach coping strategy, with all participants seeking and engaging with HCV treatment (Leventhal et al. 1980; Leventhal et al. 1984; Samo et al. 2015).

The final stage involves the appraisal of the selected coping strategy. This is the time at which participants were interviewed for the qualitative study and when they completed the follow-up illness perception score for the quantitative study. The significant reduction in illness threat suggest that participants' appraisal of treatment (their selected coping strategy) was positive and effective. The un-infected status quo had been achieved and the illness representation had been modified according to their successful experience of treatment (Leventhal et al. 1984; Ogden, 2012)

8.2.3 Trauma and trauma-informed care

Interesting divergent results of the two studies, quantitative and qualitative, regarded trauma, a topic that developed from different viewpoints but that ultimately converged towards mutual implications for practice. A plethora of evidence associates traumatic experiences with substance use disorders, and specifically traumatic

experiences and injecting drug use (Dube et al. 2003; Felitti, 2003; Huang et al. 2011; Kerr et al. 2009; Khoury et al. 2010; Ompad et al. 2005; Pearce et al. 2008; Quinn et al. 2016; Roy et al. 2003). Felitti's (2003) study on Adverse Childhood Experiences (abuse, neglect, household dysfunction) pinpointed the origins of addiction in traumatic experiences in childhood.

Experience of trauma is common. Scottish evidence indicates that up to 20% of children experience sexual abuse, one in six 11-17 year-olds experience severe maltreatment and 20% of women experience domestic abuse (NHS Education for Scotland, 2017). For some populations experience of trauma is even higher. The World Health Organization estimates that 75% of people who attend substance use services have experience of trauma (Krug et al. 2002), with other evidence suggesting up to 80% of people who inject heroin have experienced childhood trauma (Wang et al. 2010). The findings of the present study found 76% of the sample self-reported symptoms of posttraumatic stress disorder at baseline, in line with the available evidence on prevalence in this population.

NHS Education for Scotland (2017) launched a training framework to transform psychological trauma and up-skill the Scottish Workforce enabling everyone, at different skill levels, to understand and respond to the needs of people affected by trauma. All healthcare should be provided in a trauma-informed way. However, healthcare services, including substance use services, tend to assume controlling, supervised and restrictive strategies, including negative operant conditioning to control behaviours, when caring for PWID (Duff, 2013; Earnshaw et al. 2013; Fraser, 2006). When considering that between 75 and 80% of PWID have experienced trauma, this type of power dynamic between provider and patient offers little chance for patients to increase their agency and internalise the locus of control, in addition to increasing the possibility of developing damaging patient-practitioner relationships (NHS Education for Scotland, 2017).

The qualitative study findings showed that the approach that the viral hepatitis nurses applied when offering treatment to study participants respected the trauma-informed values of working with patients affected by trauma. It allowed participants to experience a sense of free will and choice, allowing them to act independently,

welcoming a sense of ownership over the desire to be cured and a sense of agency over their treatment (Chapter 7; Braun et al. 2018). There is evidence that actively involving individuals in treatment can improve outcomes and experience of treatment (NHS England, 2014; Vahdat, 2014).

Unfortunately, no outcome measures regarding trauma-informed working were collected in the quantitative study, so these observations and findings are drawn from the qualitative interviews. These are outcomes that should be researched further to enable the understanding of, and facilitate the implementation of, trauma-informed work at a systems level to improve the experience of PWID engaging with general and specialist health services.

8.3 Recruitment

Failure to recruit to target is the top reported inefficiency in UK registered trials (Duley et al. 2018). Reviews of funded RCTs show only 55% of studies recruit to their required sample size, with 44% failing to meet target and 22% achieving less than 80% of their target sample size (Duley et al. 2018; Sully et al. 2013). The current study managed to recruit 74.6% of the required sample, although only 47.8% of the target sample completed the randomisation tasks. This led to significant restrictions on the strength and generalisability of the analyses.

8.3.1 Settings

Recruitment took place in two injecting equipment provision (IEP) services (Dundee and Perth). Participants were receiving their HCV treatment at these IEPs. The accessibility and familiarity of these locations facilitated treatment: participants' familiarity with the environment and the staff reduced potential anxiety and discrimination (Harris et al. 2013; Treloar et al. 2013b). It allowed participants to avoid unfamiliar healthcare settings which can be perceived as stigmatising and can be associated to discriminatory experiences (Harris et al. 2013; Treloar et al. 2013b).

The co-location of the treatment clinics and the IEP service allowed participants to collect injecting paraphernalia whilst visiting the service for their HCV treatment. This

was highly encouraged given the target population for the treatment was active drug users and the nurses were keen to adopt a holistic approach to the care they offered. It is possible, however, that this might have played a part in the low uptake and retention of this study. Visits for the ADAPT study were between 20 and 30 minutes, sometimes longer when participants were very talkative. By asking them to participate and give up their time, the researcher was also delaying their drug taking. Delaying gratification can have a substantial impact on substance users' physical and cognitive wellbeing. The best example that can be provided in the study is that of participant 32. This participant was being seen for their third visit. Half way through the visit they asked to stop the visit as they were in withdrawal and physically unable to stay in the room any longer. The study visit had stopped them from leaving the IEP service straight after being dispensed his HCV treatment to inject heroin. The protein drinks offered at the end of each visits were obviously not beneficial enough for him to stay an extra 5 or 10 minutes to finish the visit. Incentives such as the protein drinks and monetary reward will rarely triumph over immediate heroin gratification.

Previous research has found that heroin users delay discounting rates are twice those of non-addicted controls, with discounting rates positively correlated with impulsivity traits (Kirby e al. 1999). Delay discounting refers to the choice an individual makes to receive a reward of reduced value in the present compared to a higher value reward in the future (Kirby et al. 1999). As rewards become more remote, their present value decreases. For some participants, the present value of the protein drinks they would receive after 20/30 minutes of research visit was negligible, or in fact negative, when considering physical and cognitive gratification from illicit substance use had to be delayed. In addition, the participants were receiving protein drinks from the nurses for their HCV treatment too, so part of the reward had already been obtained.

8.3.2 Issues and obstacles

The first obstacle was identified in the characteristics of the physical environment. The main IEP service in Dundee where recruitment took place, the Cairn Centre, is an integrated service for harm reduction and BBV care. A third sector agency (Gowrie Care) manages the site and provides the IEP service. NHS nurses tend to the physical

harm reduction needs of patients, such as caring for injecting-related injuries, and use clinic rooms to test patients for BBVs and treat HCV infections. The service is placed within a ground floor space, with 5 sitting spaces and 2 clinical rooms. The clinical rooms need to be available for clinical purposes, and the 5 sitting spaces in the office are used by 3 Gowrie Care staff and 2 or 3 nurses every day. This meant there was no space for the researcher to stay in the needle-exchange, to be visible and easily approachable when potential participants came in. Within the same building there was a large office on the second floor with NHS node points. This office was vacant so the researcher used this space daily to be physically present in the building. Yet given the physical separation (2 floors, locked doors, flights of stairs) of these offices, researcher visibility was poor, and nurses had to proactively ask patients if they were interested in participating and contact the researcher to join them on the ground floor.

Another obstacle was identified in the recruitment process. Active HCV infection was an inclusion criterion for the study. The sponsor of the study did not allow the researcher to approach the potential participants herself because of medical confidentiality, but required the nurses providing the HCV treatment to ask patients for their consent to speak to the researcher about the ADAPT study. If they agreed, the researcher would see them immediately after their HCV treatment visit to explain the study and ask if they wanted to participate. This required nurses to remember to ask patients if they wanted to speak to the researcher. At the start of the trial this was identified as a substantial obstacle to successfully recruiting participants.

In order to facilitate patients' attendance for HCV medication dispensing, the nurses did not assign appointment timeslots for patients but just asked them to come in during opening hours on specific days. This allowed participants to attend when it most suited them, empowering them and allowing them to take control of their own treatment. It also meant that, at times, a participant was missed because the researcher was seeing another participant or was away at a meeting or training. Nurses would employ strategies to remind participants to attend for their treatment. They would verbalise the reminder at each patient visit; they would write on the medication packaging the date the patient was expected to return for further dispensing; they would phone the patients directly if they had failed to showed up on

the assigned day by lunchtime; and lastly, if patients were on a prescription for opiate substitution therapy (OST) at a pharmacy, they would phone that pharmacy to ask if the patient had already collected their OST and, where they hadn't, would ask the pharmacist to remind clients to attend the IEP service.

Issues arose when recruitment opened in the second site (Drumhar, Perth – over 20 miles from Dundee). As an individual researcher was running the trial, she could not be in both the recruitment sites at the same time. The researcher discussed with the nurses which day was the busiest in the Perth clinic for HCV patients and they agreed she would attend the second site every Thursday. In order not to miss participants from the main site in Dundee on Thursdays, she ran through the trial materials with two of the nurses and asked them if they felt comfortable being on the trial's delegation log. This allowed the trial visits to be completed by the 2 nurses. Over the course of the trial, a total of two end of treatment visits (visit 3) and one final visit (visit 4) were completed by the nurses.

8.3.3 Strategies to increase recruitment and retention

The Health Behaviour Change Competency framework developed by Dixon and Johnston (2010) describes a route MAP that does not utilise behaviour change models but assembles the 93 behaviour change techniques from Michie's (2013) Taxonomy into three main routes to behaviour change: Motivation development, Actions & control, and Prompts & cues (MAP). Albeit this framework and route map are mostly NHS Education for Scotland to upskill healthcare staff in health behaviour change, the researcher found it useful in order to develop strategies to change the behaviour of nurses to increase recruitment and retention in the ADAPT trial.

Nurses were very motivated to recruit participants in the HCV treatment trial, mostly driven by motivation to treat and cure patients. Due to their passion for patient welfare, it was apparent that they were also motivated to help the researcher recruit to the ADAPT trial in order to reduce instances of sharing of injecting equipment, but also from intrinsic curiosity around the psychosocial factors measured in the trial. The researcher and the nurses discussed the best plan (Action) to enable recruitment to ADAPT. When patients attended, the nurses would explain briefly that there was a

study conducted by a psychology student to aid behaviour change. If they agreed to see the researcher, the nurses would reach her by phone (mobile number) and she would see patients immediately.

So the Motivation and Action components of the behaviour change framework were present. What the researcher identified as missing were prompts and cues. Prompts rely on the automatic and associative cognitive system to change behaviour, which was identified as the target component to facilitate the desired behaviour. Prompts were introduced in the physical and social environment at different stages.

Initially the researcher added a post-it with her name and phone number above the telephone by the PCs used by the nurses in the office and clinical rooms. Potential participants were still being missed, so the researcher added another prompt by using the nursing team's diary. Nurses on shift would check the diary first thing in the morning so the researcher added her name next to the patients that were booked in.

By keeping on top of patient's treatment schedule for participants that had been consented onto ADAPT, the researcher would then socially prompt the nurses by going to speak to them during the working day about the specific participants she wanted to see.

One of the nurses (the one working most with these patients) then decided to create their own physical environmental cue by adding a blank matrix to the medicine cabinet from which patient were dispensed their HCV medication, in order that the researcher could add the patients ADVANCE participation number (the medicinal trial) for the patients she needed to see that week. The researcher would update this daily in case someone had not shown up on their scheduled day. This prompting worked for a while, but then the nurses got too used to seeing the prompts on the cabinet and stopped paying attention to the numbers written on them.

Consequently, the researcher decided to use social prompts as the next strategy to increase recruitment and retention. She would stay in the needle-exchange every morning until the nurses arrived to work to socialise and to request to the nurse on shift to see selected participants. During the working day the researcher would also return to the needle-exchange as an additional cue and to specifically enquire whether

any of the patients had attended. The nurses often reported that patients would attend but refuse to see the researcher because of time constraints.

The last strategy applied was the most successful one. A further environmental cue was added to the individual patients' dispensing logs. The researcher would add a post-it inside the patients' file at the start of each week for any consented participants she needed to see. As the nurses opened the file and recorded the dispensing, they were prompted to phone the researcher whilst the patient had just been dispensed (fortnightly doses) or was still consuming their daily dose (daily dispensed).

The optimal option for recruitment would have been for the researcher to be physically present in the needle-exchange area the whole time. As this was not possible given space restrictions, the described trial and error of prompts resulted in the selection of the best available cues to enhance recruitment and retention.

8.3.3.1 Contingency management

As discussed previously, participants were offered protein drinks at the end of each visit. Among the HCV-positive injecting population, these protein drinks have gained value over the years as they were provided in concomitance to HCV treatment. During the Interferon-era of treatment, the protein drinks served a physiological purpose. As the DAA-era of treatment started, the protein drinks became a form of contingency management.

Contingency management refers to providing patients with rewards such as vouchers, privileges or modest financial incentives to increase health promoting behaviours (Department of Health and Social Care, 2017; National Institute for Health and Care Excellence - NICE, 2007b). It is one of the few psychosocial interventions actively recommended within NICE guidelines because of the strong evidence supporting it.

Anecdotally, the protein drinks were not solely used for the purpose of consumption. They were also sold on the street. This, indirectly, drastically increased their value as a form of contingency management. However, the protein drinks were provided with the patients' HCV treatment so, in turn, the value of the reward for the ADAPT study reduced. The ADAPT visits were longer and participants were already in possession of protein drinks after being dispensed HCV treatment. Some participants felt that there

was no need to stay longer to get another few protein drinks, whilst other still appreciated the extra bottles.

The small cash reward provided in the qualitative sub-study was substantially more attractive. Participants were keen to take part in the interview, even though they were told it would take around 30 minutes. In this case, the value of the reward, albeit not in the present moment but in the immediate future, was considered worth the effort and wait. This delayed (monetary) gratification might have been considered beneficial because of a possible anticipated future gratification (in the form of drug use).

Ethical considerations were given in regards to the provision of monetary incentives. Some research suggests that compensation to PWID should be provided in vouchers or food (Ritter et al. 2003). This is because monetary incentives are believed to attract PWID for the economical gain rather than the willingness or interest in participating in research, impairing voluntary consent (Ritter et al. 2003). There are also preconceptions about the way PWID will use the monetary incentives, i.e. to buy illicit drugs, placing researchers and ethics committees in a moral conundrum (Murdoch & Caulfield, 2016). However, research has shown that, although there is a lack of these preconceptions for the general population, 30% of participants in RCTs from the general population state money as the main motivator for participating and that less than 5% of participants thought of money as a coercive incentive (Byrne et al. 2012; Murdoch & Caulfield, 2016). Therefore, avoiding monetary incentives only in research with PWID reinforces negative stereotypes and stigma towards this population, preconceiving participants as untrustworthy (Murdoch & Caulfield, 2016).

8.3.3.2 Lost to follow-up

Attrition rates in RCTs are common, with mean attrition falling between 21.1% and 66% (Cooper et al. 2018; Gindi et al. 2009; Gratton et al. 2007; Horyniak et al. 2013; Manstead & Semin, 1999; Rigotti et al. 1997; Samo et al. 2016). The current study showed an even higher overall attrition rate of 84%.

As explored in Chapter 6, there were different reasons why people were lost to follow-up (LTFU). The cost-benefit analysis of time employed to complete a visit and the protein drinks incentive was undoubtedly one of the reasons why participants were LTFU. The researcher believes this cost-benefit analysis was one of the explanations for

some of the twenty-two participants that were lost to follow-up for unknown reason (LTFU= 44%). Nine people were withdrawn from their HCV treatment (18%) because they did not attend their dispensing appointment for up to 7 days after their assigned date (Inglis et al. 2019). HCV is capable of developing viral resistance to treatment (Sagnelli et al. 2018) so this mechanism was put in place to reduce emergence of DAA resistance among HCV-positive participants. Eight people went to prison (16%). Their HCV treatment was continued via the prison healthcare facilities but the ADAPT study could not take place in prison. One participant was withdrawn as cognitively incapacitated due to being under the influence of heroin (2%). One participant was hospitalised due to severe injecting-related injury (2%). One participant was in withdrawal and left half way through visit 3 and was then LTFU (2% - Visit 3 data completed as LOCF).

Visit disruptions were also common with staff in the needle-exchange looking for available rooms or recovery workers, social workers, and at one time even police, looking for the people being seen in the study. This was considered the nature of the population under investigation and strategies could not be employed to reduce the interruptions and study drop-outs.

8.3.3.3 Time and repetition

After the first few participants had been recruited to the trial, the first repeated measures took place. Some participants commented on the length of the visits and the repetitiveness of some of the measures. The researcher discussed this feedback with her supervisors and the decision was taken to amend the protocol to facilitate participants' engagement. Amendment 02 (AM02), reported in Chapter 4, was submitted to shorten the first two visits and reduce the repetition of some of the measures taken at both these visits.

8.3.4 Substance influence: assessing cognitive and physical capacity

The researcher was aware of the issue of substance influence on the ability of participants to give informed consent and to complete study visits. As a population which is characterised by the use of both prescribed and illicit opioids, benzodiazepines, and often other substances, expecting the participants to be fully

sober would have been unrealistic and would have lacked ecological validity. PWID are able to perform daily tasks under the influence of substances and this ability differs individually person to person (Aldridge & Charles, 2008). Therefore, the researcher did not assess intoxication categorically, but assessed the level of intoxication using her experience of working with the population to appraise excessive influence and intoxication. Three examples of excessive influence are described below.

On one occasion, a follow-up visit was interrupted and the little data that had been collected was deleted, as the participant showed severe levels of heroin influence and the nurses were called. Naloxone was offered to the person, who refused it. On another occasion, a potential participant was being seen for consent. Heavy benzodiazepine intoxication became quickly apparent, so the researcher could not take inform consent and instead offered the person a cup of coffee and sat with him to ensure his health and safety. A third example relates to assessing physical capability due to withdrawal symptoms. As presented in the LTFU section, one participant left half way through visit 3 because he was experiencing heroin withdrawals. He was not capable of sitting physically still, was sweating and agitated albeit very lucid. The researcher asked him if he wanted to stop. He was grateful she had asked and left.

Cognitive capacity was also assessed for the qualitative study, as participants were required to reflect and express their lived experience of HCV. All the participants that were approached, consented and interviewed were not incapacitated by undue influence. However, conducting the qualitative interviews proved quite difficult. As discussed in the section on trauma-informed care, PWID are used to controlling, punitive and, at times, stigmatising experiences of healthcare services. As a population, they are not generally used to being asked about their thoughts and opinions, not to reflect on situations and feelings or to be involved in their own care plans (other than in research settings). In addition, chronic drug use reduces neural processing of frontal regions, impairing cognitive function (Dregan & Gulliford, 2012; Jentsch & Taylor, 1999; Severtson et al. 2012). When prompted to say more, participants would generally just repeat what had been said or not develop the topic any further, producing a series of short interviews. However, the analysis proved the

interviews to have been fruitful, engaging and generating stimulating content (Chapter 7).

8.4 Implications for clinical practice

Direct implications for practice cannot be stated regarding the intervention as the results on the effect of implementation intentions are not reported with confidence, but some implications can be reported for secondary outcomes and findings.

Harm reduction staff and viral hepatitis nurses should implement routine enquiry about all individual injecting paraphernalia (e.g. water, filters, spoons) when asking active injectors whether they have put themselves at risk. Asking clients and patients about sharing in general terms results in a significantly lower number of self-reported sharing contacts, compared to asking the same question after enquiring about each individual injecting equipment piece. The findings showed that water continued to be the most shared equipment piece and that participants would not recall water sharing as a risk until specifically being reminded about it, as supported by previous literature (Gaskin et al. 2000; Gossop et al. 1997).

The strong significance of identification with a drug network as a predictor of injecting sharing behaviour also has implications for practice. Since usually identification with a social group is associated with improved health, these findings are a reminder that some forms of social identifications may pose health risks depending on the type of group people are identifying with. Substance use practitioners, BBV practitioners and harm reduction staff should ask patients and clients about their strength of identification with a social group that injects drugs. This will help them assess the degree of individual risk for each person.

The viral hepatitis nurses and the harm reduction staff in the needle-exchanges have been made aware of these results and their implications for practice.

8.5 Strengths and limitations of the study

8.5.1 Strengths of the study

Although literature has called for the use of implementation intentions with people who use drugs for some time now (Gagnon & Godin, 2009; Palfai, 2006; Prestwich et al. 2006), the results of chapter 2 showed no such studies had been carried out and published. ADAPT is the first study to use implementation intentions as an intervention to reduce risk behaviour in people who inject drugs.

The methodology devised for the study was sound (Chapter 4). Most of the outcomes selected were previously developed and validated measures. Where previously published scales were not available or appropriate, adaptations of validated scales were made to ensure the quality of the measurements collected. Using validated measures reduces research waste and allows more scientific evidence to be collected, disseminated and critically evaluated (McDowell, 2006). The randomisation in the trial was also very rigorous, as demonstrated by the randomisation checks reported in chapter 6.

The intervention was innovative for a variety of reasons. Firstly, the intervention was carried out with people who inject drugs. Although one study reported using implementation intentions with people who used drugs in opiate withdrawal (Brandstätter et al. 2001), the participants in the study were asked to form implementation intentions to create a curriculum vitae rather than to change or reduce their substance use behaviour. In addition, they were patients admitted to a hospital for detoxification and were not currently injecting. No studies to date have reported the use of this intervention with actively injecting drug users. Furthermore, the implementation of the intervention was carried out with a clinical population as the participants were all on treatment for HCV.

This leads onto the second innovative aspect of ADAPT. Since 2013, both the UK and the Scottish Governments have produced legislation to facilitate the integration of health and social care (Department of Health and Social Care, 2013; Scottish Government, 2015b). ADAPT was integrated in a needle-exchange setting and with a viral hepatitis service, increasing the holistic approach to health, care and support needs of patients that required HCV treatment (Department of Health and Social Care,

2013).

Lastly, the integration of ADAPT within a third sector needle-exchange and an NHS clinical team, enabled the researcher to develop multidisciplinary ties. The researcher, a health psychologist, was collaborating with the nursing and medical team of the viral hepatitis service, the gastroenterology service, the harm reduction service, in addition to public health workers from the sexual health and BBV managed care network, the clinical psychologist in the substance use service and the third sector harm reduction staff. Multidisciplinary working allows professionals to learn about colleagues' activities and roles which can improve communication (Finkelman, 2006). It also allows for collaboration between disciplines which improves quality of care and increases professionals' knowledge and skills (Finkelman, 2006; Ndoro, 2014).

8.5.2 Limitations of the study

Limitations of the study (ADAPT and the qualitative sub-study) were discussed individually in each chapter and most of the obstacles and issues encountered during the study were discussed in the preceding paragraphs. However, an overall discussion of limitations is presented here.

The main limitation of ADAPT was the difficulty to recruit to target and to retain participants in the trial. The design of the trial was adapted during the study and different recruitment strategies were employed to increase recruitment and minimise drop-out rates. Despite this, the target sample was not reached and attrition rates remained high throughout the study. This issue resulted in the impossibility to run the planned multivariate analyses in chapter 6. It also meant that one of the secondary research questions could not be investigated, as the outcome for the longevity of the intervention effectiveness 4 months post-intervention (i.e. 12 weeks post HCV treatment) presented too many missing data.

To deal with missing data and allow for a degree of the planned modified intention-to-treat analysis, a Last Observation Carried Forward (LOCF) strategy was applied. This strategy is widely used in clinical trial analyses plans but it can introduce bias as it implies no change has occurred over time for participants that have been lost to follow-up. It also ignores data trends prior to drop-out (Streiner, 2008; Streiner &

Geddes, 2001). These negatives aspects are thought to be offset by the advantages of using this strategy. It allows for testing of the effects of the intervention on a larger sample, minimising the participants excluded and therefore the research waste associated with the trial (Conroy et al. 2015; Streiner, 2008).

In order to keep the time of research visits to under 30 minutes, the baseline measures and the interventions were divided into 2 visits (visit 1 – start of treatment & visit 2 – mid treatment). This resulted in a loss of data as 18 participants did not return for visit 2, not allowing the analysis in chapter 5 to include one of the main outcomes (self-efficacy) and some of the secondary outcomes (social connectedness and social norms). A sample of 32 was considered too small to be able to result in reliable inferences about the data even with bootstrapping, given the skewed sampling distribution and that bootstrapping cannot be used as a justification for a small sample size (Rousselet et al. 2019). Therefore the association and predicting role of self-efficacy on injecting risk behaviour, evidenced in published literature, could not be tested (Bonar & Rosenberg, 2011; Cox et al. 2008; Gagnon & Godin, 2009; Gibson et al. 1993; Nasir et al 2009; Thiede et al. 2007; Wagner et al. 2010a).

Despite dividing the baseline measures and attempting to keep the visits to under 30 minutes, the visits were too long for the population in the study and the number of questionnaires and measures was too high. Participants repeatedly reported they would not have time to stay for a visit. This issue was pre-empted in the planning stages and incentives were put in place to increase recruitment and retention. The incentives were not enough to serve this purpose. These limitations and the results reported in these chapters will, however, help inform and guide future selection of psychosocial factors to be tested, alongside appropriate incentives and contingency management strategies to aid recruitment and retention.

The sample size of the qualitative sub-study was also small, due to the pool of available participants diminishing towards the end of the trial. Although the sample size presented in chapter 7 was considered adequate for the methodology applied, a larger sample would have helped consolidate the results.

A further limitation was the initial lack of familiarity of the population (needle-exchange clients) with the researcher. As discussed above, around 80% of this

population has experience traumatic events. Experience of trauma can affect people's trust in others (NHS Education for Scotland, 2017). As the researcher was not offering a treatment or a service and was simply asking personal questions about consumption of illicit drugs and intimate mental health and social details, issues with trust might have influenced people's decisions for taking part in the study and returning for future visits. The lack of initial familiarity might have also influenced participants' self-reported responses. As some of the outcomes were of a sensitive nature (injecting risk, trauma, depression, anxiety), the validity and reliability of the self-reported outcomes might be limited. For example, some participants might not have wanted to disclose traumatic experience to the researcher after only meeting them once. Nonetheless, evidence shows that behavioural self-reports of people who use drugs are reliable and valid when compared to biomarkers, collateral interviews and criminal records (Darke et al. 1998). No such evidence has been produced for self-reported psychosocial outcomes.

Finally, the effect of implementation intentions was only tested at a 4-week follow-up. Evidence shows that sustained behaviour change is commonly defined as 6 months since the initial behavioural modification (Prochaska & DiClemente, 1983). A 6-month follow-up was initially planned, but given the difficulty in retaining participants, it was amended to a 4-month follow-up as participants were expected to attend in this timeframe for the conclusion of their HCV treatment. Despite the change the attrition rate was extremely high and it did not allow any meaningful analysis of the data.

8.6 Directions for future research

This chapter has so far presented a number of 'lessons learnt' which will help improve and guide future research with this population in this setting. ADAPT showed that implementation intentions can be created with people who actively inject drugs and are on treatment for HCV. The effectiveness of the intervention, however, could not be reported with confidence given the small sample which was analysed. The large effect size observed for self-efficacy indicates that implementation intentions could aid self-efficacy to remain high over time. The effects of the intervention on sharing behaviour

were less clear. The effect sizes reported suggest a larger trial would increase the understanding and confidence of the results reported and would likely find interesting results.

Additionally, the contradicting results on self-efficacy and powerlessness in the quantitative and qualitative studies suggest that the self-efficacy measure used, adapted from Martin's (1995) Self-Efficacy Scale for Drug Avoidance and recommended by the European Monitoring Centre for Drugs and Drug Addiction, had questionable validity and reliability. The administration of this scale to a large sample of PWID would allow a factor analysis to identify item factor loadings and result in the modification of the scale.

Future research should consider conducting all main outcomes and interventions in the first baseline visit with people who inject drugs to ensure all main measures are captured in the first instance. Additionally, given the highly correlated nature of the mental health scales, considerations should be made about the need to measure all variables as separate constructs. If possible, the outcomes should be integrated in patients' treatment visits and collected by nursing staff that have already established a therapeutic relationship with the patients and that are more likely to see patients returning for their treatment. Further considerations in regards to incentives for participants should be given in order to increase recruitment and retention.

Interventions on social network identification to reduce sharing of injecting equipment should be designed and piloted with the PWID population. The change in illness perception should also be explored in future research as a potential predictor of HCV reinfection and as a target for intervention.

8.7 Conclusions

This pilot randomised controlled trial demonstrates that it is feasible and acceptable to create implementation intentions with people actively injecting drugs and on treatment for HCV. It reveals major difficulties with retaining PWID in a longitudinal trial not allowing firm conclusions in regards to the effectiveness of implementation intentions in reducing sharing of injecting equipment. However, it does suggest that

the behavioural intervention functioned as risk limitation rather than as active instrument producing positive change in regards to the self-efficacy outcome. A larger study is needed to confirm and consolidate these findings.

Despite the small sample size, ADAPT revealed some interesting secondary results. First, it identified the strong influence of identification with a drug network on injecting sharing behaviour. Group identification, usually associated with improved mental and physical health outcomes, was exposed as a negative influencing factor of drug using behaviour. Second, the importance of enquiring about each singular piece of injecting paraphernalia when assessing injecting risk was highlighted as an essential aspect of risk assessments for staff working in harm reduction, substance use and viral hepatitis. Last, the changing perception of HCV throughout treatment was thoroughly explored and it suggest HCV risk increases as patients undergo treatment and as treatment becomes faster, easier, more effective and essentially nullifies side effects.

References

*Articles included in the meta-analysis (Chapter 2)

A

Aarts, H., Dijksterhuis, A. P. and Midden, C. (1999). To plan or not to plan? Goal achievement or interrupting the performance of mundane behaviors. *European Journal of Social Psychology, 29(8),* 971-979. Doi:10.1002/(SICI)1099-0992(199912)29:8<971::AID-EJSP963>3.0.CO;2-A

Abraha, I. and Montedori, A. (2010). Modified Intention to Treat Reporting in Randomised Controlled Trials: Systematic Review. *BMJ, 340*: 1-8. Doi:10.1136/bmj.c2697

Adamson, K., Jackson, L.. and Gahagan, J. (2017). Young people and injection drug use: Is there a need to expand harm reduction services and support? *International Journal of Drug Policy, 39*: 14-20. Doi:10.1016/j.drugpo.2016.08.016

Adriaanse, M. A., Vinkers, C. D. W., De Ridder, D. T. D., Hox, J. J. and De Wit J. B. F. (2011). Do implementation intentions help to eat a healthy diet? A systematic review and meta-analysis of the empirical evidence. *Appetite, 56*(1), 183-193. Doi:10.1016/j.appet.2010.10.012

Ahern, J., Stuber, J. and Galea, S. (2007). Stigma, discrimination and the health of illicit drug users. *Drug & Alcohol Dependence, 88(2-3)*: 188-196. Doi:10.1016/j.drugalcdep.2006.10.014

Ajzen, I. (1991). The theory of planned behaviour. *Organizational Behavior and Human Decision Processes, 50,* 179-211. Doi:10.1016/0749-5978(91)90020-T

Ajzen, I. (2002a). *Constructing a TPB Questionnaire: Conceptual and Methodological Considerations*. Accessed online on 24 January 2018 at chuang.epage.au.edu.tw/ezfiles/168/1168/attach/20/pta_41176_7688352_57138.pdf

Ajzen, I. (2002b). Perceived behavioural control, self-efficacy, locus of control, and the theory of planned behaviour. *Journal of Applied Social Psychology,32(4)*: 665-683. Doi:10.1111/j.1559-1816.2002.tb00236.x

Ajzen I. and Madden, T. J. (1986). Prediction of goal oriented behavior: Attitudes, intentions, and perceived behavioral control. *Journal of Experimental Social Psychology, 22*: 453-474. Doi:10.1016/0022-1031(86)90045-4

Alavi, M., Spelman, T., Matthews, G. V., Haber, P. S., Day, C., van Beek, I., Walsh, N., Yeung, B., Bruneau, J., Petoumenos, K., Dolan, K., Kaldor, J. M., Dore, G. J., Hellard, M., Grebeley, J., on behalf of the ATAHC Study Group (2015). Injecting risk behaviours following treatment for hepatitis C virus infection among people who inject drugs: The Australian Trial in acute hepatitis C. *International Journal of Drug Policy, 26,* 976-983. Doi:10.1016/j.drugpo.2015.05.003

Aldridge, J. and Charles, V. (2008). Researching the intoxicated: informed consent implications for alcohol and drug research. *Drug and Alcohol Dependence, 93*: 191–196. Doi:10.1016/j.drugalcdep.2007.09.001

American Psychiatric Association -APA (2000). *Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR (Text Revision).* 4th ed. Washington, DC: American Psychiatric Association.

American Psychological Society Publications and Communications Board Working Froup on Kournal Article Reporting Standards (APA) (2008). Reporting standards for research in psychology: Why do we need them? What might they be? *American Psychologist, 63(9),* 848-849. doi:10.1037/0003-066X.63.9.839

American Psychiatric Association -APA (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5).* 5th ed. Arlington: American Psychiatric Association.

*Arden, M. A. and Armitage, C. J. (2012). A Volitional help sheet to reduce binge drinking in students: a randomized exploratory trial. *Alcohol and Alcoholism, 47(2),* 156-159. Doi:10.1093/alcalc/agr164

*Armitage, C. J. (2007). Efficacy of a brief worksite intervention to reduce smoking: the roles of behavioural and implementation intentions. *Journal of Occupational Health Psychology, 12(4),* 376-390. Doi:10.1037/1076-8998.12.4.376

*Armitage, C. J. (2008). A volitional help sheet to encourage smoking cessation: a randomised exploratory trial. *Health Psychology, 27(5),* 557-566. Doi:10.1037/0278-6133.27.5.557

*Armitage, C. J. (2009). Effectiveness of experimenter-provided and self-generated implementation intentions to reduce alcohol consumption in a sample of the general populations: a randomized exploratory trial. *Health Psychology, 28(5)*, 545-553. Doi:10.1037/a0015984

*Armitage, C. J. (2015). Evidence that a volitional help sheet reduces alcohol consumption among smokers: a pilot randomized controlled trial. *Behavioral Therapy, 46(3)*, 342-349. Doi:10.1016/j.beth.2014.12.003

*Armitage, C. J. (2016). Evidence that implementation intentions can overcome the effects of smoking habits. *Health Psychology, 35(9)*, 935-943. Doi:10.1037/hea0000344

*Armitage, C. J. and Arden, M. A. (2008). How useful are the stages of change for targeting interventions? Randomized test of a brief intervention to reduce smoking. *Health Psychology, 27(6)*, 789-798. Doi:10.1037/0278-6133.27.6.789

*Armitage, C. J. and Arden, M. A. (2012). A volitional help sheet to reduce alcohol consumption in the general population: a field experiment. *Prevention Science, 13*, 635-643. Doi: 10.1007/s11121-012-0291-4

*Armitage, C. J. and Arden, M. A. (2016). Enhancing the effectiveness of alcohol warning labels with a self-affirming implementation intention. *Health Psychology, 35(10),* 1159-1163. Doi: 10.1037/hea0000376

Armitage, C., J. and Conner, M. (2001). Efficacy of the theory of planned behaviour: a meta-analytic review. *British Journal of Social Psychology, 40*: 471-499. Doi:10.1348/014466601164939

*Armitage, C. J., Harris, P. R. and Arden, M. A. (2011). Evidence that self-affirmation reduces alcohol consumption: randomized exploratory trial with a new, brief means of self-affirming. *Health Psychology, 30(5),* 633-641. Doi: 10.1037/a0023738

*Armitage, C. J., Rowe, R., Arden, M. A. and Harirs, P. R. (2014). A brief psychological intervention that reduces adolescent alcohol consumption. *Journal of Consulting and Clinical Psychology, 82(3),* 546-550. Doi: 10.1037/a0035802

Artenie, A. A., Zang, G., Daniel, M., Fortier, E., Jutras-Aswad, D., Puzhko, S. and Bruneau, J. (2017). Short-term injection drug use changes following hepatitis C virus (HCV) assessment and treatment among persons who inject drugs with acute HCV infection. *International Journal of Drug Policy, 47*: 239–243. Doi:10.1016/j.drugpo.2017.05.033

Artenie, A. A., Cunningham, E., Dore, G. J., Conway, B., Dalgard, O., Powis, J., Bruggmann, P., Hellard, M., Cooper, C., Read, P., Feld, J. J., Hajarizadeh, B., Amin, J., Lacombe, K., Stedman, C., Litwin, A. H., Marks, P., Matthews, G. V., Quiene, S., Erratt, A., Bruneau, J. and Grebely, J. (2020). Patterns of drug and alcohol use and injection equipment sharing among people with recent injecting drug use or receiving opioid agonist treatment during and following hepatitis C virus treatment with direct-acting antiviral therapies: an international study. *Clinical Infectious Diseases, 70(11)*: 2369-2376. Doi: 10.1093/cid/ciz633.

Aspinall, E. J., Corson, S., Doyle, J. S., Grebely, J., Hutchinson, S., Dore, G. J., Goldberg, D. J. and Hellard, M. E. (2013). Treatment of hepatitis C virus infection among people who are actively injecting drugs: a systematic review and meta-analysis. *Clinical Infectious Diseases, 57,* s80-9. Doi:10.1093/cid/cit306

Audit Scotland (2019). *Drugs and Alcohol Services: An update*. Audit Scotland: Edinburgh. Accessed online on 14 August 2019 at audit-scotland.gov.uk/uploads/docs/report/2019/briefing_190521_drugs_alcohol.pdf

Avants, S. K., Warbuton, L. A. and Margolin, A. (2000). The influence of coping and depression on abstinence from illicit drug use in methadone-maintained patients. *American Journal of Alcohol Abuse, 26(3)*: 399-416. Doi:10.1081/ADA-100100252

B

Bahorik, A. L., Satre, D. D., Kline-Simon, A. H., Weisner, C. M. and Campbell C. I. (2017). Alcohol, Cannabis, and Opioid Use Disorders, and Disease Burden in an Integrated Healthcare System. *J Addict Med, 11(1),* 3-9. Doi:10.1097/ADM.0000000000000260

Bailey, S. L., Ouellet, L. J., Mackesy-Amiti, M. E., Golub, E. T., Hagan, H., Hudson, S. M., Latka, M. H., Gao, W., Garfein, R. S., DUIT Study Team (2007). Perceived risk, peer influences, and injection partner type predict receptive syringe sharing among young adult injecting drug users in five U. S. Cities. *Drug & Alcohol Dependence, 91s*: s18-s29. Doi:10.1016/j.drugalcdep.2007.02.014

Bandura, A. (1977). Self-efficacy: Toward a unifying theory of behavioral change. *Psychological Review, 84(2)*: 191-215. Doi:10.1037/0033-295x.84.2.191.

Bandura, A. (1986). *Social foundations of thought and action: A social cognitive theory*. Englewood Cliffs, NJ: Prentice-Hall.

Batchelder, A. W., Peyser, D., Nahvi, S., Arnsten, J. H. and Litwin, A. H. (2015). "Hepatitis C treatment turned me around:" Psychological and behavioural transformation related to hepatitis C treatment. *Drug & Alcohol Dependence, 153,* 66-71. Doi:10.1016/j.drugalcdep.2015.06.007

Barker, C. (2002). *Making Sense of Cultural Studies: Central problems and critical debates.* London: Sage. 1st Edition.

Baumeister, R. F., Heatherton, T. F. and Tice, D. M. (1994). *Losing control: how and why people fail at self-regulation.* San Diego, CA: Academic Press.

Bechara, A., Noel, X. and Crone, E. A. (2006). Loss of willpower: abnormal neural mechanisms of impulse control and decision making in addiction. In Wiers, R.

W. and Stacy, A. W. (Eds). *Handbook of Implicit Cognition and Addiction* (pp. 215-232). Thousand Oaks, California: SAGE Publications Inc.

Becker, G. and Arnold, R. (1986). Stigma as a social and cultural construct. In: Ainlay, S. C., Becker, G. and Coleman, L. M. (eds) *The Dilemma of Difference. Perspectives in Social Psychology (A series of texts and monographs.* Springer: Boston, MA. Doi:10.1007/978-1-4684-7568-5_3

Begg, C. B. and Mazumdar, M. (1994). Operating characteristics of a rank correlation test for publication bias. *Biometrics, 50(4),* 1088-1101. Doi: 10.2307/2533446

Bélanger-Gravel, A., Godin, G. and Amireault, S. (2013). A meta-analytic review of the effect of implementation intentions on physical activity. *Health Psychology Review, 7(1),* 23-54. Doi: 10.1080/17437199.2011.560095

Bentler, P. M. and Chou, C. P. (1987). Practical issues in structural modelling. *Sociological Methods & Research, 16*: 78-117. Doi:10.1177/0049124187016001004

Berridge, K. C., and Robinson, T. E. (2016). Liking, wanting, and the incentive-sensitization theory of addiction. *The American psychologist*, *71*(8): 670–679. Doi:10.1037/amp0000059

Best, D., Beckwith, M., Haslam, C., Haslam, S. A., Jetten, J., Mawson, E. and Lubman, D. I. (2016). Overcoming alcohol and other drug addiction as a process of social identity transition: the social identity model of recovery (SIMOR). *Addiction Research & Theory, 24(2)*: 111-123. Doi:10.3109/16066359.2015.1075980

Best, D., Rome, A., Hanning, K., White, W., Gossop, M., Taylor, A., & Perkins, A. (2010). *Research for recovery: A review of the drugs evidence base. Crime and Justice Social Research*, Scottish Government. Edinburgh: Scottish Government. Accessed online on 27 July 2020 at gov.scot/resource/doc/321958/0103435.pdf

Bloor, M., Robertson, M., McKegancy, N. and Neale, J. (2008). Theorising equipment-sharing in a cohoty of Scottish Drug users. *Health, Risk & Society, 10,* 599-607. Doi:10.1080/13698570802533697

Bolman, C., Eggers, S. M., van Osch, L., Poel, F. T., Candel, M. and de Vries, H. (2015). Is action planning helpgul for smoking cessation? Assessing the effects of action planning in a web-based computer-tailored intervention. *Substance Use & Misuse, 50(10)*: 1249-1260. Doi:10.3109/10826084.2014.977397

Bonar, E. E. and Rosenberg , H. (2011). Using the health belief model to predict injecting drug users' intentions to employ harm reduction strategies. *Addictive Behaviors, 36*: 1038–1044. Doi:10.1016/j.addbeh.2011.06.010

Bonnington, O. and Harris, M. (2017). Tensions in relation: How peer support is experienced and received in a hepatitis C treatment intervention. *International Journal of Drug Policy, 47,* 221-229. Doi: 10.1016/j.drugpo.2017.05.031.

Borenstein, M., Hedges, V., Higgins, J. P. and Rothstein, H. R. (2009). *Introduction to meta-analysis.* Chichester, UK: John Wiley & Sons Ltd.

Borland, R., Balmford, J. and Swift, E. (2015). Effects of encouraging rapid implementation and/or structured planning of quit attempts on smoking cessation outcomes: a randomized controlled trial. *Annals of Behavioral Medicine, 49*: 732-742. Doi:10.1007/s12160-015-9706-3

Brandstätter, V., Lengfelder, A. and Gollwitzer, P. M. (2001). Implementation intentions and efficient action initiation. *Journal of Personality and Social Psychology, 81(5),* 946-960. Doi:10.1037/0022-3514.81.5.946

Braun, N., Debener, S., Spychala, N., Bongartz, E., Sörös, P., Müller, H. H. O. and Philipsen, A. (2018). The Senses of Agency and Ownership: A review. *Frontiers in Psychology, 9*: 535-572. Doi:10.3389/fpsyg/2018/00535

Braun, V. and Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology, 3(2)*: 77-101. Doi:10.1191/1478088706qp063oa

Braun, V. and Clarke, .V. (2013). *Successful qualitative research: A practical guide for beginners*. London: Sage. 1st Edition.

Brener, L., Horwitz, R., von Hippel, C., Bryant, J. and Treloar, C. (2014). Discrimination by health care workers versus discrimination by others: Countervailing forces on HCV treatment intentions. *Psychology, Health & Medicine, 20(2)*: 148-153. Doi:10.1080/13548506.2014.923103

van den Brink, W., Hendricks, V. M., Blanken, P., Koeter, M. W., van Zwieten, B. J. and van Ree, J. M. (2003), Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials. *British Medical Journal, 327*: 310–316. Doi:10.1136/bmj.327.7410.310

British Medical Journal – BMJ (2017). *BMJ Best Practice - Hepatitis C: The right clinical information, right where it's needed*. Accessed online on 19 September 2017 at bestpractice.bmj.com

British Psychological Society – BPS (2019). *Health psychology in applied settings: A guide for employers*. Accessed online on 25 September 2019 at bps.org.uk/dhp

Broadbent, E., Petrie, K. J., Main, J. and Weinman, J. (2006). The Brief Illness Perception Questionnaire. *Journal of Psychosomatic Research, 60,* 631-637. Doi:10.1016/j.jpsychores.2005.10.020

Brown, E. M., Smith, D. M. and Armitage, C. J. (2019). Self-incentives uniquely boost cessation in community-based stop smoking programs: randomized controlled trial. *Annals of Behavioral Medicine, 53(5)*: 442-452. Doi:10.1093/abm/kay056

Broz, D. and Ouellet, L. J. (2010). Prevalence and correlates of former injection drug use among young noninjecting heroin users in Chicago. *Substance Use & Misuse, 45,* 2000-2025. Doi:10.3109/10826081003682875

Buckingham, S. A., Frings, D. and Albery, I. P. (2013). Group membership and social identity in addiction recovery. *Psychology of Addictive Behaviors, 27(4)*, 1132-1140. Doi:10.1037/a0032480

Buitenhuis, A. H., Tuinman, M. A. and Hagedoorn, M. (2018). A dyadic planning intervention to quit smoking in single-smoking couples: design of a randomized controlled trial. *BMC Psychology, 6*: 53. Doi:10.1186/s40359-018-0266-8

Butler, M. (2017). *Two sides of the same coin: Patient Adherence and Staff Turnover in Substance Misuse Settings*. Thesis submitted for the Doctorate in Clinical Psychology (DClinPsychol), The University of Edinburgh: May 2017.

Butler, S. F., Budman, S. H., McGee, M. D., Davis, M. S., Cornelli, R. and Morey L. C. (2006). Addiction severity assessment tool: Development of a self-report measure for clients in substance abuse treatment. *Drug and Alcohol Dependence, 80,* 349-360. Doi:10.1016/j.drugalcdep.2005.05.005

Byrne, M. M., Croft, J. R., French, M. T., Dugosh, K. L. and Festinger, D. S. (2012). Development and preliminary results of the Financial Incentive Coercion Assessment questionnaire. *Journal of Substance Abuse Treatment, 43*: 86-93. Doi:10.1016/j.jsat.2011.10.002

C

Cama, E., Brener, L., Wilson, H. and von Hipple, C. (2016). Internalized stigma among people who inject drugs. *Substance Use & Misuse, 51(12)*: 1664-1668. Doi:10.1080/10826084.2016.1188951

Cameron, D., Epton, T., Norman, P., Sheeran, P., Harris, P. R., Webb, T. L., Julious, S. A., Brennan, A., Thomas, C., Petroczi, A., Naughton, D. and Shah, I. (2015). A theory-based online health behaviour intervention for new university students (U@Uni: LifeGuide): results from a repeat randomized controlled trial. *Trials, 16*: 1-15. Doi:10.1186/s13063-015-1092-4

Caven, M., Malaguti, A., Robinson, E., Fletcher, E. And Dillon, J. F. (2019). Impact of Hepatitis C treatment on behavioural change in relation to drug use in people who inject drugs: A systematic review. *International Journal of Drug Policy 72*: 169-176. Doi:10.1016/j.drugpo.2019.05.011

Caudwell, K. M., Mullan, B. A. and Hagger, M. S. (2016). Combining motivational and volitional approaches to reducing excessive alcohol consumption in pre-drinkers: a theory-based intervention protocol. *BMC Public Health, 16*: 1-12. Doi:10.1186/s12889-015-2648-7

*Caudwell, K. M., Mullan, B. A. and Hagger, M. S. (2018). Testing an online, theory-based intervention to reduce pre-drinking alcohol consumption and alcohol-related harm in undergraduates: a randomized controlled trial. *International Journal of Behavioural Medicine, 25(5),* 592-604. Doi:10.1007/s12529-018-9736-x

Cepeda, A., Kaplan, C., Neaigus, A., Cano, M. A., Villarreal, Y. and Valdez, A. (2012). Injecting transition risk and depression among Mexican American non-injecting heroin users. *Drug & Alcohol Dependence, 125,* S12-17. Doi:10.1016/j.drugalcdep.2012.05.035

Chatzisarantis, N. L. D. and Hagger, M. S. (2010). Effects of implementation intentions linking suppression of alcohol consumption to socializing goals on alcohol-related decisions. *Journal of Applied Social Psychology, 40(7)*: 1618–1634. Doi:10.1111/j.1559-1816.2010.00632.x

Cheng, J., Lu, Y., Han, X., González-Vallejo, C.and Sui, N. (2012). Temporal discounting in heroin-dependent patients: no sign effect, weaker magnitude effect, and the relationship with inhibitory control. *Experimental & Clinical Psychopharmacology, 20(5)*: 400-409. Doi:10.1037/a0029657

Churchill, S. and Jessop D. C. (2011). Too impulsive for implementation intentions? Evidence that impylsivity moderates the effectiveness of an implementation intention intervention. *Psychology & Health, 26(5),* 517-530. Doi:10.1080/08870441003611536

Cloud, D. H., Ibragimov, U., Prood, N., Young, A. M. and Cooper, H L. F. (2019). Rural risk environments for hepatitis c among young adults in Appalachian Kentucky. *International Journal of Drug Policy, 72*: 47-54. Doi:10.1016/j.drugpo.2019.05.006

Cohen, J. (1988). *Statistical power analysis for the behavioural sciences*. Hillside, New Jersey: Lawrence Earlbaum Associates.

Collins, R. L., Parks, G. A. and Marlatt, G. A. (1985). Social determinants of alcohol consumption: the effects of social interaction and model status on the self-administration of alcohol. *Journal of Consulting & Clinical Psychology, 53(2),* 189-200. Doi:10.1037/0022-006X.53.2.189

*Conner, M. and Higgins, A. R. (2010). Long-term effects of implementation intentions of prevention of smoking uptake among adolescents: a cluster randomized controlled trial. *Health Psychology, 29(5),* 529-538. Doi: 10.1037/a0020317.

Conroy, D., Sparks, P. and de Visser, R. (2015). Efficacy of a non-drinking mental simulation intervention for reducing student alcohol consumption. *British Journal of Health Psychology, 20(4)*: 688-707. Doi:10.1111/bjhp.12133

Contreras, R. and Jason, L. A. (2013). Experiences of Oxford House residents living with the hepatitis C virus. *Frontiers in Psychological and Behavioral Science, 2(2)*: 57-63.

Cooper, H., Hedges, L. V. and Valentine, J. C. (2009). *The Handbook of Research Synthesis and Meta-analysis.* New York City, USA: Russell Sage Foundation.

Cooper, C. L., Whitehead, A., Pottrill, E., Julious, S. A. and Walters, S. J. (2018). Are pilot trials useful for predicting randomisation and attrition rates in definitive studies: A review of publicly funded trials. *Clinical trials, 15(2)*: 189-196. Doi:10.1177/1740774517752113

Copenhaver, M. M., Johnson, B. T., Lee, I.C., Harman, J. J., Carey, M. P. and SHARP Research Team (2006). Behavioral HIV Risk Reduction among People Who Inject Drugs: Meta-Analytic Evidence of Efficacy. *Journal of Substance Abuse Treatment, 31(2),* 163-171. Doi:10.1016/j.jsat.2006.04.002

Copenhaver, M. M. and Lee, I. C. (2006). Optimizing a community-friendly HIV risk reduction intervention for injection drug users in treatment: A structural equation modeling approach. *Journal of Urban Health, 83*(6), 1132-1142. Doi:10.1007/s11524-006-9090-1

Courneya, K. S. and McAuley, E. (1995). Reliability and discriminant validity of subjective norm, social support and cohesion in an exercise setting. *Journal of Sport and Exercise Psychology, 17(3)*, 325-337. Doi:10.1123/jsep.17.3.325

Cox, J., De, P., Morissette, C., Tremblay, C., Stephenson, R., Allard, R., Graves, L. And Roy, É. (2008). Low perceived benefits and self-efficacy are associated with hepatitis C virus (HCV) infection-related risk among injection drug users. *Social Science & Medicine, 66(2)*: 211-220. Doi:10.1016/j.socscimed.2007.08.022

Cox, W. M., Fadardi, J. S. and Klinger, E. (2006).Motivational processes underlying implicit cognition in addiction. In Wiers, R. W. and Stacy, A. W. (Eds). *Handbook of Implicit Cognition and Addiction* (pp. 253-266). Thousand Oaks, California: SAGE Publications Inc.

Crutzen, R., Viechtbauer, W., Spigt, M., Kotz, D. (2015). Differential attrition in health behaviour change trials: a systematic review and meta-analysis. *Psychology & Health*, 30(1):122-134. Doi:10.1080/08870446.2014.953526

Cruz, H. M., de Paula, V. S. and Villar, L. M. (2018). A Cross-Sectional Study of Viral Hepatitis Perception among Residents from Southeast and North Regions of Brazil. *International Journal of Environmental Research and Public Health, 15*: 189. Doi:10.3390/ijerph15020189

Cummings, C. and O'Donohue, W. T. (2018). Sexual Abuse and PTSD in Children. In: Maragakis, A. and O'Donohue, W. (eds). *Principle-Based Stepped Care and Brief Psychotherapy for Integrated Care Settings*. Springer, Cham: 379-387.

D

Dallal, G. E. (2008). *Randomization.com online generator*. Access on 22 January 2018 at randomization.com .

Darke, S. (1998). Self-report among injecting drug users: A review. *Drug & Alcohol Dependence, 51(3)*: 253-263. Doi:10.1016/S0376-8716(98)00028-3

Darke, S. and Hall, W. (1995). Levels and correlates of polydrug use among heroin users and regular amphetamine users. *Drug & Alcohol Dependence, 39*: 231-235. Doi:10.1016/0376-8716(95(01171-9

Darke, S., Hall, W., Ross, M. and Wodak, A. (1992). Benzodiazepine use and HIV risk-taking behaviour among injecting drug users. *Drug & Alcohol Dependence, 31(1)*: 31-36. Doi:10.1016/0376-8716(92(90005-W

Darke, S., Ross, J., Cohen, J., Hando, J. and Hall, W. (1995). Injecting and sexual risk-taking behaviour among regular amphetamine users. *AIDS Care, 7(1)*: 19-26. Doi:10.1080/09540129550126920

Davey-Rothwell M. A., Latkin, C. A. and Tobin, K. E. (2010). Longitudinal analysis of the relationship between perceived norms and sharing injection paraphernalia. *AIDS Behavior, 14(4)*: 878-84. Doi:10.1007/s10461-008-9520-z

Davey-Rothwell M. A., Siconolfi, D. E., Tobin, K. E. and Latkin, C. A. (2015). The role of neighbourhoods in shaping perceived norms: An exploration of neighbourhood disorder and norms among injection drug users in Baltimore, MD. *Health &Place, 33*: 181–186. Doi:10.1016/j.healthplace.2015.03.009

Day, C. A., Ross, J., Dietze, P. and Dolan, K. (2005). Initiation to heroin injecting among heroin users in Sydney, Australia: Cross sectional survey. *Harm Reduction Journal, 2(2)*: 1-7. Doi: 10.1186/1477-7517-2-2

Day, C. A., Islam, M., White, A., Reid, S. E., Hayes, S. and Haber, P. S. (2011). Development of a nurse-led primary healthcare service for injecting drug users in inner-city Sydney. *Australian Journal of Primary Health, 17,* 10-15. Doi:10.1071/PY10064

De, P., Cox, J., Boivin, J. F., Platt, R. W. and Jolly, A. M. (2007). Social network-related risk factors for bloodborne virus infections among injection drug users receiving syringes through secondary exchange. *Journal of Urban Health: Bulletin of the NY Academy of Medicine, 85,* 77-89. Doi:10.1007/s11524-007-9225-z

DeLamater, J. D. and Hyde, J. S. (1998). Essentialism vs social constructionism in the study of human sexuality. *The Journal of Sex Research, 35(1)*: 10-18. Doi:10.1080/00224499809551913

Department of Health and Social Care (2013). *Integrated Care and Support: Our Shared Commitment*. Accessed online on 31 July 2020 at assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/198748/DEFINITIVE_FINAL_VERSION_Integrated_Care_and_Support_-_Our_Shared_Commitment_2013-05-13.pdf

Department of Health and Social Care - Independent Expert Working Group (2017). *Drug misuse and dependence: UK guidelines on clinical management. Clinical Guidelines on Drug Misuse and Dependence Update 2017*. London: Department of Health. Accessed online on 20 July 2020 at gov.uk/government/publications/drug-misuse-and-dependence-uk-guidelines-on-clinical-management

DeStasio, K. L., Hill, A. P. and Berkman, E. T. (2018). Efficacy of an SMS-based smoking intervention using message self-authorship: a pilot study. *Journal of Smoking Cessation, 13(1)*: 55-58. Doi:10.1017/jsc.2016.27.

Dixon, D. and Johnston, M. (2010). *Health Behaviour Change Competency Framework: Competences to deliver interventions to change lifestyle behaviours that affect health*. Accessed online on 20 July 2020 at healthscotland.com/uploads/documents/4877-Health_behaviour_change_competency_framework.pdf

Dolan, S. L., Rohsenow, D. J., Martin, R. A. and Monti, P. M. (2013). Urge-specific and lifestyle coping strategies of alcoholics: Relationships of specific strategies to treatment outcome. *Drug & Alcohol Dependenve, 128*: 8-14. Doi:10.1016/j.drugalcdep.2012.07.010

Dowsett, L. E., Coward, S., Lorenzetti, D. L., MacKean, G. and Clement, F. (2017). Living with Hepatitis C Virus: A Systematic Review and Narrative Synthesis of Qualitative Literature. *Canadian Journal of Gastroenterology and Hepatology, 2017*: 1-11. Doi:10.1155/2017/3268650

Dregan, A. and Gulliford, M. C. (2012). Is Illicit Drug Use Harmful to Cognitive Functioning in the Midadult Years? A Cohort-based Investigation, *American Journal of Epidemiology, 175(3)*: 218–227. Doi:10.1093/aje/kwr315

Dube, S. R., Felitti, V. J., Dong, M., Chapman, D. P., Giles, W. H. and Anda, R. F. (2003). Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics, 111*: 564-572. Doi:10.1542/peds.111.3.564

Duff, C. (2013). The social life of drugs. *International Journal of Drug Policy 24(3)*: 167-172. Doi:10.1016/j.drugpo.2012.12.009

Duley, L. Gillman, A., Duggan, M., Belson, S., Knox, J., McDonald, A., Rawcliffe, C., Simon, J., Spronsen, T., Watson, J. and Wood, W., (2018). What are the main inefficiencies in trial conduct: a survey of UKCRC registered clinical trials units in the UK. *Trials, 19*: 1-7. Doi:10.1186/s13063-017-2378-5

Dunn, M., Degenhardt, L. and Bruno, R. (2010). Transition to and from injecting drug use among regular ecstasy users. *Addictive Behaviors, 35,* 909-912. Doi:10.1016/j.addbeh.2010.06.007

Duval, S. J. and Tweedie, R. L. (2000). A nonparametric "trim and fill" method of accounting for publication bias in meta-analysis. *Journal of the American Statistical Association, 95*(449), 89–98. Doi:10.1080/01621459.2000.10473905

Dziura, J. D., Post, L. A., Zhao, Q., Fu, Z. and Peduzzi, P. (2013). Strategies for Dealing with Missing Data in Clinical Trials: From Design to Analysis. *Yale Journal of Biological Medicine, 86,* 343-358. PMCID: PMC3767219

E

Earnshaw, V., L. Smith and M. Copenhaver (2013). Drug addiction stigma in the context of methadone maintenance therapy: an investigation into understudied sources of stigma. *International journal of mental health and addiction 11(1)*: 110-122. Doi:10.1007/s11469-012-9402-5.

Easton, P., Entwistle, V. A and Williams, B. (2013). How the stigma of low literacy can impair patient-professional spoken interactions and affect health: insights from a qualitative investigation. *BMC Health Services Research, 13(319)*: 1-12. Doi:10.1186/1472-6963-13-319

Egger, M., Davey-Smith, G., Schneider, M., and Minder, C. (1997). Bias in meta-analysis detected by a simple graphical test. *BMJ, 315*, 629-35. Doi:10.1136/bmj.315.7109.629

*Ehret, P. J. and Sherman, D. K. (2018). Integrating self-affirmation and implementation intentions: effects on college student drinking. *Annals of behavioral medicine, 52*, 633-644. Doi:10.1093/abm/kax032

El-Bassel, N., Shaw, S. A., Dasgupta, A. and Strathdee, S. A. (2014). People Who Inject Drugs in Intimate Relationships: It Takes Two to Combat HIV. *Current HIV/AIDS Report s, 11,* 45-51. Doi:10.1007/s11904-013-0192-6

El-Sayed, H., Mehanna, S., Hassan, A., Sheded, M., Elmaraghy, N., Lofty, N. and Khadr, Z. (2019). Knowledge, perception and practices of Suez Canal University students regarding Hepatitis C Virus infection risk and means of prevention. *International Journal of Clinical Microbiology and Biochemical Technology,* 2: 20-27. Doi:10.29328/journal.ijcmbt.1001007

Elfeddali, I., Bolman, C., Candel, M. J. J. M., Wiers, R. W., and de Vries, H. (2012). Preventing smoking relapse via web-based computer-tailored feedback: a randomized controlled trial. *Journal of Medical Internet Research, 14(4)*: e109. Doi:10.2196/jmir.2057

Elfeddali, I., Bolman, C. And de Vries, H. (2013). Situational and affective risk situations of relapse and the quality of implementation intentions in an e-health smoking relapse prevention programme. *Substance Use & Misuse, 48*: 635-644. Doi:10.3109/10826084.2013.800113

Ellis, P. D. (2010). *The essential guide to effect sizes: statistical power, meta-analysis, and the interpretation of research results.* Cambridge: Cambridge University Press. Doi: 10.1017/CBO9780511761676

Epton, T., Norman, P., Dadzie, A. S., Harris, P. R., Webb, T. L., Sheeran, P., Julious, S. A., Ciravegna, F., Brennan, A., Meier, P. S., Naughton, D., Petroczi, A., Kruger, J. and Shah, I. (2014). A theory-based online health behaviour intervention for new university students (U@Uni): Results from a randomised controlled trial. *BMC Public Health, 14*: 563. Doi:10.1186/1471-2458-14-563

European Monitoring Centre for Drugs and Drug Addiction – EMCDDA (2001). *Insights Series: Injecting drug use, risk behaviour and qualitative research in the time of AIDS.* Luxembourg: Office for Official Publications of the European Communities.

European Monitoring Centre for Drugs and Drug Addiction - EMCDDA (2012). *Insights Series: New heroin-assisted treatment. Recent evidence and current practices of*

supervised injectable heroin treatment in Europe and beyond. Luxembourg: Office for Official Publications of the European Communities.

European Monitoring Centre for Drugs and Drug Addiction - EMCDDA (2018). *Perspectives on drugs. Drug consumption rooms: an overview of provision and evidence.* Luxembourg: Office for Official Publications of the European Communities.

F

Fairbarn, N., Small, W., van Borek, N., Wood, E. and Kerr, T. (2010). Social structural factors that shape assisted injecting practices among injection drug users in Vancouver, Canada: a qualitative study. *Harm Reduction Journal, 7,* 1-7. Doi:10.1186/1477-7517-7-20

Falade-Nwulia, O., Sulkowski, M. S., Merkow, A., Latkin, C. and Metha, S. (2018). Understanding and addressing hepatitis C reinfection in the oral direct acting antiviral era. *Journal of Viral Hepatitis, 25(3)*: 220-227. Doi:10.1111/jvh.12859

Falck, R. S., Siegal, H. A., Wang, J. and Carlson, R. G. (1995). Usefulness of the health belief model in predicting HIV needle risk practices among injection drug users. *AIDS Education & Prevention, 7(6)*: 523-533. PMID:8924349

Fast Forward (2016). *Performance and Image Enhancing Drugs (PIEDs) Research Report Nov 2016*. Accessed online on 25 January 2018 at sdf.org.uk/wp-content/uploads/2017/05/PIED_Research_Report.pdf .

Faul, F., Erdfelder, E., Lang, A.-G. and Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39,* 175-191. Doi:10.3758/BF03193146

Felitti, V. J. (2003). The origins of addiction: Evidence from the adverse childhood experiences study. [English translation.]. *Praxis der Kinderpsychologie und Kinderpsychiatrie*, 52(8): 547–559.

Field, A. (2018). *Discovering Statistics Using IBM SPSS Statistics*. London: Sage Publications Ltd. 5th Edition.

Field, M., Mogg, K. and Bradley, B. P. (2006). Attention to drug-related cues in drug abuse and addiction: component processes. In Wiers, R. W. and Stacy, A. W. (Eds). *Handbook of Implicit Cognition and Addiction* (pp. 151-166). Thousand Oaks, California: SAGE Publications Inc.

Finkelman, A. W. (2006). *Leadership and Management in Nursing*. Upper Saddle River, NJ: Prentice Hall.

Fisher, L. D., Dixon, D. O., Herson, J., Frankowski, R. K., Hearron, M. S. and Peace, K. E. (1990). Intention to treat in clinical trials. In: Peace, K. E. (Eds). *Statistical issues in drug research and development*. New York: Marcel Dekker.

Fitzsimons, G. M. and Bargh, J. A. (2004). Automatic self-regulation. In Baumeister, R. F. and Vohs, K. D. (Eds.) *Handbook of self-regulation: Research, theory and applications* (pp. 492-508). New York City, NY: Guilford Press.

Fraser, A. and George, M. (1988). Changing trends in drug use: an initial follow-up of a local heroin community. *British Journal of Addiction, 83*: 655-663. Doi:10.1111/j.1360-0443.1988.tb02594.x

Fraser, S. (2004). 'It's your life!': injecting drug users, individual responsibility and hepatitis C prevention. *Health*, *8(2)*: 199–221. Doi:10.1177/1363459304041070

Fraser, S. (2006). The chronotope of the queue: Methadone maintenance treatment and the production of time, space and subjects. *International Journal of Drug Policy, 17(3)*: 192-202. Doi:10.1016/j.drugpo.2006.02.010

Fraser, S., Rance, J. and Treloar, C. (2016). Hepatitis C prevention and convenience: why do people who inject drugs in sexual partnerships 'run out' of sterile equipment? *Critical Public Health, 26(3)*: 294-306. Doi:10.1080/09581596.2015.1036839

Fraser, S. and Treloar, C. (2006). 'Spoiled identity' in hepatitis C infection: The binary logic of despair. *Critical Public Health, 16(2)*: 99-110. Doi:10.1080/09581590600828683

G

Gagnon, H. and Godin, G. (2009). Psychosocial factors explaining drug users' intention to use a new syringe at each injection. *Addiction Research & Theory, 17(5)*: 481-492. Doi:10.1080/16066350801902475

Gardner, B., Lally, P. and Wardle, J. (2012). Making health habitual: the psychology of 'habit-formation' and general practice. *British Journal of General Practice, 62(605)*: 664-666. Doi:10.3399/bjgp12X659466

Gaskin, S., Brazil, C. And Pickering, D. (2000). The sharing of injecting paraphernalia by intravenous drug users (IDUs) within a Worcestershire cohort, with specific reference to water and filters. *International Journal of Drug Policy, 11(6)*: 423-435. Doi:10.1016/s0955-3959(00)00069-4.

Gerlach, J. T., Depolder, H. M. and Zachoval, R. (2003). Acute hepatitis C: high rate of both spontaneous and treatment-induced viral clearance. *Gastroenterology, 125,* 80-88. Doi:10.1016/S0016-5085(03)00668-1

Gibson, D. R., Choi,, KH., Catania, J. A., Sorensen, J. L. and Kegeles, S. (1993). Psychosocial Predictors of Needle Sharing among Intravenous Drug Users, *International Journal of the Addictions, 28(10):* 973-981. Doi:10.3109/10826089309062177

Gindi, R. M., Rucker, M. G., Serio-Chapman, C. E., Sherman, S. G. (2008). Utilization patterns and correlates of retention among clients of the needle exchange program in Baltimore, Maryland. Drug & Alcohol Dependence, 103: 93–98. Doi:10.1016/j.drugalcdep.2008.12.018

Glanz, K., Rimer, B. K. and Lewis, F. M. (eds) (2002). *Health Behavior and Health Education: Theory, Research and Practice*. Jossey-Bass: San Francisco, CA. 3rd Edition.

Glasgow City Council (2019). *Scotland's first heroin-assisted treatment unveiled*. Accessed online on 5 December 2019 at glasgow.gov.uk/article/25326/Scotlands-First-Heroin-Assisted-Treatment-Unveiled

Global Burden of Disease - Tobacco Collaborators (2015). Smoking prevalence and attributable disease burden in 195 countries and territories, 1990–2015: a systematic analysis from the Global Burden of Disease Study 2015. *Lancet, 389*(10082), 1885-1906. Doi:10.1016S0140-6736(17)30819-X

Gollwitzer, P.M. (1993). Goal achievement: the role of intentions. *European Review of Social Psychology, 4(1)*: 141–185. Doi:10.1080/14792779343000059.

Gollwirzer, P. M. (1999). How can good intentions become effective behaviour change strategies. *American Psychologist, 54(7)*: 493-503. Doi:10.1037/0003-066X.54.7.493

Gollwitzer, P. M. and Sheeran, P. (2006). Implementation intentions and goal achievement: A meta-analysis of effect and processes. *Advances in Experimental Social Psychology, 38*: 69-119. Doi:10.1016/S0065-2601(06)38002-1

Gossop, M., Griffiths, P., Powis, B., Williamson, S., Fountain, J. and Strang, J. (1997). Continuing drug risk behaviour: Shared use of injecting paraphernalia among London heroin injectors. *AIDS Care, 9(6)*: 651-660. Doi:10.1080/09540129750124687

Gossop, M., Marsden, J., Stewart, D. and Treacy, S. (2002). Reduced injection risk and sexual risk behaviours after drug misuse treatment: results from the National Treatment Outcome Research Study. *AIDS Care, 14(1)*: 77-93. Doi:10.1080/09540120220097955

Gowing, L., Farrell, M., Bornemann, R., Sullivan, L. E. and Ali, R. (2008). Substitution treatment of injecting opioid users for prevention of HIV. *Cochrane Database Systematic Reviews*, 21-85. Doi:10.1002/14651858.CD004145.pub3

Gratton, L., Povey, R. and Clark-Carter, D. (2007). Promoting children's fruit and vegetable consumption: Interventions using the Theory of Planned Behaviour as a framework. British Journal of Health Psychology, 12(4): 639-650. Doi:10.1348/135910706X171504

Grebely, J., Matthews, G. V., Hellard, M., Shaw, D., van Beek, I., Petoumenos, K., Alavi, M., Yeung, B., Haber, P. S., Lloyd, A. R., Kaldor, J. M. and Dore, G. J. (2011). Adherence to treatment for recently acquired hepatitis C virus (HCV) infection among injecting drug users. *Journal of Hepatology, 55*: 76-85. Doi:10.1016/j.jhep.2010.10.033

Green, S. B. (1991) How Many Subjects Does It Take To Do A Regression Analysis, Multivariate *Behavioral Research, 26 (3)*: 499-510. Doi:10.1207/s15327906mbr2603_7

Gupta, S. K. (2011). Intention-to-treat concept: A review. *Perspectives in Clinical Research, 2(3)*: 109-112. Doi:10.4103/2229-3485.83221

Gyamarthy, A., Li, N., Tobin, K. E., Hoffman, I. F., Sokolov, N., Levchenko, J., Barluk, J., Kozlov, A. A., Kozlov, A. P. and Latkin, C. A. (2009). Correlates of unsafe injecting among injecting drug users in St Petersburg, Russia. *European Addiction Research, 15(3)*: 163-170. Doi:10.1159/000220344

H

Haasen, C., Verthein, U., Degkwitz, P., Berger, J., Krausz, M. and Naber, D. (2007). Heroin-assisted treatment for opioid dependence. *British Journal of Psychiatry, 191*: 55–62. Doi:10.1192/bjp.bp.106.026112

Haber, P. S., Demirkol, A., Lange, K. and Murnion, B. (2009). Management of injecting drug users admitted to hospital. *Lancet, 374,* 1284-1293. Doi:10.1016/S0140-6736(09)61036-9

*Hagger, M. S., Lonsdale, A. and Chatzisarantis, N. L. D. (2012a). A theory-based intervention to reduce alcohol drinking in excess of guideline limits among undergraduate students. *British Journal of Health Psychology, 17*, 18-43. Doi:10.1111/j.2044-8287.2010.02011.x

*Hagger, M. S., Lonsdale, A., Koka, A., Hein, V., Pasi, H., Lintunen, T., Chatzisarantis, N. L. D. (2012b). An intervention to reduce alcohol consumption in undergraduate students using implementation intentions and mental simulations: a cross-

national study. *International Journal of Behavioral Medicine, 19*, 82-96. Doi:10.1007/s12529-011-9163-8

Hagger, M. S. and Luszczynska, A. (2014). Implementation intention and action planning intervention in health contexts: state of the research and proposals for the way forward. *Applied Psychology: Health and Well-being, 6(1)*: 1-47. Doi:10.1111/aphw.12017

Hajarizadeh, B., Cunningham, E. B., Valerio, H., Martinello, M., Law, M., Janjua, N., Midgard, H., Dalgard, O., Dillon, J. F., Hickman, M., Bruneau, J., Dore, G. J., Grebely, J. (in press). Hepatitis C reinfection after successful antiviral treatment among people who inject drugs: A meta-analysis. *Journal of Hepatology.* Doi:10.1016/j.jhep.2019.11.012

Hanafiah, K. M., Groeger, J., Flaxman, A. D. and Wiersma, S. T. (2013). Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody HCV seroprevalence. *Hepatology, 57(4),*1333-1342. Doi:10.1002/hep.26141

Harris, M., Rhodes, T. and Martin, A. (2013). Taming systems to create enabling environment for HCV treatment: Negotiating trust in the drug and alcohol setting. *Social Science & Medicine, 83*: 19-26. Doi:10.1016/j.socscimed.2013.01.031

Harris, P. and Middleton, W. (1994). The illusion of control and optimism about health: On being less at risk but no more in control than others. *British Journal of Social Psychology, 33(4)*: 369-386. Doi:10.1111/j.2044-8309.1994.tb01035.x

Harvey, E., Strathdee, S. A., Patrick, D. M., Ofner, M., Archibald, C. P., Eades, G. and O'Shaughnessy, M. V. (1998). A qualitative investigation into an HIV outbreak among injecting drug users in Vancouver, British Columbia. *AIDS Care, 10,* 313-321. Doi:10.1080/713612412

Haslam, S.A. (2014). Making good theory practical: Five lessons for an Applied Social Identity Approach to challenges of organizational, health, and clinical psychology. *British Journal of Social Psychology, 53*: 1–20. Doi:10.1111/bjso.12061

Hatcher, R. L. and Gillaspy, J. A. (2006). Development and validation of a revised short version of the working alliance inventory. *Psychotherapy Research, 16(1)*, 12-25. Doi:10.1080/10503300500352500

Hauri, A. M., Armstrong, G. L. and Hutin, Y. J. F. (2003). Contaminated injections in health care settings. In: Ezzati, M., Lopez, A. D., Rodgers, A., Murray, C. J. L., editors. *Comparative quantification of health risks: global and regional burden*

of disease attributable to selected major risk factors. Geneva: World Health Organisation; 2003.

Health Improvement Scotland – HIS (2017). *National Clinical Guidelines for the treatment of HCV in adults*. NHS National Services Scotland - Version 3, January 2017. Accessed online on 20 September 2017 at hps.scot.nhs.uk

Health Protection Scotland – HPS, prepared by Codere, G. Weir, A., McAuley, A., McLeod, A., Watt, C., Hutchinson, S., Goldberg, D. and Quinn, L. (2017a). *Surveillance of known hepatitis C antibody positive cases in Scotland: results to 31 December 2016*. HPS Weekly Report Volume 51 No.2017/24. Accessed online on 20 September 2017 at hps.scot.nhs.uk/documents/ewr/pdf2017/1724.pdf

Health Protection Scotland (2017b). *Needle Exchange Surveillance Initiative (NESI) 2008-09 to 2015-17*. Accessed online on 10 October 2017 at hps.scot.nhs.uk/resourcedocument.aspx?id=5863

Health Protection Scotland (2019). *Needle Exchange Surveillance Initiative (NESI) 2008-09 to 2017-18*. Accessed online on 10 December 2019 at hpspubsrepo.blob.core.windows.net/hps-website/nss/2721/documents/1_NESI%202018.pdf

Healthcare Improvement Scotland and NHS National Services Scotland (2018). *National Clinical Guidelines for the treatment of HCV in adults.* Version 5, June 2018. Accessed on 1 April 2020 at hps.scot.nhs.uk/web-resources-container/national-clinical-guidelines-for-the-treatment-of-hcv-in-adults/

Hedges, L. V. And Vevea, J. L. (1998). Fixed- and random-effects models in meta-analysis. *Psychological Methods, 3*(4), 486-504. Doi:10.1037/1082-989X.3.4.486

Hedric, D., Kerr, T. and Dubois-Arber, F. (2010). Drug consumption facilities in Europe and beyond. In Rhodes, T. and Hedric, D. (Eds), *EMCDDA Monographs: Harm reduction: evidence, impacts and challenges* (305-331). Luxembourg: Publications Office of the European Union, 2010.

Heimer, R., Eritsyan, K., Barbour, R., Levina, O. S. (2014a). Hepatitis C virus seroprevalence among people who inject drugs and factors associated with infection in eight Russian cities. *BMC Infectious Diseases, 14 (6)*: 1-9. Doi:10.1186/1471-2334-14-S6-S12

Heimer, R., Barbour, R., Palacios, W. R., Nichols, L. G. and Grau, L. E. (2014b). Associations between injection risk and community disadvantage among suburban injection drug users in southwestern Connecticut, USA. *AIDS & behavior, 18,* 452-463. Doi:10.1007/s10461-013-0572-3

Hellard, M., Sacks-Davis, R. and Gold, J. (2009). Hepatitis C treatment for injection drug users: A review of the available evidence. *Clinical Infectious Diseases, 49,* 561-573. Doi:10.1086/600304

Hendrickson, B., Rosen, D. and Aune, K. R. (2011). An analysis of friendship networks, social connectedness, homesickness, and satisfaction levels of international students. *International Journal of Intercultural Relations, 35(3)*, 281-295. Doi:10.1016/j.ijintrel.2010.08.001

Heydari, A., Dashtgard, A. and Moghada, Z. E. (2014). The effect of Bandura's social cognitive theory implementation on addiction quitting of clients referred to addiction quitting clinics. *Iranian Journal of Nursing and Midwifery Research, 19(1)*, 19-23. PMCID: PMC3917180

Hickman, M., Dillon, J. F., Elliot, L., DeAngelis, D., Vickerman, P., Foster, G., Donnan, P., Eriksen, A., Flowers, P., Goldberg, D., Hollingworth, W., Ijas, S., Liddell, D., Mandal, S., Martin, N., Beer, L. J. Z., Drysdale, K., Fraser, H., Glass, R., Graham, L., Gunson, R. N, Hamilton, E., Harris, H., Harris, M., Harris, R. et al. (2019). Evaluating the population impact of hepatitis C direct acting antiviral treatment as prevention for people who inject drugs (EPIToPe) – a natural experiment (protocol). *BMJ Open, 9(9)*: e029538. Doi:10.1136/bmjopen-2019-029538

Higgins, A. and Conner, M. (2003). Understanding adolescent smoking: the role of the Theory of Planned Behaviour and implementation intentions. *Psychology, Health & Medicine, 8(2)*: 173-186. Doi:10.1080/1354850031000087555

Higgins, J. P. T. (2008). Commentary: heterogeneity in meta-analysis should be expected and appropriately quantified. *International Journal of Epidemiology, 37,* 1158–1160. Doi:10.1093/ije/dyn204

Higgins, J. P. T. and Green, S. (editors) (2011). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011].* The Cochrane Collaboration, 2011. Accessed online on 12/11/18 at handbook-5-1.cochrane.org

von Hippel, C., Brener, L. and Horwitz, R. (2018). Implicit and explicit internalized stigma: Relationship with risky behaviours, psychosocial functioning and healthcare access among people who inject drugs. *Addictive Behaviors, 76*: 305–311. Doi:10.1016/j.addbeh.2017.08.036

Hodder, R. K., Freund, M., Bowman, J., Wolfenden, L., Gillham, K., Dray, J. and Wiggers, J. (2016). Association between adolescent tobacco, alcohol and illicit drug use and individual and environmental resilience protective factors. *BMJ Open, 6*, e012688. Doi:10.1136/bmjopen-2016-012688

Hoffmann, T., Erueti, C. and Glasziou, P. (2013). Poor description of non-pharmacological interventions: analysis of consecutive sample of randomised trials. *BMJ, 347,* 1-10. Doi:10.1136/bmj.f3755

Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D., Altman, D. G., Barbour, V., MacDonald, H., Johnston, M., Lamb, S. E., Dixon-Woods, M., McCulloch, P., Wyatt, J. C., Chan, A. and Michie, S. (2014). Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ, 348,* 1-12. Doi:10.1136/bmj.g1687

Hofmann, W., Friese, M. and Wiers, R. W. (2008) Impulsive versus reflective influences on health behavior: a theoretical framework and empirical review. *Health Psychology Review, 2(2)*: 111-137. Doi:10.1080/17437190802617668

Hohman, Z. P., Crano, W. D., Siegel, J. T. and Alvaro, E. M. (2014). Attitude ambivalence, friend norms, and adolescent drug use. *Prevention Science, 15(1),* 65-74. Doi:10.1007/s11121-013-0368-8

Hooper, M. W., Baker, E. A. and McNutt, M. D. (2013). Associations between coping, affect, and social support among low-income African American smokers. *Addictive Behaviors, 38*: 2736-2740. Doi:10.1016/j.addbeh.2013.07.005

Horyniak, D., Higgs, P., Jenkinson, R., Degenhardt, L., Stoové, M., Kerr, T., Hickman, M., Aitken, C. and Dietze, P. (2013). Establishing the Melbourne injecting drug user cohort study (MIX): rationale, methods, and baseline and twelve-month follow-up results. *Harm Reduction Journal, 10*: 1-14. Doi:10.1186/1477-7517-10-11

Hovart, A. O. and Greenberg, L. S. (1989). Development and validation of the Working Alliance Inventory. *Journal of Counselling Psychology, 36(2),* 223-233. Doi:10.1037/0022-0167.36.2.223

Huang, S., Trapido, E., Fleming, L., Arheart, K., Crandall, L., French, M.,. Malcolm, S. and Prado, G. (2011). The long-term effects of childhood maltreatment experiences on subsequent illicit drug use and drug-related problems in young adulthood. *Addictive Behaviours, 36*: 95-102. Doi:10.1016/j.addbeh.2010.09.001

Hunt, K. and Burns, S. (2017). Is There an Association between Social Connectedness, Social Identity, Alcohol Consumption and Mental Health among Young University Students? *Open Journal of Preventive Medicine, 7,* 99-114. Doi:10.4236/ojpm.2017.76009

Hurley, B., Lin, K., Jani, S. N. and Kapila, K. (2017). Screening and Assessment of Trauma in Clinical Populations. In: Eckstrand, K., Potter, J. (eds). *Trauma, Resilience, and Health Promotion in LGBT Patients*. Springer, Cham: 183-190.

Hurley, R. (2018). Slashed cost of hepatitis C drugs spurs drive to eliminate the disease: Unimaginable just a few years ago, new drugs for hepatitis C are becoming affordable for all. *BMJ, 361,* 1-2. Doi: 10.1136/bmj.k1679

I

Information Services Division ISD Scotland, NHS Scotland (2018a). *Prescribing for Opioid Dependence in Scotland – BNF Section 04.10.03*. Accessed online on 14 August 2019 at isdscotland.org

Information Services Division ISD Scotland, NHS Scotland (2018b). *Injecting Equipment Provision in Scotland 2016/17*. Accessed online on 21 November 2019 at isdscotland.org/Health-Topics/Drugs-and-Alcohol-Misuse/Publications/2018-08-07/2018-08-07-IEP-Report.pdf

Ingiliz, P., Wehmeyer, M. H., Boesecke, C., Schulze Zur Wiesch, J., Schewe, K., Lutz, T., Baumgarten, A., Simon, K. G., Hueppe, D., Rockstroh, J. K., Mauss, S., Christensen, S. European AIDS Treatment Network (NEAT) Study Group, German Hepatitis C Cohort (GECCO) Study Group (2019). Reinfection With the Hepatitis C Virus in Men Who Have Sex With Men After Successful Treatment With Direct-acting Antivirals in Germany: Current Incidence Rates, Compared With Rates During the Interferon Era. *Clinical Infectious Diseases, ciz949*.Doi:10.1093/cid/ciz949

Inglis, S. K., Beer, L. J. Z., Byrne, C., Malaguti, A., Robinson, E., Sharkey C., Gillings, K., Stephens, B. and Dillon, J. F. (2019). Randomised controlled trial conducted in injecting equipment provision sites to compare the effectiveness of different hepatitis C treatment regimens in people who inject drugs: A Direct observed therapy versys fortnightly CollEction study for HCV treatment – ADVANCE HCV protocol study. *BMJ Open, 9*: e029516. Doi:10.1136/bmjopen-2019-029516

International Alliance for Responsible Drinking – IARD (2018). *Drinking guidelines: General population*. Accessed online on 30 November 2018 at iard.org/resources/drinking-guidelines-general-population/

Islam, N., Krajden, M., Shoveller, J., Gustafson, P., Gilbert, M., Buxton, J. A., Wong, J., Tyndall, M. W., Janjua, N. Z., British Columbia Hepatitis Testers Cohort (BH-HTC) team. Incidence, risk factors, and prevention of hepatitis C reinfection: a population-based cohort study. *Lancet Gastroenterology & Hepatology, 2(3)*: 200-210. Doi:10.1016/S2468-1253(16)30182-0

J

Jafari, M., Shahidi, S. H. and Abedin, A. R. (2012). Comparing effectiveness of cognitive behavioural therapy and stages of change model on improving abstinence self-

efficacy in Iranian substance dependent adolescents. *Iranian Journal of Psychiatry and Behavioural Sciences, 6(2),* 7-15. PMCID: PMC3940013

Janda, M. and Mergenhagen, K. A. (2017). The Effect of Psychosocial Factors on Success Rates of Hepatitis C Treatment. *Psychosomatics, 58,* 624-663. Doi:10.1016/j.psym.2017.07.003

Janke, A. E., McGraw, S., Fraenkel, L. and Garcia-Tsao, G. (2008). Psychosocial correlates of hepatitis C: Interaction and impact on quality of life. *Psychosomatics, 49(6)*: 494-501. Doi:10.1176/appi.psy.49.6.494

Jauffret-Roustide, M., Cohen, J., Poisot-Martin, I., Spire, B., Gossop, M., Carrieri, M. P., Manif 2000 Study Group (2012). Distributive sharing among HIV-HCV co-infected injecting drug users: the preventive role of trust in one's physician. *AIDS Care, 24(2),* 232-238. Doi:10.1080/09540121.2011.596515

Jentsch, J. D. and Tayor, J. R. (1999). Impulsivity resulting from frontostriatal dysfunction in drug abuse: implications for the control of behavior by reward-related stimuli. *Psychopharmacology, 146(4)*: 373-390. Doi:10.1007/pl00005483

Jetten, J., Haslam, S. A., Cruwys, T., Greenway, K. H., Haslam, C. and Steffens, N. K. (2017). Advancing the social identity approach to health and well-being: Progressing the social cure research agenda. *European Journal of Social Psychology, 47*: 789-802. Doi:10.1002/ejsp.2333

Johnson, C. F., Barnsdale, L. R. and McAuley, A., (2016). *Investigating the role of benzodiazepines in drug-related mortality: A systematic review undertaken on behalf of the Scottish National Forum on Drug-Related Deaths*. Edinburgh: NHS Health Scotland.

Johnston, L., Ahmad, F., Stephens, B. S. and Dillon, J. F. (2017). *The Eradicate-C study – curing people who are actively injecting drugs of hepatitis C: The first step to elimination*. Abstract # ILC2017-RS-2530 presented at the International Liver Congress of the European Association for the Study of the Liver (EASL); 2017 19-23 April; Amsterdam, The Netherlands.

Jordan, A. E., Masson, C. L., Mateu-Gelabert, P., McKnight, C., Pepper, N., Bouche, K., Guzman, L., Kletter, E., Seewald, R. M., Des-Jarlais, D. C., Sorensen, J. L. and Perlman, D. C. (2013). Perceptions of drug users regarding hepatitis C screening and care: a qualitative study. *Harm Reduction Journal, 10(10)*: 1-8.

K

Kang, SY., Deren, S., Andia, J., Colón, H. M. and Robles, R. (2004). Effects of changes in

perceived self-efficacy on HIV risk behaviors over time. *Addictive Behaviors, 29(3)*: 567-574. Doi:10.1016/j.addbeh.2003.08.026

Karataş, T., Özen, S. and Kutlutürkan, S. (2017). Factor Structure and Psychometric Properties of the Brief Illness Perception Questionnaire in Turkish Cancer Patients *Asian-Pacific Journal of Oncology Nursing, 4(1)*, 77-83. Doi:10.4103/2347-5625.199080

Kemode, M., Crofts, N., Kumar, M. S. and Dorabjee, J. (2011). Opiod substitution therapy in resource-poor settings. *Bulletin of the WHO, 89,* 243. Doi:10.2471/BLT.11.086850

Kerr, T., Stoltz, J. A., Marshall, B. D. L., Lai, C., Strathdee, S. A. and Wood, E. (2009). Childhood Trauma and Injection Drug Use Among High-Risk Youth. *Journal of Adolescent Health, 45(3)*: 300-302. Doi:10.1016/j.jadohealth.2009.03.007

Khoury, L., Tang, Y. L., Bradley, B., Cubells, J. F. And Ressler, K. J. (2010). Substance use, childhood traumatic experience, and posttraumatic stress disorder in an urban civilian population. *Depression & Anxiety, 27*: 1077-1086. Doi:10.1002/da.20751

Kimber, J., Copeland, L., Hickman, M., Macleod, J., McKenzie, J., De Angelis, D. and Robertson, J. R. (2010). Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution treatment. *BMJ, 341,* 1-8. Doi:10.1136/bmj.c3172

Kirby, K. N., Petry, N. M., & Bickel, W. K. (1999). Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. *Journal of Experimental Psychology: General, 128(1)*; 78-87. Doi:10.1037/0096-3445.128.1.78

Kober, H. (2014). Emotion regulation in substance use disorders. In Gross, J. J. (Ed.) *Handbook of emotion regulation* (pp 428-446). New York City, NY: Guildford Press. 2nd Edition.

Kroenke, K., Spitzer, R. L. and Williams, J. B. W. (2001). The PHQ-9: Validity of a Brief Depression Severity Measure. *Journal of General Internal Medicine, 16(9)*, 606-613. Doi:10.1046/j.1525-1497.2001.016009606.x

Kroenke, K. and Spitzer, R. L. (2002). The PHQ-9: A New Depression Diagnostic and Severity Measure. *Psychiatric annals, 32(9),* 509-515. Doi:10.3928/0048-5713-20020901-06

Krug, E. G., Dahlberg, L. L., Mercy, J. A., Zwi, A. B. And Lozano, R. (eds). *World report on violence and health*. Geneva, World Health Organization, 2002. Accessed online

on 28 July 2020 at apps.who.int/iris/bitstream/handle/10665/42495/9241545615_eng.pdf?sequence=1

Krzeczkowska, A., Flowers, P., Chouliara, Z., Hayes, P. and Dickson, A. (2019). Experiences of diagnosis, stigma, culpability and disclosure in male patients with hepatitis C virus: An interpretative phenomenological analysis. *Health*: 1-17. Doi:10.1177/1363459319846939

Kumar, P. C., McNeely, J. and Latkin, C. A. (2016). 'It's not what you know but who you know'. Role of social capital in predicting risky injection drug use behaviour in a sample of people who inject drugs in Baltimore city. *Journal of substance Use, 21(6)*: 620-626. Doi:10.3109/14659891.2015.1122098

Kwasnicka, D., Presseau, J., White, M. and Sniehotta, F. F. (2013). Does planning how to cope with anticipated barriers facilitate health-related behaviour change? A systematic review. *Health Psychology Review, 7(2),* 129-145. Doi:10.1080/17437199.2013.766832

L

Lakon, C. M., Ennerr, S. T. and Norton, E. C. (2006). Mechanisms through which drug, sex partner and friendship network characteristics relate to risky needle use among high risk youth and young adults. *Social Science & Medicine, 63*: 2489-2499. Doi:10.1016/j.socscimed.2006.06.015

Lally, P. and Gardner, B. (2011). Promoting habit formation. *Health Psychology Review, 7(1)*: S137-S158. Doi:10.1080/17437199.2011.603640

Lambers, F. A. E., Prins, <., Xiomara, T., Molenkamp, R., Kwa, D., Brinkman, K., van der Meer, J. T. M., Schinkel, J., on behalf of the MOSAIC (MSM Observational Study of Acute Infection with hepatitis C) study group. *AIDS, 25(17)*: F21-F27. Doi:10.1097/QAD.0b013e32834bac44

Langston, S., Edwards, M. S., Lyvers, M. and Stapleton, P. (2016). Illness perceptions and treatment outcomes in Hepatitis C. *New Zealand Journal of Psychology, 45(2)*, 22-28. No doi.

Langston, S., Edwards, M. S., Lyvers, M. and Stapleton, P. (2017). The self-regulatory model of illness and adjustment outcomes in hepatitis C. *Professional Psychology: Research and Practice, 48(5)*, 317-326. Doi:10.1037/pro0000136

Langston, S., Edwards, M. S. and Lyvers, M. (2018). Illness Perceptions, Coping, Benefit Finding, and Adjustment in Individuals with Hepatitis C. *Australian Psychologist, 53(1)*, 87-96. Doi:10.1111/ap.12255

Latka, M. H., Hagan, H., Kapadia, F., Golub, E. T., Bonner, S., Campbell, J. V., Coady, M. H., Garfein, R. S., Pu, M., Thomas, D. L., Thiel, T. K. and Strathdee, S. A. (2008). A Randomized Intervention Trial to Reduce the Lending of Used Injection Equipment Among Injection Drug Users Infected With Hepatitis C. *American Journal of Public Health, 98(5)*: 853-861. Doi:10.2105/AJPH.2007.113415

Latkin, C. A., Forman, V., Knowlton, A. and Sherman, S. (2003). Norms, social networks, and HIV-related risk behaviours among urban disadvantaged drug users. *Social Science & Medicine, 56(3)*, 465-476. Doi:10.1016/S0277-9536(02)00047-3

Latkin, C., Yang, C., Srikrishnan, A. K., Solomon, S., Mehta, S. H., Celentano, D. D., Kumar, M. S., Knowlton, A. and Solomon, S. S. (2011). The relationship between social network factors, HIV, and Hepatitis C among injection drug users in Chennai, India. *Drugs & Alcohol Dependence, 117(1)*: 50-54. Doi:10.1016/j.drugalcdep.2011.01.005

Lazarus, J. V., Safreed-Harmon, K., Thursz, M. R., Dillon, J. F., El-Saved, M. H., Elsharkawy, A. M., Hatzakis, A., Jadoul, M., Prestileo, T., Razavi, H., Rockstroh, J. K., Wiktor, S. Z. and Colombo, M. (2018). The Micro-Elimination Approach to Eliminatinf Hepatitis C: Strategic and Operational Considerations. *Seminars in Liver Disease, 38(3)*: 181-192. Doi:10.1055/s-0038-1666841

Lee, K. H., Bowen S. and An-Fu, B. (2010). Psychosocial outcomes of mindfulness-based relapse prevention in incarcerated substance abusers in Taiwan: A preliminary study. *Journal of Substance Use, 16(6)*, 476-483. Doi:10.3109/14659891.2010.505999

Lee, R. M. and Robbins, S. B. (1995). Measuring belongingness: The Social Connectedness and the Social Assurance scales. *Journal of Counselling Psychology, 42(2)*, 232-241. Doi:10.1037/0022-0167.42.2.232

Leightley, D., Puddephatt, J. A., Jones, N., Mahmoodi, T., Chui, Z., Field, M., Drummond, C., Rona, R. J., Fear, N. T. and Goodwin, L. (2018). A Smartphone App and Personalized Text Messaging Framework (InDEx) to Monitor and Reduce Alcohol Use in Ex-Serving Personnel: Development and Feasibility Study. *Journal of Medical Internet Research Mhealth & Uhealth, 6(9)*:e10074. Doi:10.2196/10074

Lengfelder,A. and Gollwitzer, P. M. (2000). Reflective and reflexive action control in frontal lobe patients. *Neuropsychology, 15*: 80-100. Doi:10.1037/0894-4105.15.1.80

Leventhal, H., Meyer, D., Nerenz, D. R. (1980). The common sense model of illness danger. In: Rachman, S. (ed). *Medical Psychology*. Vol 2. New York, NY: Pergamon; 7–30.

Leventhal, H., Nerenz, D. R., Steele, D. J. (1984). Illness representations and coping with health threats. In: Baum, A., Taylor, S. E., Singer, J. E. (Eds). *Handbook of Psychology and Health: Social Psychological Aspects of Health*. Vol 4. Hillsdale, NJ: Erlbaum; 219–252.

Lewis, M. A., McBride, C. M., Pollak, K. I., Puleo, E., Butterfield, R. M. and Emmon, K. M. (2006). Understanding health behavior change among couples: An interdependence and communal coping approach. *Social Sciences & Medicine (62)*: 1369-1380. Doi:10.1016/j.socscimed.2005.08.006

Lim, S., Powell, T. W., Xue, Q.L., Towe, V. L., Taylor, R. B., Ellen, J. M. and Sherman, S. G. (2018). Exploratory and confirmatory factor analyses and invariance assessment f the perceived powerlessness scale among youth in Baltimore. *Journal of Health Psychology*: 1-13. Doi: 10.1177/1359105318769349

Løchting, I., Garrat, A. M., Storheim, K., Werner, E. L. and Grotle, M. (2013). Evaluation of the Brief Illness Perception Questionnaire in Sub-Acute and Chronic Low Back Pain Patients: Data Quality, Reliability and Validity. *Journal of Pain & Relief, 2(3)*, 1-6. Doi:10.4172/2167-0846.1000122

Luty, J. (2015). Drug and alcohol addiction: do psychosocial treatments work? *British Journal of Psychiatric Advances, 21(2)*, 132-143. Doi:10.1192/apt.bp.114.013177

Lyons, R. F., Michelson, K. D., Sullivan, M. J., Coyne, J. C. (1998). Coping as a communal process. *Journal of Social & Personal Relationships, 15(5),* 579-605. Doi:10.1177/0265407598155001

M

Mackesy-Amiti, M. E., Donenberg, G. R. and Ouellet, L. J. (2014). Psychiatric correlates of injection risk behaviour among young people who inject drugs. *Addictive Behaviours, 28(4)*: 1089-1095. Doi:10.1037/a0036390

Magura, S., Grossman, J. I., Lipton, D. S., Siddigi, Q., Shapiro, J., Marion, I. and Amann, K. R. (1989). Determinants of needle sharing among intravenous drug users. *American Journal of Public Health, 79(4)*: 459-462. Doi:10.2105/ajph.79.4.459

Magura, S., Rosenblum, A. and Fong, C. (2012). Factors associated with medication adherence among psychiatric outpatients at substance abuse risk. *Open Addiction Journal, 4,* 58-64. Doi:10.2174/1874941001104010058

Mann, A. G., Ramsay, M. E., Brant, L. J., Balogun, M. A., Costella, A. and Harris, H. E. (2013). Diagnoses of, and deaths from, severe liver disease due to hepatitis C in

England between 200 and 2005 estimated using multiple data sources. *Epidemiology & Infections, 137(4),* 513-518. Doi:10.1017/S0950268808001350

Manstead, A. S. R. and Semin, G. R. (1999). Methodology in social psychology: Putting ideas to the test. In Hewston, M., Stroebe, W. and Stephenson, G. M. (eds). *Introduction to social psychology*. Oxford: Blackwell Publishers. 75-106.

March, J. C., Oviedo-Joekes, E., Perea-Milla, E., Carrasco, F. and the PEPSA Team (2006). Controlled trial of prescribed heroin in the treatment of opioid addiction. *Journal of Substance Abuse Treatment, 31*: 203–211. Doi:10.1016/j.jsat.2006.04.007

Marsden, J., Gossop, M., Stewart, D., Best, D., Farrel, M., Ann, P. L., Edwards, C. and Strang J. (1998). The Maudsley Addiction Profile (MAP): a brief instrument for assessing treatment outcome. *Addiction, 93(12)*, 1857-1868. Doi: 10.1046/j.1360-0443.1998.9312185711.x

Martin, G. W., Wilkinson, D. A. and Poulos, C. X. (1995). The Drug Avoidance Self-Efficacy Scale. *Journal of Substance Abuse, 7(2)*, 151-163. Doi:10.1016/0899-3289(95)90001-2

Mathei, C., Shkedy, X., Denis, B., Kabali, C., Aerts, M., Molenberghs, G., Van Damme, P. and Buntix, F. (2006). Evidence for a substantial role of sharing of injecting paraphernalia other than syringes/needles to the spread of hepatitis C among injecting drug users. *Journal of Viral Hepatitis, 13(8)*: 560-570. Doi:10.1111/j.1365-2893.2006.00725.x

*Matcham, F., McNally, L. and Vogt, F. (2014). A pilot randomized controlled trial to increase smoking cessation by maintaining National Health Service Stop Smoking Service attendance. *British Journal of Health Psychology, 19*, 795-809. Doi:10.1111/bjhp.12078

Matthieu, M. M., Wilson, A., and Casner, R. W. (2017). Interdisciplinary Issues at the Intersection of Assessing and Treating Substance Use Disorders and Post Traumatic Stress Disorder: Clinical Social Work and Clinical Behavioral Analysis with Veterans. *Advances in Social Work, 18(1)*, 217-234. Doi:10.18060/21320

Mcdonald, S. A., Hutchinson. S. J., Schnier, C., McLeod, A. and Goldberg, D. J. (2014). Estimating the number of injecting drug users in Scotland's HCV-diagnosed population using capture-recapture methods. *Epidemiology & Infections, 142(1),* 200-207. Doi:10.1017/S0950268813000617

McDowell, I. (2006). *Measuring health: a guide to rating scales and questionnaires*. Oxford University Press: Oxford. Third Edition.

McGowan, C., Harris, M. and Rhodes, T .(2013). Hepatitis C avoidance in injection drug users: a typology of possible protective practices. *PLoS ONE, 8(10)*: 1-7. Doi:10.1371/journal.pone.0077038

McHugh, M. L. (2012). Inter-rater reliability: The kappa statistic. *Biochemia Medica, 22(3),* 276-282. Doi:10.11613/BM.2012.031

McLeod, J. (2011). *Qualitative research in counselling and psychotherapy.* London: Sage. 2nd Edition.

Medić, Dzelalija, B., Sonicki, Z. and Zekanović, D. (2008). Characteristics of hepatitis C infection in injecting drug users in Zadar County, Croatia. *Collegium Antrolopogicum , 32(3)*: 697-702. PMID:18982740

Mehta, S. H., Genberg, B. L., Astemborski, J., Kavasery, R., Kirk, G. D., Vlahov, D., Strathdee, S. A. and Thomas, D. L. (2008). Limited uptake of hepatitis C treatment among injection drug users. *Journal of Community Health, 33(3)*: 126-133. Doi:10.1007/s10900-007-9083-3

Meier, P. S., Barrowclough, C. and Donmall, M. C. (2005). The role of the therapeutic alliance in the treatment of substance misuse: a critical review of the literature. *Addiction, 100(3),* 304-316. Doi:10.1111/j.1360-0443.2004.00935.x

Menard, S. (1995). *Applied logistic regression analysis.* Sage University Paper Series on Quantitative Applications in the Social Sciences, 07-106. Thousand Oaks, CA: Sage.

Michie, S., Richardson, M., Johnston, M., Abraham, C., Francis, J., Hardeman, W., Eccles, M. P., Cane, J. and Wood, C. E. (2013). The Behavior Change Technique Taxonomy (v1) of 93 Hierarchically Clustered Techniques: Building an International Consensus for the Reporting of Behavior Change Interventions. *Annals of Behavioral Medicine, 46(1),* 81-95. Doi:10.1007/s12160-013-9486-6

Midgard, H., Bjøro, B., Mæland, A., Konopski, Z., Kileng, H., Damås, J. K., Paulsen, J., Heggelund, L., Sandvei, P. K., Ringstad, J. O., Karlsen, L. N., Stene-Johansen, K., Pettersson, J. H. O., Dorenberg, D. H. and Dalvarg, O. (2016a). Hepatitis C reinfection after sustained virological response. *Journal of Hepatology, 64(5)*: 1020-1026. Doi:10.1016/j.jhep.2016.01.001.

Midgard, H., Weir, A., Palmateer, N., Lo Re III, V., Pineda, J. A., Macías, J. and Dalgard, O. (2016b). HCV epidemiology in high-risk groups and the risk of reinfection. *Journal of Hepatology, 65(1)*: S33-S45. Doi:10.1016/j.jhep.2016.07.012

Midgard, H., Hajarizadeh, B., Cunningham, E. B., Conway, B., Backmund, M., Bruggmann, P., Bruneau, J., Bourgeois, S., Dunlop, A., Foster, G. R., Hellard, M.,

Robaeys, G., Thurnheer, M. C., Weltman, M., Amin, J., Mark, P. S., Quiene, S., Dore, G. J., Dalgard, O., Grebeley, J. on behalf of the ACTIVATE Study Group (2017). Changes in risk behaviours during and following treatment for hepatitis C virus infection among people who inject drugs: The ACTIVATE study. *International Journal of Drug Policy, 47,* 230-238. Doi:10.1016/j.drugpo.2017.05.040

Miller, K., Wakefield, J. R. H. and Sani, F. (2017). On the reciprocal effects between multiple group identifications and mental health: A longitudinal study of Scottish adolescents. *British Journal of Clinical Psychology, 54(4)*, 357-371. Doi:10.1111/bjc.12143

Miller, P. G. (2005). Scapegoating, self-confidence and risk comparison: the functionality of risk neutralisation and lay epidemiology by injecting drug users. *International Journal of Drug Policy*, *16(4)*: 246–53. Doi:10.1016/j.drugpo.2005.05.001

Milne, S., and Sheeran, P. (2002). *Combining motivational and volitional interventions to prevent testicular cancer: Testing the interaction between protection motivation theory and implementation intentions*. Paper presented at the 13th General Meeting of the European Association of Experimental Social Psychology: San Sebastian, Spain.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G. and The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Medicine 6(7),* e1000097. Doi:10.1371/journal.pmed.1000097

Morgan, K., Lee, J. and Sebar, B. (2015). Community health workers: A bridge to healthcare for people who inject drugs. *International Journal of Drug Policy, 26(4),* 380-387. Doi:10.1016/j.drugpo.2014.11.001

Muñoz, F., Burgos, J. L., Cuevas-Mota, J., Teshale, E. and Garfein, R. S. (2015). Individual and socio-enironmental factors addociated with unsafe injection practices among young adult injection drug users in San Diego. *AIDS Behavior, 19(1)*: 199-210. Doi:10.1007/s10461-014-0815-y

Murdoch, B. and Caulfield, T. (2016). Doing Research with Vulnerable Populations: The Case of Intravenous Drug Users. *BioéthiqueOnline: Canadian Journal of BioEthics, 5/32*: 1-11

*Murgraff, V., Abraham, C. and McDermott, M. (2007). Reducing Friday alcohol consumption among moderate, women drinkers: evaluation of a brief

evidence-based intervention. *Alcohol & Alcoholism, 42(1),* 37-41. Doi:10.1093/alcalc/ag1083

Murray, T., Rodgers, W. and Fraser, S. (2005). The effects of implementation intentions on exercise self-efficacy and behaviour. *Psychology and Health, 20*: 186–187. No doi.

Myers, R. (1990). *Classical and modern regression with applications*. 2nd Edition. Boston, Duxbury.

N

Nasir, S. and Rosenthal, D. (2009). The social context of initiation into injecting drugs in slums of Makassar, Indonesia. *International Journal of Drug Policy, 20(3)*: 327-343. Doi:10.1016/j.drugpo.2008.02.001

National Institute for Drug Abuse (2020). *Drug Misuse and Addiction*. Accessed online on 26 July 2020 at drugabuse.gov/publications/drugs-brains-behavior-science-addiction/drug-misuse-addiction

National Institute for Health & Care Excellence - NICE (2007a). *Methadone and buprenorphine for the management of opioid dependence*. Accessed online on 1 August 2019 at nice.org.uk/guidance/ta114

National Institute for Health & Care Excellence – NICE (2007b). *Drug misuse in over 16s: psychosocial interventions.* Accessed online on 20 July 2020 at nice.org.uk/guidance/cg51

National Records of Scotland (2019). *Drug-related deaths in Scotland in 2018*. Accessed online on 26 November 2019 at nrscotland.gov.uk/files/statistics/drug-related-deaths/2018/drug-related-deaths-18-pub.pdf

Ndoro, S. (2014). Effective multidisciplinary working: the key to high-quality care. *British Journal of Nursing, 23(13)*: 724-727. Doi:10.12968/bjon.2014.23.13.724

Neaigus, A., Friedman, S. R., Jose, B., Goldstein, M. F., Curtis, R., Ildefonso, G. and Des Jarlais, D. C. (1996). High-risk personal networks and syringe sharing as risk factors for HIV infection among new drug injectors. *Journal of Acquired Immune Deficiency Syndromes, 11(5)*: 499–509. Doi:10.1097/00042560-199604150-00011

Neaigus, A., Gyarmathy, A., Miller, M., Frajzyngier, V. M., Friedman, S. R. and Des Jarlais, D. C. (2006). Transitions to injecting drug use among noninjecting heroin users – Social network influence and individual susceptibility. *Journal of Acquired Immune Deficiency Syndromes, 41(4)*: 493-503. Doi:10.1097/01.qai.0000186391.49205.3b

Neale, J., Tompkins, C. and Shear, L. (2008). Barriers to accessing generic health and social care services: A qualitative study of injecting drug users. *Health and Social Care in the Community, 16(2),* 147-154. Doi:10.1111/j.1365-2524.2007.00739.x

Nelson, P. K., Mathers, B. M., Cowie, B., Hagan, H., Des Jarlais, D., Horyniak, D. and Degenhardt, L. (2011). Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet, 378(9791)*, 571-583. Doi: 10.1016/S0140-6736(11)61097-0

Newcombe, R. (1992). The reduction of drug related harm: a conceptual framework for theory, practice and research. In, O'Hare et al (Eds.)*. The reduction of drug related harm*. London Routledge.

NHS Education for Scotland (2017). *NES Transforming psychological trauma: A knowledge and skills framework for the Scottish workforce*. Accessed online on 9 April 2020 at nes.scot.nhs.uk/media/3983113/NationalTraumaTrainingFramework-execsummary-web.pdf

NHS England (2014). *The NHS five year forward view*. Accessed online on 16 April 2020 at england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.pdf

Nicolls, J., Cramer, S., Ryder, S., Gold, D., Priyadarshi, S., Millar, S., Hunter, C., Hogg, R., Jones, A., Measham, F., Stevens, A., Hamilton, I., McPhee, I., Eastwood, N. and Powell, M. (2019). The UK Government must help end Scotland's drug-related death crisis. *The Lancet Psychiatry, 6 (10)*: 804. Doi:10.1016/S2215-0366(19)30301-3

*Norman, P. and Wrona-Clarke, A. (2016). Combining self-affirmation and implementation intentions to reduce heavy episodic drinking in university students. *Psychology of Addictive Behaviors, 30(4),* 434-441. Doi:10.1037/adb0000144

*Norman, P., Cameron, D., Epton, T., Webb, T. L., Harris, P. R., Millings, A. and Sheeran, P. (2018). A randomized controlled trial of a brief online intervention to reduce alcohol consumption in new university students: Combining self-affirmation, theory of planned behaviour messages, and implementation intentions. *British Journal of Health Psychology, 23*, 108-127. Doi: 10.1111/bjhp.12277

Nunnally, J. C. (1967). *Psychometric theory.* New York: McGraw-Hill.

Nydegger, L. A., Keeler, A. R., Hood, C., Siegel, J. T. and Stacy, A. W. (2013). Effects of a one-hour intervention on condom implementation intentions among drug users in Southern California. *AIDS Care, (25: 12)*: 1586-1591.

Doi:10.1080/09540121.2013.793271

O

O'Keefe, D., Bluthenthal, R. N., Kral, A. H., Aitken, C. K., McCormack, A. and Dietze, P.M. (2019). Measures of harm reduction service provision for people who inject drugs. *Bulletin of the World Health Organisation, 97*: 605-611. Doi:10.2471/BLT.18.224089

Ogden, J. (2012). *Health Psychology: A Textbook*. Berkshire, England. Open University Press: McGraw-Hill Education. 5th Edition.

Ompad, D. C., Ikeda, R. M., Shah, N., Fuller, C. M, Bailey, S., Morse, E., Kerndt, P., Maslow, C., Wu, Y., Vlahov, D., Garfein, R., Strathdee, S. A. and for The Collaborative Injectiion Drug Users Study II (2005). Childhood sexual abuse and age at initiation of injection drug use. *American Journal of Public Health, 95(4)*: 703-709. Doi:10.2105/AJPH.2003.019372

Orne, M.T. (1962). On the social psychology of the psychological experiment: With particular reference to demand characteristics and their implications. *American Psychologist, 17,* 776-783. Doi:10.1037/1522-3736.5.1.535a

Orosz, G., Dombi, E., Tóth-Király, I., Bőthe, B., Jagodics, B. and Zimbardo, P. G. (2016). Academic cheating and time perspective: Cheaters live in the present instead of the future. *Learning and Individual Differences, 52,* 39-45. Doi:10.1016/j.lindif.2016.10.007

Orosz, G., Dombi, E., Tóth-Király, I. And Roland-Levy, C. (2017). The less is more: the 17-item Zimbardo Time Perspective Inventory. *Current Psychology, 36(1),* 39-47. Doi:10.1007/s12144-015-9382-2

Oviedo-Joekes, E., Brissette, S., Marsh, D., Lauzon, P., Guh, D., Anis, A. and Schechter, M. T. (2009). Diacetylmorphine versus methadone for the treatment of opiate addiction. *The New England Journal of Medicine, 361*: 777–786. Doi: 10.1056/NEJMoa0810635

Owiti, J. A., Greenhalgh, T., Sweeney, L., Foster, G. R. and Bhiu, K. S. (2015). Illness perceptions and explanatory models of viral hepatitis B & C among immigrants and refugees: a narrative systematic review. *BMC Public Health, 15*:151. Doi:10.1186/s12889-015-1476-0

P

Palfai, T. P. (2006). Automatic processes in the self-regulation of addictive behaviors. In Wiers, R. W. and Stacy, A. W. (Eds). *Handbook of Implicit Cognition and Addiction* (pp. 411-424). Thousand Oaks, California: SAGE Publications Inc.

Palmateer, N. E., Hutchinson, S. J., McLeod, A., Codere, G. and Goldberg, D. J. (2007). Comparison of deaths related to Hepatitis C and AIDS in Scotland. *Journal of Viral Hepatitis, 14(12),* 870-4. Doi:10.1111/j.1365-2893.2007.00876.x

Pawa, D. and Areesantichai, C. (2016). Effectiveness of the behaviour change intervention to improve harm reduction self-efficacy among people who inject drugs in Thailand. *Psychology Research Behavior Management, 9*: 247-252. Doi:10.2147/PRBM.S112147

Pawlotsky, J. M. (2004). Pathophysiology of hepatitis C virus infection and related liver disease. *Trend in Microbiology, 12(2),* 96-102. Doi:10.1016/j.tim.2003.12.005

Pawlotsky, J., Field, J., Zeuzem, S. and Hoofnagle, J. (2015). From non-A, non-B hepatitis to hepatitis C virus cure, *Journal of Hepatology, 62(1),* S87-S99. Doi:10.1016/j.jhep.2015.02.006

Pearce, M. E., Christian, W. M., Patterson, K., Norris, K., Moniruzzaman, A., Craib, K. J. P., Schechter, M. T., Spittal, P. M., for The Cedar Project Partnership (2008). The Cedar Project: Historical trauma, sexual abuse and HIV risk among young Aboriginal people who use injection and non-injection drugs in two Canadian cities. *Social Science & Medicine, 66(11)*: 2185-2194. Doi:10.1016/j.socscimed.2008.03.034

Penrose Enquiry (2015). *The Penrose Enquiry – Final report (Lord Penrose)*. Accessed online on 10 October 2017 at penroseinquiry.org.uk/finalreport/

Perdue, T., Hagan, H., Thiede, H. and Valleroy, L. (2003). Depression and HIV risk behaviour among Seattle-area injection drug users and young men who have sex with men. *AIDS Education & Prevention, 15(1)*: 81-92. Doi:10.1521/aeap.15.1.81.23842

Perneger, T. V., Giner, F., del Rio, M. and Mino, A. (1998), Randomised trial of heroin maintenance programme for addicts who fail in conventional drug treatment. *British Medical Journal 317*: 13–18. Doi:10.1136/bmj.317.7150.13

Petrie, K. J., Lana, A. and Devcich, D. A. (2007). The role of illness perceptions in patients with medical conditions. *Current Opinion in Psychiatry, 20(2)*, 163-167. Doi:10.1097/YCO.0b013e328014a871

Platt, L., Wall, M., Rhodes, T., Judd, A., Hickman, M., Johnston, L. G., Renton, A., Bobrova, N. and Sarang, A. (2006). Methods to Recruit Hard-to-Reach Groups: Comparing Two Chain Referral Sampling Methods of Recruiting Injecting Drug Users Across Nine Studies in Russia and Estonia. *Journal of Urban Health: Bulletin of the New York Academy of Medicine, 83(7)*, i39-i53. Doi:10.1007/s11524-006-9101-2

Plumridge, E. and Chetwynd, J. (1998). The moral universe of injecting drug users in the era of AIDS: Sharing injecting equipment and the protection of moral standing. *AIDS Care: Psychological and Socio-medical Aspects of AIDS/HIV, 10(6)*: 723-733. Doi:10.1080/09540129848343

Prestwich, A., Conner, M. and Lawton, R. J. (2006). Implementation Intentions: Can they be used to prevent and treat addiction?. In Wiers, R. W. and Stacy, A. W. (Eds). *Handbook of Implicit Cognition and Addiction* (pp. 455-470). Thousand Oaks, California: SAGE Publications Inc.

Prins, A., Bovin, M. J., Smolenski, D. J., Marx, B. P., Kimerling, R., Jenkins-Guarnieri M. A., Kaloupek, D. G., Schnurr, P. P., Kaiser, A. P., Leyva, Y. E. and Tiet Q. Q. (2016). The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): Development and Evaluation Within a Veteran Primary Care Sample. *Journal of Generic Internal Medicine, 31 (10)*, 1206-1211. Doi:10.1007/s11606-016-3703-5.

Prochaska, J. O., and DiClemente, C. C. (1983). Stages and processes of self-change in smoking: Toward an integrative model of change. *Journal of Consulting and Clinical Psychology, 51(3)*: 390–395. Doi:10.1037//0022-006x.51.3.390

Przepiorka, A. and Blachnio, A. (2016). Time perspective in Internet and Facebook addiction. *Computers in Human Behavior, 60,* 13-18. Doi:10.1016/j.chb.2016.02.045 0747-5632

Public Health England – PHE (2014). *Hepatitis C in the UK, 2014 report*. Accessed online on 13 August 2015 at gov.uk/government/uploads

Public Health England – PHE (2017a). *Hepatitis C in England 2017 report: Working to eliminate hepatitis C as a major public health threat.* Accessed online on 19 September 2017 at gov.uk/government/publications/hepatitis-c-in-the-uk

Public Health England - PHE Department of Health & Social Care, Medicines & Healthcare Products Regulatory Service (2017b). *Widening the availability of Naloxone*. Accessed online on 18 November 2019 at gov.uk/government/publications/widening-the-availability-of-naloxone/widening-the-availability-of-naloxone

Public Health England – PHE (2019). *Hepatitis C in the UK 2019: Working to eliminate hepatitis C as a major public health threat.* Accessed online on 02 July 2019 at assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/831155/Hepatitis_C_in_the_UK_2019_report.pdf

Puhan, M. A., Soesilo, I., Guyatt, G. H. and Schünemann, H. J. (2006). Combining scores from different patient reported outcome measures in meta-analyses: when is it

justified? *Health Quality of Life Outcomes, 4(94),* 1-8. Doi:10.1186/1477-7525-4-94

Putnam, R. D. (2001). *Bowling Alone: The Collapse and Revival of American Community*. New York: Simon and Schuster Paperbacks.

Q

Quinn, K., Boone, L., Scheidel, J. D., Mateu-Gelabert, P., McGorray, S. P., Beharie, N., Cottler, L. B. and Khan, M. R. (2016). The relationships of childhood trauma and adulthood prescription pain reliever misuse and injection drug use. *Drug & Alcohol Dependence, 169*: 190-198. Doi:10.1016/j.drugalcdep.2016.09.021

R

Rachlin, H. (2000). *The science of self-control*. Cambridge, MA: Harvard University Press.

Rácz, J., Gyarmathy, V. A., Neaigus, A. and Ujhelyi, E. (2007). Injecting equipment sharing and perception of HIV and hepatitis risk among injecting drug users in Budapest. *AIDS Care, 19(1)*: 59-66. Doi:10.1080/09540120600722742

Radley, A., de Bruin, M., Inglis, S. K., Donnan, P. T. and Dillon, J. F. (2018). Clinical effectiveness of pharmacy-led versus conventionally delivered antiviral treatment for hepatitis C in patients receiving Opioid substitution therapy: a study protocol for a pragmatic cluster randomised trial. *Gastroenterology and hepatology, 8(12)*: 1-8. Doi:10.1136/ bmjopen-2017-021443

Rance, J., Treloar, C., Fraser, S., Bryant, J., Rhodes, T. (2017). "Don't think I'm going to leave you over it": Accounts of changing hepatitis C status among couples who inject drugs. *Drug & Alcohol Dependence, 173,* 78-84. Doi:10.1016/j.drugalcdep.2016.12.020

Reicher, S. (2000). Against methodolatry: Some comments on Elliott, Fischer, and Rennie. *British Journal of Clinical Psychology, 39*: 1-10. Doi:10.1348/014466500163031

Reynolds, B. (2006). A review of delay-discounting research with humans: relations to drug use and gambling. *Behavioural Pharmacology, 17*: 651-667. Doi:10.1097/FBP.0b013e3280115f99

Rhodes, T. (2008). Risk environments and drug harms: A social science for harm reduction approach. Editorial Essay. *Journal of Drug Policy, 20*: 193-201. Doi:10.1016/j.drugpo.2008.10.003

Rhodes, T., Davis, M. and Judd, A. (2004). Hepatitis C and its risk management among

drug injectors in London: renewing harm reduction in the context of uncertainty. *Addiction, 99(5),* 621-633. Doi:10.1111/j.1360-0443.2004.00692.x

Rhodes, T., Singer, M., Bourgois, P., Friedman, S. R. and Strathdee, S. A. (2005). The social production of HIV risk among injecting drug users. *Social Science & Medicine, 61*: 1026-1044. Doi:10.1016/j.socscimed.2004.12.024

Rhodes, T. and Trealor, C. (2008). The social production of hepatitis C risk among injecting drug users: a qualitative synthesis. *Addiction, 103*: 1593-1603. Doi:10.1111/j/1360-0443.2008.02306.x

Rigotti, N. A., Arnsten, J. H., McKool, K. M., Wood-Reid, K. M., Pasternak, R. C. and Singer, D. E. (1997). Efficacy of a smoking cessation program for hospital patients. Archives of Internal Medicine, 157(22): 2653–2660. Doi:10.1001/archinte.1997.00440430135016

Ritter, A. J., Fry, C. L. and Swan, A. (2003). The ethics of reimbursing injecting drug users for public health research interviews: what price are we prepared to pay? *International Journal of Drug Policy, 14(1)*: 1-3. Doi:10.1016/S0955-3959(02)00094-4

Rivis, A. and Sheeran, P. (2003). Descriptive norms as an additional predictor in the theory of planned behaviour: A meta-analysis. *Current Psychology, 22(3)*, 218-233. Doi:10.1007/s12144-003-1018-2

*Rivis, A. and Sheeran, P. (2013). Automatic risk behaviour: direct effects of binge drinkers stereotypes on drinking behaviour. *Health Psychology, 32(5),* 571-580. Doi:10.1037/a0029859

Robinson, T. E. and Berridge, K. C. (2003). Addiction. *Annual Review of Psychology, 54*: 25-53. Doi:10.1146/annurev.psych.54.101601.145237

Robles, R. R., Reyes, J. C., Colón, H. M., Sahai, H., Marrero, A., Mator, T. D., Calderón, J. M. and Shepard, E. W. (2004). Effects of combined counseling and case management to reduce HIV risk behaviors among Hispanic drug injectors in Puerto Rico: A randomized controlled study. *Journal of Substance Abuse Treatment, 27(2)*: 145-152. Doi:10.1016/j.jsat.2004.06.004

Rodgers, W. M., Hall, C. R., Blanchard, C. M., McAuley, E., & Munroe, K. J. (2002). Task and scheduling self-efficacy as predictors of exercise behaviour. *Psychology and Health, 17*: 405–516. Doi:10.1080/0887044022000004902

Ronksley, P. E., Brien, S. E., Turner, B. J., Mukamal, K. J. and Ghali, W. A. (2011). Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. *BMJ, 342*, d671.

Doi:10.1136/bmj.d671

Rosenthal, R. (1991). *Meta-analytic procedures for social research*. Newbury Park, CA: Sage. Revised Edition.

Rotily, M., Weilandt, C., Bird, S. M., Kall, K., van Haastrecht, H. J. A., Landolo, E., Rousseau, S. (2001). Surveillance of HIV infection and related risk behaviour in European prisons: A multicentre pilot study. *European Journal of Public Health, 11(3),* 243-250. Doi:10.1093/eurpub/11.3.243

Rousselet, G. A., Pernet, C. R., & Wilcox, R. R. (2019). A practical introduction to the bootstrap: A versatile method to make inferences by using data-driven simulations [Preprint]. Retrieved from PsyArXiv Website on 19.06.2020 Doi:0.31234/osf.io/h8ft7

Roux, P., Lions, C., Michel, L., Mora, M., Daulouède, JP, Marcellin, F., Spire, B., Morel, A., Carrieri, P. M., and the ANRS Methaville study group (2014). Factors associated with HCV risk practices in methadone-maintained patients: the importance of considering the couple in prevention interventions. *Substance abuse treatment, prevention, and policy, 9(37)*: 1-10. Doi: 10.1186/1747-597X-9-37

Roy, E., Haley, N., Leclerc, P., Cédras, L., Blais, L. And Boivin, J. F. (2003). Drug injection among street youths in Montreal: predictors of initiation. *Journal of Urban Health, 80(1)*: 92-105. Doi:10.1093/jurban/jtg092

Roy, E., Nonn, E., Haley, N. and Cox J. (2007). Hepatitis C meanings and preventative strategies among street-involved young injection drug users in Montréal. *International Journal of Drug Policy, 18*: 397–405. Doi:10.1016/j.drugpo.2007.02.005

S

Sabin, C. A., Lepri, A. and Phillips, A. N. (2000). A practical guide to applying the intention-to-treat principle to clinical trials in HIV infection. *HIV Clinical Trials, 1 (2)*: 31-38. Doi:10.1310/hct.2000.1.2.006

Safo, S. A., Batchelder, A., Peyser, D. and Litwin, A. H. (2015). The common sense model applied to hepatitis C: a qualitative analysis of the impact of disease comparison and witnessed death on hepatitis C illness perception. *Harm Reduction Journal, 12***:** 1-8. Doi:10.1186/s12954-015-0054-1

Sagnelli, E., Starace, M. and Minichini C., Pisauro, M., Macera, M., Sagnelli, C. and Coppola, N. (2018). Resistance detection and retreatment options in hepatitis C virus-related chronic liver diseases after DAA-treatment failure. *Infection, 46*:

761-783. Doi:10.1007/s15010-018-1188-3

Saleh, D. A., Amr, S., Jillson, I. A., Wang, J. H., Khairy, W. A. and Loffredo C. A. (2014). Knowledge and perception of hepatitis c infection and pesticides use in two rural villages in Egypt. *BMC Public Health, 14*: 501. Doi:10.1186/1471-2458-14-501

Samo, R. N., Agha, A., Shah, S. A., Altaf, A., Memon, A., Blevins, M., Qian, H. Z. And Vermund, S. H. (2016). Risk factors for loss to follow-up among people who inject drugs in a risk reduction program at Karachi, Pakistan. A case-control study. *PLoS One, 11(2)*: 1-11. Doi:10.1371/journal.pone.0147912

Sani, F., Madhok, V., Norbury, M., Dugard, P. and Wakefield, J. R. H. (2015a). Greater number of group identifications is associated with lower odds of being depressed: evidence from a Scottish community sample. *Social Psychiatry and Psychiatric Epidemiology, 50*: 1389-1397. Doi:10.1007/s00127-015-1076-4

Sani, F., Madhok, V., Norbury, M., Dugard, P. and Wakefield, J. R. H. (2015b). Greater number of group identifications is associated with healthier behaviour: Evidence from a Scottish community sample. *British Journal of Health Psychology, 20(3),* 466-481. Doi:10.1111/bjhp.12119

Savolainen, I., Kaakinen, M., Sirola, A. and Oksanen, A. (2018). Addictive behaviours and psychological distress among adolescents and emerging adults: A mediating role of peer group identification. *Addictive Behaviors Reports, 7*: 75-81. Doi:10.1016/j.abrep.2018.03.002

Schneider, J., Kaplan, S. H., Greenfield, S., Li, W. and Wilson, I. B. (2004). Better Physician-Patient Relationships Are Associated with Higher Reported Adherence to Antiretroviral Therapy in Patients with HIV Infection. *Journal of General Internal Medicine, 19(11),* 1096-1103. Doi:10.1111/j.1525-1497.2004.30418.x

Schofield, P.E., Pattison, P.E., Hill, D.J., & Borland, R. (2001). Youth culture and smoking: Integrating social group processes and individual cognitive processes in a model of health-related behaviours. *Journal of Health Psychology, 8*: 291–306. Doi:10.1177/13591053030083001

Schuckit, M. (2009). Alcohol-use disorders. *Lancet, 373,* 493-501. Doi:10.1016/S0140-6736(09)60009-X

Schulkind, J., Stephens, B., Ahmad, F., Johnston, L., Hutchinson, S., Thain, D., Ward, Z., Vicerman, P., Hickman, M. and Dillon, J. F. (2019). High response and re-infection rates among people who inject drugs treated for hepatitis C in a

community needle and syringe programme. *Journal of Viral Hepatitis, 26(5)*: 519-528. Doi:10.1111/jvh.13035

Schultz, K. F., Altman, D. G., Moher, D. and the CONSORT group (2010). CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMC Medicine, 8(18),* 1-9. Doi:10.1136/bmj.c332

Scottish Drugs Forum - SDF (2018). *MSPs support Scottish Government's pursuit of drug consumption facility.* Accessed online on 26 November 2019 at sdf.org.uk/msps-support-scottish-governments-pursuit-of-drug-consumption-facilities/

Scottish Drugs Forum – SDF (2019). *Heroin-assisted treatment to be provided in Glasgow.* Accessed online on 05 December 2019 at sdf.org.uk/heroin-assisted-treatment-provided-glasgow/

Scottish Government (2004). *Residential detoxification and rehabilitation services for drug users: a review*. Scottish Executive Effective Interventions Unit: Edinburgh. Accessed online on 21 November 2019 at dldocs.stir.ac.uk/documents/0012675.pdf

Scottish Government (2015a). *Sexual Health and Blood Borne Virus Framework 2015-2020 Update.* Accessed online on 15 May 2020 at gov.scot/publications/sexual-health-blood-borne-virus-framework-2015-2020-update/

Scottish Government (2015b). *Localities Guidance: Guidance on what localities are for, the principles upon which they should be established, and the ethos under which they should operate*. Accessed online on 31 July 2020 at gov.scot/publications/localities-guidance/

Scottish Government (2017). *2017-18 ADP Funding Allocations for Alcohol and Drug prevention, treatment and recovery support services*. Accessed online on 2 August 2019 at gov.scot/binaries/content/documents/govscot/publications/transparency-data/2019/03/alcohol-and-drug-partnerships-funding-allocations/documents/alcohol-and-drug-partnerships-funding-allocation-2017-2018/alcohol-and-drug-partnerships-funding-allocation-2017-2018/govscot%3Adocument/ADPs%2Bfunding%2Ballocation%2B2017-2018.pdf

Scottish Government (2019). *Policy in detail: Overdose prevention.* Accessed online on 19 November 2019 at gov.scot/Topics/Justice/policies/drugs-alcohol/overdose-prevention

Scottish Health Protection Network – Dillon, J. F. And Aspinall, E. J. (2019). *Recommendations on Hepatitis C Virus Case Finding and Access to Care. Report*

of the National Short Life Working Group. Glasgow: Health Protection Scotland. Accessed online on 19 November 2019 at hps.scot.nhs.uk/web-resources-container/recommendations-on-hepatitis-c-virus-case-finding-and-access-to-care/

Scottish Intercollegiate Guidelines Network - SIGN (2018*). Critical appraisal notes and checklists*. Accessed online on 6 September 2018 at sign.ac.uk/checklists-and-notes.html

Scottish Parliament Information Centre (SPICe) – part of the Scottish Parliament (2007). *SPICe Briefing: Drug Misuse.* SPICe, Scottish Parliamentary Corporate Body: Edinburgh. Accessed online on 2 August 2019 at parliament.scot/ResearchBriefingsAndFactsheets/S5/SB_17-22_Drug_Misuse.pdf

Severtson, S. G., Hedden, S. L., Martins, S. S. and Latimer, W. W. (2012). Patterns of cognitive impairments among heroin and cocaine users: the association with self-reported learning disabilities and infectious disease. *Journal of Learning Disabilities, 45(2)*: 139-150. Doi:10.1177/0022219409355481

Shahesmaeili, A., Mirzazadeh, A., McFarland, W., Sharifi, H., Haghdoost, A. A., Soori, H. (2018). Syringe Sharing in Drug Injecting Dyads: A Cross‐Classified Multilevel Analysis of Social Networks. *AIDS and Behavior, 22*: S10-S18. Doi: 10.1007/s10461-018-2144-z

Shaw, S. Y., Shah, L., Jolly, A. M., Wylie, J. L. (2007). Determinants of injection drug users (IDU) syringe sharing: the relationship between availability of syringes and risk network member characteristics in Winnipeg, Canada. *Addiction, 102(10),* 1626-1635. Doi:10.1111/j.1360-0443.2007.01940.x

Sheeran, P. (2002). Intention-behaviour relations: A conceptual and empirical review. *European Review of Social Psychology, 12*, 1-36. Doi:10.1080/14792772143000003

Sheeran, P., Milne, S., Webb, T. L. and Gollwitzer, P. M. (2005). Implementation intentions and health behaviour. In Conner, M. and Norman, P. (Eds): *Predicting health behaviour* (2nd Edition): 276-323. Maidenhead: Open University Press.

Sherman, S. G., Latkin, C. A. and Gielen, A. C. (2001). Social factors related to syringe sharing among injecting partners: a focus on gender. *Substance use and Misuse, 36(14)*: 2113-2136. Doi:10.1081/ja-100108439

Simmons, J., Rajan, S., McMahon, J. M. (2012). Retrospective accounts of injection initiation in intimate partnerships. *International Journal of Drug Policy, 23(4),* 303-311. Doi:10.1016/j.drugpo.2012.01.009

Skeer, M. R., Ladin, K., Wilkins, L. E.,, Landy, D. M. and Stopka, T. J. (2018). 'Hep C's like the common cold': understanding barriers along the HCV care continuum among young people who inject drugs. *Drug and Alcohol Dependence, 190*: 246–254. Doi: 10.1016/j.drugalcdep.2018.06.013

Skolnik, A. A., Noska, A., Yakovchenko, V., Tsai, J., Jones, N., Gifford, A. L., and McInnes, D. K. (2019). Experiences with interferon-free hepatitis C therapies: addressing barriers to adherence and optimizing treatment outcomes. *BMC Health Services Research, 19*: 1-7. Doi:10.1186/s12913-019-3904-9

Simpson, D. D., Jow, G. W. and Rowan-Szal, G. A. (1997). Drug abuse treatment retention and process effects on follow-up outcomes. *Drug & Alcohol Dependence, 47(3),* 227-235. Doi:10.1016/S0376-8716(97)00099-9

Siu, N. Y. F., Lam, H. H. Y., Le, J. J. Y. And Przepiorka, A. M (2014). Time perception and time perspective differences between adolescents and adults. *Acta Psychologica, 151*: 222-229. Doi:10.1016/j.actpsy.2014.06.013

Smith, L. R., Strathdee, S. A., Metzger, D. And Latkin, C. (2017). Evaluating network-level predictors of behaviour change among injection networks enrolled in the HPTN 037 randomized controlled trial. *Drug and Alcohol Dependence, 175*: 164-170. Doi:10.1016/j.drugalcdep.2017.02.007

Sniehotta, F. F., Presseau, J., and Araújo-Soares, V. (2014). Time to retire the theory of planned behaviour. *Health Psychology Review, 8(1)*: 1-7. Doi: 10.1080/17437199.2013.869710

Spitzer, R. L., Kroenke, K., Williams, J. B. W. and the Patient Health Questionnaire Primary Care Study Group (1999). Validation and Utility of a Self-report Version of PRIME-MD: The PHQ Primary Care Study. *Journal of American Medical Association, 282(18)*, 1737-1744. Doi:10.1001/jama.282.18.1737

Spitzer, R. L., Kroenke, K., Williams, J. B. W. and Löwe, B. (2006). A Brief Measure for Assessing Generalized Anxiety Disorder – The GAD-7. *Archived of Internal Medicine ,166(10)*,1092-1097. Doi:10.1001/archinte.166.10.1092

Steiberg, L., Graham, S., O'Brien, L., Woolard, J., Cauffman, E. and Banich, M. (2009). Age differences in future orientation and delay discounting. *Child Development, 80(1)*: 28-44. Doi:10.1111/j.1467-8624.2008.01244.x

Stevens, V. J., & Hollis, J. F. (1989). Preventing smoking relapse, using an individually tailored skills-training technique. *Journal of Consulting and Clinical Psychology, 57*(3): 420-424. Doi:10.1037/0022-006X.57.3.420

Stimson, G. V., Jones, S., Chalmers, C. and Sullivan, D. (1998). A short questionnaire (IRQ) to assess injecting risk behaviour. *Addiction, 93(3)*, 337-347.

Doi:10.1046/j.13600443.1998.9333373.x

Stoicescu, C., Cluver, L. D., Spreckelsen, T. F., Mahanani, M. M. and Ameilia, R. (2019). Intimate partner violence and receptive syringe sharing among women who inject drugs in Indonesia: A respondent-driven sampling study. *International Journal of Drug Policy, 63*: 1-11. Doi:10.1016/j.drugpo.2018.08.009

Strack, F., & Deutsch, R. (2004). Reflective and impulsive determinants of social behavior. *Personality and Social Psychology Review, 8(3)*: 220_247. Doi:10.1207/s15327957pspr0803_1

Strang, J., Metrebian, N., Lintzeris, N., Potts, L., Carnwath, T., Mayet, S., Williams, H., Zador, D., Evers, R., Groshkova, T., Charles, V., Martin, A. and Forzisi, L. (2010). Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin addicts in England after persistent failure in orthodox treatment (RIOTT): a randomised trial. *Lancet 375*: 1885–1895. Doi:10.1016/S0140-6736(10)60349-2

Streiner, D. L. (2008). Missing data and the trouble with LOCF. *Evidence Based Mental Health*, *11***:** 3– 5. Doi:10.1136/ebmh.11.1.3-a

Streiner, D. L. and Geddes, J. (2001). Intention to treat analysis in clinical trials when there are missing data. *Evidence-Based Mental Health, 4*: 70-71. Doi:10.1136/ebmh.4.3.70

Sublette, V. A., Smith, S. K., George, J., McCaffery, K. and Douglas, M. W. (2015). The hepatitis C treatment experience: Patients' perceptions of the facilitators of and barriers to uptake, adherence and completion. *Psychology & Health, 30(8)*: 987-1004. Doi:10.1080/08870446.2015.1012195

Sugarman, D. E., Nich, C. And Carroll, K. M. (2010). Coping strategy use following computerized cognitive-behavioural therapy for substance use disorders. *Psychology of Addictive Behaviors, 24(4)*: 689-695. Doi:10.1037/a0021584

Sully, B. G., Julious, S. A. and Nicholl, J. (2013). A reinvestigation of recruitment to randomised, controlled, multicenter trials: a review of trials funded by two UK funding agencies. *Trials,14*: 1-9. Doi:10.1186/1745-6215-14-166

Sussman, S., Dent, C. W. And McCullar, W. J. (2000). Group self-identification as a prospective predictor of drug use and violence in high-risk youth. *Psychology of Addictive Behaviors, 14(2)*: 192-196. Doi:10.1037/0893-164X.14.2.192

Sutton, S. (1998). Predicting and explaining intentions and behavior: how well are we doing? *Journal of Applied Social Psychology, 28(15),* 1317-1338. Doi:10.1111/j.1559-1816.1998.tb01679.x

Sutton, A. J., Abrams, K. R. and Jones, D. R. (2001). An illustrated guide to the methods of meta-analysis. *Journal of Evaluation in Clinical Practice, 7(2)*, 135-148. Doi:10.1046/j.1365-2753.2001.00281.x

Sutton, S., McVey, D. And Glanz, A. (1999). A comparative test of the theory of reasoned action and the theory of planned behaviour in the prediction of condom use intentions in a national sample of English young people. *Health Psychology (18:1)*: 72-81. Doi:10.1037/0278-6133.18.1.72

Swartzman, S., Sani, F. and Munro, A. J. (2017). The role of social support, family identification, and family constraints in predicting posttraumatic stress after cancer. *Psycho-oncology, 26(9)*, 1330-1335. Doi:10.1002/pon.4304

T

Tajfel, H., & Turner, J.C. (1979). An integrative theory of intergroup conflict. In W.G. Austin & S. Worchel (Eds.), *The social psychology of intergroup relations* (pp. 33–47). Monterey, CA: Brooks/Cole.

Tanner-Smith, E. E, Wilson, S. J. And Lipsey, M. W. (2013). The comparative effectiveness of outpatient treatment for adolescent substance abuse: a meta-analysis. *Journal of Substance Abuse Treatment, 44(2),* 145-158. Doi:10.1016/j.jsat.2012.05.006.

Terrault, N. A. (2002). Sexual activity as a risk factor for hepatitis C. *Hepatology, 36(5)*: S99– S105. Doi:10.1053/jhep.2002.36797

Thiede, H., Hagan, H., Campbell, J. V., Strathdee, S. A., Bailey, S. L., Hudson, S. M., Kapadia, F., Garfein, R. S. and DUIT Study Team (2007). Prevalence of correlated of indirect sharing practices among young adult injection drug users in give US cities. *Drug & Alcohol dependence (91:1)*: s39-s47. Doi:10.1016/j.drugalcdep.2007.03.001

Tiffany, S. T. (1990). A cognitive model of drug urges and drug-use behaviour: role of automatic and nonautomatic processes. *Psychological Review, 97(2)*: 147-168. Doi: 10.1037/0033-295x.97.2.147

Trafimow , D., Sheeran, P., Conner, M. And Finlay, K. A. (2002). Evidence that perceived behavioural control is a multidimensional construct: perceived control and perceived difficulty. *British Journal of Social Psychology, 41(1)*: 101-121. Doi:10.1348/014466602165081

Treloar, C., Rance, J. and Backmund, M. (2013a). Understanding barrier to hepatitis C virus care and stigmatization from a social perspective. *Clinical Infectious Diseases, 57(2)*: S51-S55. Doi:10.1093/cid/cit263

Treloar, C., Rance, J., Grebely, J. and Dore, G. J. (2013b). Client and staff experiences of a co-located service for hepatitis C care in opioid substitution treatment settings in New South Wales, Australia. *Drug & Alcohol Dependence, 133(2)*: 529-534. Doi:10.1016/j.drugalcdep.2013.07.023

Treloar, C. and Rhodes, T. (2009). The lived experience of hepatitis C and its treatment among injecting drug users: qualitative synthesis. *Qualitative Health Research, 19(9)*: 1321-1334. Doi:10.1177/1049732309341656

Tucker, D., Hayashi, K., Milloy, M. –J., Nolan, S., Dong, H., Kerr, T. and Wood, E. (2016). Risk factors associated with benzodiazepine use among people who inject drugs in an urban Canadian setting. A*ddictive Behaviors, 52*: 103-107. Doi:10.1016/j.addbeh.2015.10.002

Turner, K. M. E., Hutchinson, S., Vickerman, P., Hope, V., Craine, N., Palmateer, N., May, M., Taylor, A., De Angelis, D., Cameron, S., Parry, J., Lyons, M., Goldberg, D., Allen, E., Hickman, M. (2011). The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. *Addiction, 106(11)*, 1978-1988. Doi:10.1111/j.1360-0443.2011.03515.x

U

Unger, J. B., Kipke, M. D., De Rosa, C. J., Hyde, J., Ritt-Olson, A. and Montgomery, S. (2006). Needle-sharing among young IV drug users and their social network members: The influence of injection partner's characteristics on HIV risk behaviour. *Addictive Behaviors, 31(9)*: 1607-1618. Doi:10.1016/j.addbeh.2005.12.007

United Nations Office for Drugs and Crime - UNODC (2018). *World Drug Report 2018: Executive summary, conclusions and policy implications.* United Nations publications, Sales No. E.18.XI.9): Vienna. Accessed online on 19 November 2019 at unodc.org/wdr2018/prelaunch/WDR18_Booklet_1_EXSUM.pdf

V

Vahdat, S., Hamzehgardeshi, L., Hessam, S. and Hamzehgardeshi, Z. (2014). Patient involvement in health care decision making: A review. *Iranian Red Crescent Medical Journal, 16(1)*: e12454. Doi:10.5812/ircmj.12454

Valencia, J., Alvaro-Meca, A., Troya, J., Cuevas, G., Gutiérrez, J., Morro, A., Ivarez, J. A., Pulido, L., Cañamares, I., Escobar, I., Moreno, S. and Ryan, P. (2019). High rates of early HCV reinfection after DAA treatment in people with recent drug use attended at mobile harm reduction units. *International Journal of Drug Policy, 72*: 181-188. Doi:10.1016/j.drugpo.2019.06.016

Van Baelen, L. Plettinckx, E., Antoine, J. and Gremeaux, L. (2020). Prevalence of HCV among people who inject drugs in Brussels – a responsend-driven sampling survey. *Harm Reduction Journal, 17(11)*: 1-9. Doi:10.1186/s12954-020-00358-3

Verdejo-García, A., Lawrence, A. J., Clark, L. (2008). Impulsivity as a vulnerability marker for substance-use disorders: Review of findings from high-risk research, problem gamblers and genetic association studies. *Neuroscience & Biobehavioural Reviews, 32(4),* 777-810. Doi:1-/1-16/j/neubiorev.2007.11.003

W

Wagner, K. D., Bloom, J. J., Hathazi, S. D., Sanders, B. and Lankenau, S. E. (2013). Control over drug acquisition, preparation, and injection: Implication for HIV and HCV risk among young female injection drug users. *ISRN Addiction, 2013,* 1-9. Doi:10.1155/2013/289012

Wagner, K. D., Unger, J. B., Bluthenthal, R. N., Andreeva, V. A. and Pentz, M. A. (2010a). Cognitive Behavioural Theories used to explain injection risk behaviour among injection drug users: A review and suggestions for the integration of cognitive and environmental models. *Health Education & Behavior, 37(4)*: 504-532. Doi:10.1177/1090198109357319

Wagner, K. D., Lankenau, S. E., Palinkas, L. A., Richardson, J. L., Chou, C. P. and Unger, J. B. (2010b). The perceived consequences of safer injection: An exploration of qualitative findings and gender differences. *Psychology, Health & Medicine, 15(5),* 560-573. Doi:10.1080/13548506.2010.498890

Wallston, K. A., Wallston, B. S., Smith, S. and Dobbins, C. J. (1987). Perceived control and health. *Current Psychology, 6*: 5-25. Doi:10.1007/BF02686633

Walsh, A., Edwards, H. and Fraser, J. (2009). Attitudes and subjective norms: determinants of parents' intentions to reduce childhood fever with medications. *Health Education Research, 24(3)*, 531-545. Doi:10.1093/her/cyn055

Walters, S. T., Ondersma, S. J., Ingersoll, K. S., Rodriguez, M., Lerch, J., Rossheim, M. E. and Taxman, F. S. (2014). MAPIT: Development of a web-based intervention targeting substance abuse treatment in the criminal justice system. *Journal of Substance Abuse Treatment, 46*: 60-65. Doi:10.1016/j.sat.2013.07.003

Wang, Z., Du, J., Sun, H., Wu, H., Xiao, Z. and Zhao, M. (2010). Patterns of Childhood Trauma and Psychological Distress among Injecting Heroin Users in China. *PLoS ONE, 5(12)*: e15882. Doi:10.1371/journal.pone.0015882

Webb, T. L., and Sheeran, P. (2007). How do implementation intentions promote goal

attainment? A test of component processes. *Journal of Experimental Social Psychology, 43*: 295-302. Doi:10.1016/j.jesp.2006.02.001

Webb, T. L. and Sheeran, P. (2008). Mechanism of implementation intention effects: The role of goal intentions, self-efficacy, and accessibility of plan components. *British Journal of Social Psychology, 47(3)*, 373-395. Doi:10.1348/014466607X267010

*Webb, T. L., Sheeran, P. and Luszczynska, A. (2009). Planning to break unwanted habits: habit strength moderates implementation intention effects on behaviour change. *British Journal of Social Psychology, 48***,** 507-523. Doi:10.1348/014466608X370591

Weinstein, N. D. (1982(. Unrealistic optimism about susceptibility to health problems. *Journal of Behavioral Medicine, 5*: 441-460. Doi:10.1007/BF00845372

Whiteley, D., Whittaker, A., Elliott, L. and Cunningham-Burley, S. (2016). The lived experience of interferon-free treatments for hepatitis C: A thematic analysis. *International Journal of Drug Policy, 38*: 21-28. Doi:10.1016/j.drugpo.2016.10.013

Whiteley, D., Whittaker, A., Elliott, L. and Cunningham-Burley, S. (2017). Hepatitis C in a new therapeutic era: Recontextualising the lived experience. *Journal of Clinical Nursing, 27*: 2729-2739. Doi:10.1111/jocn.14083

Wieber, F., Odenthal, G. and Gollwitzer, P. (2010). Self-efficacy feelings moderate implementation intention effects. *Self & Identity, 9(2)*: 177-194. Doi: 10.1080/15298860902860333

Williams, K. L. and Galliher, R. V. (2006). Predicting depression and self-esteem from social connectedness, support, and competence. *Journal of Social and Clinical Psychology, 25(8)*, 855-874. Doi:10.1521/jscp.2006.25.8.855

Wilson, H., Brener, L., Mao, L. and Treloar, C. (2014). Perceived discrimination and injecting risk among people who inject drugs attending Needle and Syringe Programmes in Sydney, Australia. *Drug Alcohol Dependence, 144*: 274-278. Doi: 10.1016/j.drugalcdep.2014.08.018

Wolfe, D., Luhmann, N., Harris, M., Momenghalibaf, A., Albers, E., Byrne, J., Swan, F. (2015). Human rights and access to hepatitis C treatment for people who inject drugs. *International Journal of Drug Policy, 26(11),* 1072-1080. Doi:10.1016/j.drugpo.2015.05.007.

Wong, C. F., Silva, K., Kecojevic, A., Schrager, S. M., Bloom, J. J., Iverson, E. and Lankenau, S. E. (2013). Coping and emotion regulation profiles as predictors of

nonmedical prescription drug and illicit drug use among high-risk young adults. *Drug & Alcohol Dependence, 132 (1-2)*: 165-171. Doi: 10.1016/j.drugalcdep.2013.01.024

World Health Organization – WHO (2010). *Resolution A63/15: Viral hepatitis. 63rd World Health Assembly, 2010*. Accessed online on 19 September 2017 at apps.who.int

World Health Organization – WHO (2011). *Hepatitis C facts and figures.* Accessed online on 19 September 2017 at euro.who.int .

World Health Organization – WHO (2012). *Technical guide for countries to set targets for universal HIV services for injecting drug users.* Geneva: WHO. Accessed online on 20 November 2019 at who.int/iris/bitstream/handle/10665/77969/9789241504379_eng.pdf;jsessionid=45CA24D4892B47D438C3B76874146B95?sequence=1

World Health Organization - WHO (2014a). *Global status report on noncommunicable diseases 2014:"Attaining the nine global noncommunicable diseases targets; a shared responsibility"*. Geneva. Accessed online on 30 November 2018 at who.int/nmh/publications/ncd-status-report-2014/en/

World Health Organization -WHO (2014b). *Substance use. Community management of Opioid overdose.* Accessed online on 30 November 2018 at who.int/substance_abuse/publications/en

World Health Organization – WHO (2016a). *Global health sector strategy on viral hepatitis 2016-2012.* Geneva: WHO. Accessed online on 20 November 2019 at apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016.06-eng.pdf?sequence=1

World Health Organization – WHO (2016b). *Cannabis. The health and social effects of non-medical cannabis use*. Accessed online on 30 November 2018 at who.int/substance_abuse/publications/en

World Health Organization – WHO (2017a). *Global hepatitis report, 2017*. April 2017. Accessed online on 19 September 2017 at apps.who.int

World Health Organization – WHO (2017b). *WHO report on the global tobacco epidemic, 2017: monitoring tobacco use and prevention policies*. Geneva: World Health Organization; 2017. Accessed online on 30 November 2018 at who.int/tobacco/global_report/2017/en/

World Health Organization – WHO (2018a). *Combating hepatitis B and C to reach elimination by 2030.* Accessed online on 27 November 2019 at

who.int/iris/bitstream/handle/10665/206453/WHO_HIV_2016.04_eng.pdf;jsessionid=C96F72B8DDC1AC66F7A87CB8E99EBE98?sequence=1

World Health Organization –WHO (2018b). *Global status report on alcohol and health 2018.* Geneva. Accessed online on 30 November 2018 at who.int/substance_abuse/publications/global_alcohol_report/gsr_2018/en/

World Health Organization -WHO (2018c). *World Health Statistics data visualizations dashboard. Tobacco smoking: Prevalence of tobacco smoking.* Accessed online on 28 November 2018 at apps.who.int/gho/data/node.sdg.3-a-viz?lang=en

World Health Organization – WHO (2018d). *Progress report on access to hepatitis C treatment: focus on overcoming barriers in low- and middle-income countries, March 2018*. Geneva, Switzerland. Accessed online on 27 March 2020 at apps.who.int/iris/bitstream/handle/10665/260445/WHO-CDS-HIV-18.4-eng.pdf?sequence=1

Wozniak, L., Prakash, M., Taylor, M. and Cameron-Wild, T. (2007). Everybody's got it, but...: situational and strategic participation in normalized HCV discourse among injection drug users in Edmonton, Canada. *International Journal of Drug Policy, 18*: 388–96. Doi:10.1016/j.drugpo.2007.02.006

Z

Zalai, D., Sherman, M., McShane, K., Shapiro, C. M., Carney C. E. (2015). The importance of fatigue cognitions in chronic hepatitis C infection. *Journal of Psychosomatic Research, 78(2),* 193-198. Doi:10.1016/j.jpsychores.2014.11.011

Zapka, J. G., Stoddard, A. M., and McKusker, J. (1993). Social network, support, and influence: Relationships with drug use and protective AIDS behavior. *AIDS Education and Prevention, 5(4)*, 352–366. PMID:8297714

Zetterlind, U., Hansson, H., Åberg-Orbeck, K. and Berglund, M. (2001). Effects of coping skills training, group support, and information for spouses of alcoholics: A controlled randomized study. *Nordic Journal of Psychiatry, 55*: 257–262. No doi.

Zimbardo, P. G. And Boyd, J. N. (1999). Putting time in perspective: a valid, reliable individual-differences metric. *Journal of Personality & Social Psychology, 77(6),* 1271-88. Doi:10.1037/0022-3514.77.6.1271

Zywiak, W., Neighbors, C., Martin, R., Johnson, J., Eaton, C., & Rosenhow, D. (2009). The important people drug and alcohol interview: Psychometric properties, predictive validity and implications for treatment. *Journal of Substance Abuse Treatment, 36*: 321–330. Doi:10.1016/j.jsat.2008.08.001

10 Appendices

Appendix 10.1

Blank Case Report Form + Questionnaire Collection

ADAPT

Sponsor No. 2017PZ04

Participant ID

Site

CASE REPORT FORM

Integrating health psychology into hepatitis c treatment: a self-efficAcy intervention to reDuce injecting risk behAviour and hePatitis c reinfecTion rates

ADAPT

Chief Investigator: Prof John Dillon
Sponsor Number: 2017PZ04
ClinicalTrials.gov Number: NCT03293576
CRF Version Number: 3.1, 27/JUN/2018

Participant ID ☐☐☐ Randomised to ☐☐☐

ADAPT

Sponsor No. | 2 | 0 | 1 | 7 | P | Z | 0 | 4 |

Participant ID | | | |

Site | |

VISIT 1 (SCREENING) CONSENT AND DEMOGRAPHICS

Date of Assessment: _ _ / _ _ / _ _ _ _
(DD / MM / YYYY)

Informed Consent			
Date participant signed written consent form:	_ _ / _ _ / _ _ _ _ (DD / MM / YYYY)	**Date of first trial-related procedure:**	_ _ / _ _ / _ _ _ _ (DD / MM / YYYY)
Name of person taking informed consent: _____			

VISIT 1 (SCREENING) INCLUSION CRITERIA

The following criteria MUST be answered YES for participant to be included in the trial (except where NA is appropriate):		**Yes**	**No**
1.	Over 18 years of age;	☐	☐
2.	Chronic HCV positive infection;	☐	☐
3.	Current illicit drug use established through participants' self-report;	☐	☐
4.	Current HCV treatment provided by the NHS;	☐	☐
5.	Informed consent, agreeing to study and monitoring criteria;	☐	☐
6.	English-speaking.	☐	☐
If any of the above criteria is answered NO, the participant is NOT eligible for the trial and must not be included in the study. Please list reason(s) for ineligibility for screen failure on Participant Eligibility Review page.			

ADAPT

Sponsor No. | 2 | 0 | 1 | 7 | P | Z | 0 | 4 |

Participant ID | | | |

Site | |

VISIT 1 (SCREENING) **EXCLUSION CRITERIA**

The following criteria MUST be answered NO for the participant to be included in the trial:		**Yes**	**No**
1.	Inability to provide informed consent;	☐	☐
2.	Aggressive or violent behaviour;	☐	☐
3.	Not currently receiving HCV treatment;	☐	☐
4.	Inability to communicate in English.	☐	☐
If any of the above criteria is answered YES, the participant is NOT eligible for the trial and must not be included in the study. Please list reason(s) for ineligibility for screen failure on Participant Eligibility Review page.			

Participant's eligibility Investigator Sign-Off:	
Is the participant eligible to take part in the Clinical Trial? **Investigator's Signature**: _____ **Date** : _ _ / _ _ / _ _ _ _ (DD / MM / YYYY) **Investigator's Name:** _____	☐ Yes ☐ No, Please give reason for screen failure below
Reason(s) for screen failure:	
1.	
2.	
3.	

ADAPT

Sponsor No. | 2 | 0 | 1 | 7 | P | Z | 0 | 4 |

Participant ID | | | |

Site | |

VISIT 1 **Questionnaires**

Date of Assessment: _ _ / _ _ / _ _ _ _
(DD / MM / YYYY)

Age (in years):_____Gender: M / F / Other

Genotype: ☐ 1 or ☐ 3

Do you have a partner? ☐ Yes ☐ No ☐ Do not wish to answer

Does your partner inject drugs? ☐ Yes ☐ No ☐ Do not wish to answer ☐ N/A

Is your partner also on HCV treatment? ☐ Yes ☐ No ☐ Do not wish to answer ☐ N/A

In the last week, how many times have you injected?_____

Injecting Risk Questionnaire (IRQ)	**Completed:** ☐
Group Identification Scale (GIS)	**Completed:** ☐
Patient Health Questionnaire (PHQ-9)	**Completed:** ☐
General Anxiety Disorder (GAD-7)	**Completed:** ☐
Post-Traumatic Stress Disorder (PTSD-5)	**Completed:** ☐
Illness Perception Questionnaire (B-IPQ)	**Completed:** ☐

ADAPT

Sponsor No. | 2 | 0 | 1 | 7 | P | Z | 0 | 4 |

Participant ID | | | |

Site | |

VISIT 2 **RANDOMISATION**

Date of Visit:	__ __ / __ __ / __ __ __ __ (DD / MM / YYYY)

Participant Randomisation	
Participant study Group allocated:	_____
Date of Randomisation:	__ __ / __ __ / __ __ __ __ **(DD / MM / YYYY)**

Visit Checklist:			
		Yes	**No**
1.	**Have there been any new Adverse Events?** (If yes, please record in Adverse Events page)	☐	☐
2.	**Does participant continue to provide consent?**	☐	☐

VISIT 2 **QUESTIONNAIRES**

Date of Assessment: __ __ / __ __ / __ __ __ __ (DD / MM / YYYY)

In the last week, how many times have you injected? _____

Self-Efficacy Scale (SES) **Completed:** ☐

Social Connectedness Scale (SCS) **Completed:** ☐

Intervention/control (VHS/ZTPI) **Completed:** ☐

Social Norms Scale (SNS) **Completed:** ☐

ADAPT

Sponsor No. | 2 | 0 | 1 | 7 | P | Z | 0 | 4 |

Participant ID | | | |

Site

VISIT 3 END OF TREATMENT

Date of Visit: __ __ / __ __ / __ __ __ __
(DD / MM / YYYY)

Visit Checklist:

		Yes	No
1.	**Have there been any new Adverse Events?** (If yes, please record in Adverse Events page)	☐	☐
2.	**Does participant continue to provide consent?**	☐	☐

VISIT 3 QUESTIONNAIRES

Date of Assessment: __ __ / __ __ / __ __ __ __
(DD / MM / YYYY)

In the last week, how many times have you injected? _____

Injecting Risk Questionnaire (IRQ) **Completed:** ☐

Self-Efficacy Scale (SES) **Completed:** ☐

Social Norms Scale (SNS) **Completed:** ☐

Group Identification Scale (GIS) **Completed:** ☐

Patient Health Questionnaire (PHQ-9) **Completed:** ☐

General Anxiety Disorder (GAD-7) **Completed:** ☐

Working Alliance Inventory (WAI-SR) **Completed:** ☐

Illness Perception Questionnaire (B-IPQ) **Completed:** ☐

ADAPT

Sponsor No. | 2 | 0 | 1 | 7 | P | Z | 0 | 4 |

Participant ID | | | |

Site | |

VISIT 4 3-MONTH FOLLOW-UP

Date of Visit: __ __ / __ __ / __ __ __ __
(DD / MM / YYYY)

Visit Checklist:

		Yes	No
1.	**Have there been any new Adverse Events?** (If yes, please record in Adverse Events page)	☐	☐
2.	**Does participant continue to provide consent?**	☐	☐

VISIT 4 QUESTIONNAIRES

Date of Assessment: __ __ / __ __ / __ __ __ __
(DD / MM / YYYY)

In the last week, how many times have you injected? _____

Injecting Risk Questionnaire (IRQ) **Completed:** ☐

Self-Efficacy Scale (SES) **Completed:** ☐

Group Identification Scale (GIS) **Completed:** ☐

Illness Perception Questionnaire (B-IPQ) **Completed:** ☐

VISIT 4 SVR_{12} RESULT

SVR12 Achieved? Yes ☐ No ☐

Volitional Help Sheet

Kept in visible place ☐ Kept but not visible ☐ Did NOT keep ☐ Lost ☐ N/A (Control) ☐

ADAPT

Sponsor No. 2017PZ04

Participant ID ☐☐☐

Site ☐

TRIAL COMPLETION

Did participant complete the trial?	☐ **Yes,** Please provide **date of last visit**: __ __ / __ __ / 2 0 __ __ (DD / MM / YYYY) ☐ **No,** Please provide **date of withdrawal** and complete below: __ __ / __ __ / 2 0 __ __ (DD / MM / YYYY)

Did participant:

Achieve SVR_{12}? ☐ Yes ☐ No

Reinfect with HCV? ☐ Yes ☐ No

Early Withdrawal: please tick most appropriate reason for participant not completing the trial:

☐ **Adverse Events related:** please state related AE: _____ (add details to AE page)

☐ **Participant's decision, specify:** _____

☐ **Investigator's decision, specify:** _____

☐ **Sponsor's decision**

☐ **Withdrawn from HCV treatment**

☐ **Lost to follow up**

☐ **Patient deceased**

☐ **Prison**

☐ **Other, specify:** _____

ADAPT

Sponsor No. | 2 | 0 | 1 | 7 | P | Z | 0 | 4 |

Participant ID | | | |

Site

ADVERSE EVENTS PAGE

AE No	Event Name (Please give Diagnosis if known)	Start date (DD/MM/YYYY)	Stop date (DD/MM/YYYY)	Serious AE (SAE)?	Severity 1 – Asymptomatic 2 – Moderate 3 – Severe 4 – Life-threatening	Outcome 0 - Resolved 1- Resolved with sequelea 2 - Not resolved	Related to study?	Date reported (DD/MM/YYYY)	Signed
1		___/___/___	___/___/___	☐ No ☐ Yes			☐ No ☐ Yes	___/___/___	
2		___/___/___	___/___/___	☐ No ☐ Yes			☐ No ☐ Yes	___/___/___	
3		___/___/___	___/___/___	☐ No ☐ Yes			☐ No ☐ Yes	___/___/___	
4		___/___/___	___/___/___	☐ No ☐ Yes			☐ No ☐ Yes	___/___/___	
5		___/___/___	___/___/___	☐ No ☐ Yes			☐ No ☐ Yes	___/___/___	
6		___/___/___	___/___/___	☐ No ☐ Yes			☐ No ☐ Yes	___/___/___	
I have reviewed the AEs on this page and have assessed them for seriousness, causality, severity and outcome and confirm that, to the best of my knowledge, it accurately reflects the study information obtained for this participant **PI signature** _____ **Date:** _____ ☐ **Please check box if this is the last page used**									

Completed by: _____
Name Signature Date

ADAPT

Sponsor No. | 2 | 0 | 1 | 7 | P | Z | 0 | 4 |

Participant ID | | | |

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COMMENTS LOG

Date (DD/MM/YYY)	CRF Page	Comments	Initial

ADAPT

Sponsor No. | 2 | 0 | 1 | 7 | P | Z | 0 | 4 |

Participant ID | | | |

Site | |

PRINICIPAL INVESTIGATOR'S SIGN OFF

Principal Investigator's Signature Statement:	
I have reviewed this CRF and confirm that, to the best of my knowledge, it accurately reflects the study information obtained for this participant. All entries were made either by me or by a person under my supervision who has signed the Delegation and Signature Log.	
Principal Investigator's Signature: _____ **Principal Investigator's Name:** _____	**Date of Signature:** __ __ / __ __ / __ __ __ __ (DD / MM / YYYY)

ONCE SIGNED, NO FURTHER CHANGES CAN BE MADE TO THIS CRF WITHOUT A SIGNED DATA QUERY FORM.

ADAPT

Sponsor No. 2 0 1 7 P Z 0 4

Participant ID

Site

APPENDIX

Table 1: Treatment trial schedule

Measures \ Time	V1 Consent	V2 Randomisation and Intervention	V3 Repeated measures	V4 3-month Follow-up
Injecting risk questionnaire	■		■	■
Self-efficacy		■	■	■
Volitional help sheet (intervention)		■		
Time Perspective (Control)		■		
Subjective Norms Scale		■	■	
Social Connectedness Scale		■		
Group Identification Scale	■		■	■
PHQ-9	■		■	
GAD-7	■		■	
PC PTSD-5	■			
Working Alliance Inventory			■	
Illness Perception Questionnaire	■		■	■
Approx Time	20 mins	20 mins	30 mins	15 mins

ADAPT

Visit 1 Questionnaires

Contents: IRQ, GIS, PHQ-9, GAD-7, PTSD-5, B-IPQ

Injecting Risk Questionnaire (IRQ)

Participant ID: ____

The first two questions are about sharing injecting equipment in general.
Sharing means you using someone else's equipment, which has already been used, or someone using yours, regardless of whether you were both present at the time.
Injecting equipment includes needles, syringes, filters, spoons and cookers, and washouts.
The other questions are about using other people's equipment or them using yours. I will also ask you with how many different people you have done any of these things. Finally I will ask your age and type of drug you mainly inject (Stimson et al. 1997).

1	2	3	4
Frequently	Sometimes	Hardly ever	Never

	1	2	3	4
During the last 4 weeks, how often have you shared injecting equipment?	☐	☐	☐	☐
During the last 4 weeks, with how many different people have you shared injecting equipment? Number of people	_____			

During the last 4 weeks, how often have you done any of the following things:	1	2	3	4
- given or lent used needles/syringes to a sexual partner	☐	☐	☐	☐
- given or lent used needles/syringes to a friend or acquaintance?	☐	☐	☐	☐
- given or lent used needles/syringes to a stranger?	☐	☐	☐	☐
- injected with needles/syringes that had already been used by a sexual partner?	☐	☐	☐	☐
- injected with needles/syringes that had already been used by a friend or acquaintance?	☐	☐	☐	☐
- injected with needles/syringes that had already been used by a stranger?	☐	☐	☐	☐

1	2	3	4
Frequently	Sometimes	Hardly ever	Never

During the last 4 weeks, how often have you done any of the following things:	1	2	3	4
- filled your syringe from one that had already been used by someone else?	☐	☐	☐	☐
- let someone else fill their syringe with a syringe you had already used?	☐	☐	☐	☐
- drawn up from a container or spoon into which someone else had put a used syringe?	☐	☐	☐	☐
- put a used needle into a container or spoon that was then used by someone else?	☐	☐	☐	☐
- used a filter into which someone else had put a used syringe?	☐	☐	☐	☐
- let someone else use a filter into which you had put a used syringe?	☐	☐	☐	☐
- used the same water or bleach as someone else for flushing out or cleaning?	☐	☐	☐	☐
- used old syringes that had been kept in the same container or 'sin bin' as someone else's old syringes?	☐	☐	☐	☐
- During the last 4 weeks, with how many different people have you done any of the things on this survey? _____				

- Age (in years): _____ Gender:_____

- What type of drug do you mainly inject?

☐ Opiates e.g. heroin, methadone and similar drugs ☐ Steroids

☐ Stimulants e.g. amphetamine, cocaine and similar drugs ☐ Other:_____

Group Identification Scale

*Participant ID:*_____

Sani, F., Madhok, V., Norbury, M., Dugard, P., & Wakefield, J. R. H. (2015). Greater number of group identifications is associated with healthier behaviour: Evidence from a Scottish community sample. *British Journal of Health Psychology, 20*, 466-481.

1	2	3	4	5	6	7
Strongly Agree	Agree	Slightly Agree	Neither Agree nor Disagree	Slightly Disagree	Disagree	Strongly Disagree

	1	2	3	4	5	6	7
1 I feel a bond with my family.	☐	☐	☐	☐	☐	☐	☐
2 I feel similar to the other members of my family.	☐	☐	☐	☐	☐	☐	☐
3 I have a sense of belonging to my family.	☐	☐	☐	☐	☐	☐	☐
4 I have a lot in common with the members of my family.	☐	☐	☐	☐	☐	☐	☐

	1	2	3	4	5	6	7
1 I feel a bond with my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐
2 I feel similar to the other members of my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐
3 I have a sense of belonging to my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐
4 I have a lot in common with the members of my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐

Patient Health Questionnaire (PHQ-9)

Participant ID:_____

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Spitzer et al. 1999)

0	1	2	3
Not at all	Several days	More than half the days	Nearly every day

Over the last 2 weeks, how often have you been bothered by any of the following problems?	0	1	2	3
1 Little interest or pleasure in doing things.	☐	☐	☐	☐
2 Feeling down, depressed, or hopeless.	☐	☐	☐	☐
3 Trouble falling or staying asleep, or sleeping too much.	☐	☐	☐	☐
4 Feeling tired or having little energy.	☐	☐	☐	☐
5 Poor appetite or overeating.	☐	☐	☐	☐
6 Feeling bad about yourself — or that you are a failure or have let yourself or your family down.	☐	☐	☐	☐
7 Trouble concentrating on things, such as reading the newspaper or watching television.	☐	☐	☐	☐
8 Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving .around a lot more than usual.	☐	☐	☐	☐
9 Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐

General Anxiety Disorder (GAD-7)

*Participant ID:*_____

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Spitzer et al. 1999)

0	1	2	3
Not at all	Several days	More than half the days	Nearly every day

Over the last 2 weeks, how often have you been bothered by any of the following problems?	**0**	**1**	**2**	**3**
1 Feeling nervous, anxious or on edge.	☐	☐	☐	☐
2 Not being able to stop or control worrying.	☐	☐	☐	☐
3 Worrying too much about different things.	☐	☐	☐	☐
4 Trouble relaxing.	☐	☐	☐	☐
5 Being so restless that it is hard to sit still.	☐	☐	☐	☐
6 Becoming easily annoyed or irritable.	☐	☐	☐	☐
7 Feeling afraid as if something awful might happen.	☐	☐	☐	☐

Primary Care PTSD Screen (PTSD-5)

Participant ID:_____

Prins, A., Bovin, M. J., Kimerling, R., Kaloupek, D. G., Marx, B. P., Pless Kaiser, A., & Schnurr, P. P. (2015). *The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5).*

Sometimes things happen to people than are unusually or specifically frightening, horrible, or traumatic. For example: serious accident or fire, physical or sexual abuse or assault, seeing someone being killed or seriously injured, having a loved one dying by homicide or suicide.

Have you ever experience this kind of event? YES / NO

In your life, have you ever had any experience that was so frightening, horrible, or upsetting that, **in the past month**, you*

1 Had nightmares about it or thought about it when you did not want to?	☐ YES	☐ NO
2 Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?	☐ YES	☐ NO
3 Been constantly on guard, watchful, or easily startled?	☐ YES	☐ NO
4 Felt numb or detached from others, activities, or your surroundings?	☐ YES	☐ NO
5 Felt guilty or unable to stop blaming yourself or others for it or any problems it may have caused?	☐ YES	☐ NO

Brief Illness Perception Questionnaire

Participant ID:_____

For the following questions, please circle the number that best corresponds to your views:
(Broadbent, Petrie, Main & Weinman, 2006)

	1	2	3	4	5	6	7	8	9	10
1 How much does your Hepatitis C affect your life?	☐ No affect at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Severely affects my life
2 How long do you think your illness will continue?	☐ Very short time	☐	☐	☐	☐	☐	☐	☐	☐	☐ Forever
3 How much control do you feel you have over your illness?	☐ Absolutely no control	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extreme amount of control
4 How much do you think your treatment can help your illness?	☐ Not at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely helpful
5 How much do you experience symptoms from your illness?	☐ No symptoms at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Many sever symptoms
6 How concerned are you about your illness?	☐ Not at all concerned	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely concerned
7 How well do you feel you understand your illness?	☐ Don't understand at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Understand very clearly

8 How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?)	☐ Not at all affected emotionally	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely affected emotionally

9 Please list in rank-order the three most important factors that you believe caused your illness. The most important causes for me:

1. _____
2. _____
3. _____

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ADAPT

Visit 2 Questionnaires

Contents: SES, SCS, VHS/ZTPI, SNS

Equipment Sharing Refusal Self-efficacy Scale

Participant ID:____

Respond to these items according to your beliefs about sharing equipment (adapted from the Drug Avoidance Self-Efficacy Scale, Martin 1992 - EMCDAA).

1	2	3	4	5	6	7
Certainly Yes	Probably Yes	Likely Yes	Can't say	Likely No	Probably No	Certainly No

	1	2	3	4	5	6	7
1 Imagine that you are at a party where there are drugs going around. You haven't got clean equipment on you. Could you avoid using other people's equipment?	☐	☐	☐	☐	☐	☐	☐
2 Imagine that you are home alone and depressed. You haven't got new equipment in the house. Would you give in to the urge to use others' used works?	☐	☐	☐	☐	☐	☐	☐
3 Imagine that you are home with a loved one, and feeling angry after a fight. You want to make up but at the same time you want to score. You haven't got new equipment. Could you resist the urge to use someone else's used works?	☐	☐	☐	☐	☐	☐	☐
4 Imagine it is late, you cannot sleep and drugs are available in the house. You have no clean equipment. Could you resist the urge to use someone else's old works to help you get to sleep?	☐	☐	☐	☐	☐	☐	☐
5 Imagine that, you are going out with friends and expecting to score. Could you resist the urge to share equipment?	☐	☐	☐	☐	☐	☐	☐
6 Imagine that you are home with your loved one, and very angry after a fight. You are tempted to get back at your partner by getting loaded. You haven't got new equipment. Would you give in to the temptation to use someone else's used works?	☐	☐	☐	☐	☐	☐	☐

	1	2	3	4	5	6	7
7 Imagine that a very important relationship has just ended, and you are very depressed. You haven't got clean equipment. Would you give in to the urge to use someone else's used works?	☐	☐	☐	☐	☐	☐	☐
8 Imagine that you have run into 2 friends who have drugs on them they offer to share. You have no clean equipment on you. Could you resist the urge to join them and share their works?	☐	☐	☐	☐	☐	☐	☐
9 Imagine that you are with others and feeling uptight. Most people seem to be having a good time. You are tempted to use someone else's equipment that is lying around. Would you?	☐	☐	☐	☐	☐	☐	☐
10 Imagine you have been trying to not share equipment but gave in last night when a friend had scored and you didn't have any works. Because of last night you are feeling weak. You haven't got new equipment. Would you use others' used works?	☐	☐	☐	☐	☐	☐	☐
11 Imagine that a good friend has accused you of doing something you didn't do. You haven't got clean equipment. Now you are feeling hurt and tempted to use someone else's used works. Could you resist?	☐	☐	☐	☐	☐	☐	☐
12 Imagine that a good friend is feeling miserable. He/she wants you to join him to score. He/she only has one set of clean works. Could you resist the urge to share his/her works?	☐	☐	☐	☐	☐	☐	☐
13 Imagine that you are home alone; it is a dull weekend with nothing in particular to look forward to. You are bored but have no clean equipment. Would you give in to the urge to use used works?	☐	☐	☐	☐	☐	☐	☐
14 Imagine that you have woken up and you are in withdrawal. You have gear but don't have clean equipment on you. You find used works. Would you use them?	☐	☐	☐	☐	☐	☐	☐

Social Connectedness Scale

*Participant ID:*_____

Lee, R. M. and. Robbins, S. B. (1995). Measuring Belongingness: The Social Connectedness and the Social Assurance Scales. *Journal of Counselling Psychology (42:2)*: 232-241.

1	2	3	4	5	6
Strongly Agree					Strongly Disagree

	1	2	3	4	5	6
1 I feel disconnected from the world around me.	☐	☐	☐	☐	☐	☐
2 Even around people I know, I don't feel that I really belong.	☐	☐	☐	☐	☐	☐
3 I feel so distant from people.	☐	☐	☐	☐	☐	☐
4 I have no sense of togetherness with my peers.	☐	☐	☐	☐	☐	☐
5 I don't feel related to anyone.	☐	☐	☐	☐	☐	☐
6 I catch myself losing all sense of connectedness with society.	☐	☐	☐	☐	☐	☐
7 Even among my friends, there is no sense of brother/sisterhood.	☐	☐	☐	☐	☐	☐
8 I don't feel that I participate with anyone or any group.	☐	☐	☐	☐	☐	☐

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Volitional Help Sheet

ADAPT

*Participant ID:*_____

Situations

1. If I am tempted to share equipment when I am in withdrawal and I am offered heroin
2. If I am tempted to share equipment when I am with others who are injecting
3. If I am tempted to share equipment when things are not going my way
4. If I am tempted to share equipment when I am feeling down
5. If I am tempted to share equipment when other people encourage me to share
6. If I am tempted to share equipment when I am very anxious
7. If I am tempted to share equipment when offered equipment by someone
8. If I am tempted to share equipment when things are going really well for me
9. If I am tempted to share equipment when I am upset
10. If I am tempted to share equipment when I am under the influence of other drugs
11. If I am tempted to share equipment when I have no clean equipment with me

Solutions

- Then I will avoid situations that encourage me to share equipment
- Then I will reward myself when I do not give into my urge to share equipment
- Then I will use alternatives to calm myself
- Then I will do something else instead of injecting
- Then I will seek out someone who listens when I want to talk about my feelings
- Then I will seek out social situations where people respect the rights of others not to inject/share equipment
- Then I will remember that I have strong feelings about how much my injecting and sharing has affected the people I care about
- Then I will remember the information that people have personally given me on the benefits of not sharing equipment
- Then I will think about how my emotions affect me when I think about consequences of sharing equipment
- Then I will tell myself that I can choose to change or not to change
- Then I will tell myself that if I try hard enough I can say no to sharing equipment
- Then I will think about the type of person I will be if I am in control of my injecting
- Then I will always make sure I have enough clean equipment

Control Task. Participant ID:_____

Zimbardo's Time Perspective Inventory

"How characteristic or true is this of you?" (Orosz et al. 2017).

1	2	3	4	5
Very Untrue	Untrue	Neutral	True	Very True

	1	2	3	4	5
1 Meeting tomorrow's deadlines and doing other necessary work comes before tonight's play.	☐	☐	☐	☐	☐
2 I enjoy stories of how things used to be in the 'good old times'.	☐	☐	☐	☐	☐
3 Happy memories of good times spring readily to mind.	☐	☐	☐	☐	☐
4. I meet my obligations to friends and authorities on time.	☐	☐	☐	☐	☐
5 I've taken my share of abuse and rejection in the past.	☐	☐	☐	☐	☐
6 The past has too many unpleasant memories that I prefer not to think about. R	☐	☐	☐	☐	☐
7 I get nostalgic about my childhood.	☐	☐	☐	☐	☐
8 Taking risks keeps my life from becoming boring.	☐	☐	☐	☐	☐
9 It's hard for me to forget unpleasant images of my youth.	☐	☐	☐	☐	☐
10 You can't really plan for the future because things change so much.	☐	☐	☐	☐	☐
11 My life path is controlled by forces I cannot influence.	☐	☐	☐	☐	☐
12 It doesn't make sense to worry about the future, since there is nothing that I can do about it anyway.	☐	☐	☐	☐	☐

1	2	3	4	5
Very Untrue	Untrue	Neutral	True	Very True

13 I complete projects on time by making steady progress.	☐	☐	☐	☐	☐
14 I take risks to put excitement in my life.	☐	☐	☐	☐	☐
15 I am able to resist temptations when I know that there is work to be done.	☐	☐	☐	☐	☐
16 I find myself getting swept up in the excitement of the moment.	☐	☐	☐	☐	☐
17 I think about bad things that have happened to me in the past.	☐	☐	☐	☐	☐

Subjective Norms Scale (SNS)

Participant ID:_____

For the following questions, please circle the number that best corresponds to your views:
(adapted from Glanz, Rimer & Viswanath, 2002)

1	2	3	4	5	6	7
Strongly Agree	Agree	Slightly Agree	Neither Agree nor Disagree	Slightly Disagree	Disagree	Strongly Disagree

	1	2	3	4	5	6	7
1 Most people who are important to me think it is ok to share injecting equipment.	☐	☐	☐	☐	☐	☐	☐
2 Most people who are important to me want me to share equipment.	☐	☐	☐	☐	☐	☐	☐
3 It is expected of me to share injecting equipment.	☐	☐	☐	☐	☐	☐	☐
4 I do not feel under social pressure to share injecting equipment.	☐	☐	☐	☐	☐	☐	☐

ADAPT

Visit 3 Questionnaires

Contents: IRQ, SES, SNS, GIS, PHQ-9, GAD-7, WAI-SR, B-IPQ

Injecting Risk Questionnaire (IRQ)

Participant ID: ____

The first two questions are about sharing injecting equipment in general.
Sharing means you using someone else's equipment, which has already been used, or someone using yours, regardless of whether you were both present at the time.
Injecting equipment includes needles, syringes, filters, spoons and cookers, and washouts.
The other questions are about using other people's equipment or them using yours. I will also ask you with how many different people you have done any of these things. Finally I will ask your age and type of drug you mainly inject (Stimson et al. 1997).

1	2	3	4
Frequently	Sometimes	Hardly ever	Never

	1	2	3	4
During the last 4 weeks, how often have you shared injecting equipment?	☐	☐	☐	☐
During the last 4 weeks, with how many different people have you shared injecting equipment? Number of people	_____			

During the last 4 weeks, how often have you done any of the following things:	1	2	3	4
- given or lent used needles/syringes to a sexual partner	☐	☐	☐	☐
- given or lent used needles/syringes to a friend or acquaintance?	☐	☐	☐	☐
- given or lent used needles/syringes to a stranger?	☐	☐	☐	☐
- injected with needles/syringes that had already been used by a sexual partner?	☐	☐	☐	☐
- injected with needles/syringes that had already been used by a friend or acquaintance?	☐	☐	☐	☐
- injected with needles/syringes that had already been used by a stranger?	☐	☐	☐	☐

1	2	3	4
Frequently	Sometimes	Hardly ever	Never

During the last 4 weeks, how often have you done any of the following things:	1	2	3	4
- filled your syringe from one that had already been used by someone else?	☐	☐	☐	☐
- let someone else fill their syringe with a syringe you had already used?	☐	☐	☐	☐
- drawn up from a container or spoon into which someone else had put a used syringe?	☐	☐	☐	☐
- put a used needle into a container or spoon that was then used by someone else?	☐	☐	☐	☐
- used a filter into which someone else had put a used syringe?	☐	☐	☐	☐
- let someone else use a filter into which you had put a used syringe?	☐	☐	☐	☐
- used the same water or bleach as someone else for flushing out or cleaning?	☐	☐	☐	☐
- used old syringes that had been kept in the same container or 'sin bin' as someone else's old syringes?	☐	☐	☐	☐
- During the last 4 weeks, with how many different people have you done any of the things on this survey? _____				

- Age (in years): _____ Gender:_____

- What type of drug do you mainly inject?

☐ Opiates e.g. heroin, methadone and similar drugs ☐ Steroids

☐ Stimulants e.g. amphetamine, cocaine and similar drugs ☐ Other: _____

Equipment Sharing Refusal Self-efficacy Scale

Participant ID:____

Respond to these items according to your beliefs about sharing equipment (adapted from the Drug Avoidance Self-Efficacy Scale, Martin 1992 - EMCDAA).

1	2	3	4	5	6	7
Certainly Yes	Probably Yes	Likely Yes	Can't say	Likely No	Probably No	Certainly No

	1	2	3	4	5	6	7
1 Imagine that you are at a party where there are drugs going around. You haven't got clean equipment on you. Could you avoid using other people's equipment?	☐	☐	☐	☐	☐	☐	☐
2 Imagine that you are home alone and depressed. You haven't got new equipment in the house. Would you give in to the urge to use others' used works?	☐	☐	☐	☐	☐	☐	☐
3 Imagine that you are home with a loved one, and feeling angry after a fight. You want to make up but at the same time you want to score. You haven't got new equipment. Could you resist the urge to use someone else's used works?	☐	☐	☐	☐	☐	☐	☐
4 Imagine it is late, you cannot sleep and drugs are available in the house. You have no clean equipment. Could you resist the urge to use someone else's old works to help you get to sleep?	☐	☐	☐	☐	☐	☐	☐
5 Imagine that, you are going out with friends and expecting to score. Could you resist the urge to share equipment?	☐	☐	☐	☐	☐	☐	☐
6 Imagine that you are home with your loved one, and very angry after a fight. You are tempted to get back at your partner by getting loaded. You haven't got new equipment. Would you give in to the temptation to use someone else's used works?	☐	☐	☐	☐	☐	☐	☐

	1	2	3	4	5	6	7
7 Imagine that a very important relationship has just ended, and you are very depressed. You haven't got clean equipment. Would you give in to the urge to use someone else's used works?	☐	☐	☐	☐	☐	☐	☐
8 Imagine that you have run into 2 friends who have drugs on them they offer to share. You have no clean equipment on you. Could you resist the urge to join them and share their works?	☐	☐	☐	☐	☐	☐	☐
9 Imagine that you are with others and feeling uptight. Most people seem to be having a good time. You are tempted to use someone else's equipment that is lying around. Would you?	☐	☐	☐	☐	☐	☐	☐
10 Imagine you have been trying to not share equipment but gave in last night when a friend had scored and you didn't have any works. Because of last night you are feeling weak. You haven't got new equipment. Would you use others' used works?	☐	☐	☐	☐	☐	☐	☐
11 Imagine that a good friend has accused you of doing something you didn't do. You haven't got clean equipment. Now you are feeling hurt and tempted to use someone else's used works. Could you resist?	☐	☐	☐	☐	☐	☐	☐
12 Imagine that a good friend is feeling miserable. He/she wants you to join him to score. He/she only has one set of clean works. Could you resist the urge to share his/her works?	☐	☐	☐	☐	☐	☐	☐
13 Imagine that you are home alone; it is a dull weekend with nothing in particular to look forward to. You are bored but have no clean equipment. Would you give in to the urge to use used works?	☐	☐	☐	☐	☐	☐	☐
14 Imagine that you have woken up and you are in withdrawal. You have gear but don't have clean equipment on you. You find used works. Would you use them?	☐	☐	☐	☐	☐	☐	☐

Subjective Norms Scale (SNS)

Participant ID:_____

For the following questions, please circle the number that best corresponds to your views:
(adapted from Glanz, Rimer & Viswanath, 2002)

1	2	3	4	5	6	7
Strongly Agree	Agree	Slightly Agree	Neither Agree nor Disagree	Slightly Disagree	Disagree	Strongly Disagree

	1	2	3	4	5	6	7
1 Most people who are important to me think it is ok to share injecting equipment.	☐	☐	☐	☐	☐	☐	☐
2 Most people who are important to me want me to share equipment.	☐	☐	☐	☐	☐	☐	☐
3 It is expected of me to share injecting equipment.	☐	☐	☐	☐	☐	☐	☐
4 I do not feel under social pressure to share injecting equipment.	☐	☐	☐	☐	☐	☐	☐

Group Identification Scale

*Participant ID:*_____

Sani, F., Madhok, V., Norbury, M., Dugard, P., & Wakefield, J. R. H. (2015). Greater number of group identifications is associated with healthier behaviour: Evidence from a Scottish community sample. *British Journal of Health Psychology, 20*, 466-481.

1	2	3	4	5	6	7
Strongly Agree	Agree	Slightly Agree	Neither Agree nor Disagree	Slightly Disagree	Disagree	Strongly Disagree

	1	2	3	4	5	6	7
1 I feel a bond with my family.	☐	☐	☐	☐	☐	☐	☐
2 I feel similar to the other members of my family.	☐	☐	☐	☐	☐	☐	☐
3 I have a sense of belonging to my family.	☐	☐	☐	☐	☐	☐	☐
4 I have a lot in common with the members of my family.	☐	☐	☐	☐	☐	☐	☐

	1	2	3	4	5	6	7
1 I feel a bond with my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐
2 I feel similar to the other members of my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐
3 I have a sense of belonging to my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐
4 I have a lot in common with the members of my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐

Patient Health Questionnaire (PHQ-9)

Participant ID:_____

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Spitzer et al. 1999)

0	1	2	3
Not at all	Several days	More than half the days	Nearly every day

Over the last 2 weeks, how often have you been bothered by any of the following problems?	**0**	**1**	**2**	**3**
1 Little interest or pleasure in doing things.	☐	☐	☐	☐
2 Feeling down, depressed, or hopeless.	☐	☐	☐	☐
3 Trouble falling or staying asleep, or sleeping too much.	☐	☐	☐	☐
4 Feeling tired or having little energy.	☐	☐	☐	☐
5 Poor appetite or overeating.	☐	☐	☐	☐
6 Feeling bad about yourself — or that you are a failure or have let yourself or your family down.	☐	☐	☐	☐
7 Trouble concentrating on things, such as reading the newspaper or watching television.	☐	☐	☐	☐
8 Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving .around a lot more than usual.	☐	☐	☐	☐
9 Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐

General Anxiety Disorder (GAD-7)

Participant ID:_____

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Spitzer et al. 1999)

0	1	2	3
Not at all	Several days	More than half the days	Nearly every day

Over the last 2 weeks, how often have you been bothered by any of the following problems?	0	1	2	3
1 Feeling nervous, anxious or on edge.	☐	☐	☐	☐
2 Not being able to stop or control worrying.	☐	☐	☐	☐
3 Worrying too much about different things.	☐	☐	☐	☐
4 Trouble relaxing.	☐	☐	☐	☐
5 Being so restless that it is hard to sit still.	☐	☐	☐	☐
6 Becoming easily annoyed or irritable.	☐	☐	☐	☐
7 Feeling afraid as if something awful might happen.	☐	☐	☐	☐

Working Alliance Inventory – Short Revised

Participant ID:_____

Below is a list of statements and questions about experiences people might have with their therapy or therapist. Think about your experience in therapy, and decide which category best describes your own experience (Hatcher & Gillaspy, 2006).

1	2	3	4	5
Seldom	Sometimes	Fairly Often	Very Often	Always

	1	2	3	4	5
1 As a result of these sessions I am clearer as to how I might be able to change.	☐	☐	☐	☐	☐
2 What I am doing in therapy gives me new ways of looking at my problem.	☐	☐	☐	☐	☐
3 ____and I collaborate on setting goals for my therapy.	☐	☐	☐	☐	☐
4 ____and I are working towards mutually agreed upon goals.	☐	☐	☐	☐	☐
5 ____ and I agree on what is important for me to work on.	☐	☐	☐	☐	☐
6 I feel that the things I do in therapy will help me to accomplish the changes that I want.	☐	☐	☐	☐	☐
7 ____ and I have established a good understanding of the kind of changes that would be good for me.	☐	☐	☐	☐	☐
8 I believe the way we are working with my problem is correct.	☐	☐	☐	☐	☐

Brief Illness Perception Questionnaire

Participant ID:_____

For the following questions, please circle the number that best corresponds to your views:
(Broadbent, Petrie, Main & Weinman, 2006)

	1	2	3	4	5	6	7	8	9	10
1 How much does your Hepatitis C affect your life?	☐ No affect at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Severely affects my life
2 How long do you think your illness will continue?	☐ Very short time	☐	☐	☐	☐	☐	☐	☐	☐	☐ Forever
3 How much control do you feel you have over your illness?	☐ Absolutely no control	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extreme amount of control
4 How much do you think your treatment can help your illness?	☐ Not at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely helpful
5 How much do you experience symptoms from your illness?	☐ No symptoms at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Many sever symptoms
6 How concerned are you about your illness?	☐ Not at all concerned	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely concerned
7 How well do you feel you understand your illness?	☐ Don't understand at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Understand very clearly

8 How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?)	☐ Not at all affected emotionally	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely affected emotionally

9 Please list in rank-order the three most important factors that you believe caused your illness. The most important causes for me:

1. _____
2. _____
3. _____

ADAPT

Visit 4 Questionnaires

Contents: IRQ, SES, GIS, B-IPQ

Injecting Risk Questionnaire (IRQ)

Participant ID: ____

The first two questions are about sharing injecting equipment in general.
Sharing means you using someone else's equipment, which has already been used, or someone using yours, regardless of whether you were both present at the time.
Injecting equipment includes needles, syringes, filters, spoons and cookers, and washouts.
The other questions are about using other people's equipment or them using yours. I will also ask you with how many different people you have done any of these things. Finally I will ask your age and type of drug you mainly inject (Stimson et al. 1997).

1	2	3	4
Frequently	Sometimes	Hardly ever	Never

	1	2	3	4
During the last 4 weeks, how often have you shared injecting equipment?	☐	☐	☐	☐
During the last 4 weeks, with how many different people have you shared injecting equipment? Number of people	_____			

During the last 4 weeks, how often have you done any of the following things:	1	2	3	4
- given or lent used needles/syringes to a sexual partner	☐	☐	☐	☐
- given or lent used needles/syringes to a friend or acquaintance?	☐	☐	☐	☐
- given or lent used needles/syringes to a stranger?	☐	☐	☐	☐
- injected with needles/syringes that had already been used by a sexual partner?	☐	☐	☐	☐
- injected with needles/syringes that had already been used by a friend or acquaintance?	☐	☐	☐	☐
- injected with needles/syringes that had already been used by a stranger?	☐	☐	☐	☐

1	2	3	4
Frequently	Sometimes	Hardly ever	Never

During the last 4 weeks, how often have you done any of the following things:	1	2	3	4
- filled your syringe from one that had already been used by someone else?	☐	☐	☐	☐
- let someone else fill their syringe with a syringe you had already used?	☐	☐	☐	☐
- drawn up from a container or spoon into which someone else had put a used syringe?	☐	☐	☐	☐
- put a used needle into a container or spoon that was then used by someone else?	☐	☐	☐	☐
- used a filter into which someone else had put a used syringe?	☐	☐	☐	☐
- let someone else use a filter into which you had put a used syringe?	☐	☐	☐	☐
- used the same water or bleach as someone else for flushing out or cleaning?	☐	☐	☐	☐
- used old syringes that had been kept in the same container or 'sin bin' as someone else's old syringes?	☐	☐	☐	☐
- During the last 4 weeks, with how many different people have you done any of the things on this survey? _____				

- Age (in years): _____ Gender:_____

- What type of drug do you mainly inject?

☐ Opiates e.g. heroin, methadone and similar drugs ☐ Steroids

☐ Stimulants e.g. amphetamine, cocaine and similar drugs ☐ Other:_____

Equipment Sharing Refusal Self-efficacy Scale

Participant ID:____

Respond to these items according to your beliefs about sharing equipment (adapted from the Drug Avoidance Self-Efficacy Scale, Martin 1992 - EMCDAA).

1	2	3	4	5	6	7
Certainly Yes	Probably Yes	Likely Yes	Can't say	Likely No	Probably No	Certainly No

	1	2	3	4	5	6	7
1 Imagine that you are at a party where there are drugs going around. You haven't got clean equipment on you. Could you avoid using other people's equipment?	☐	☐	☐	☐	☐	☐	☐
2 Imagine that you are home alone and depressed. You haven't got new equipment in the house. Would you give in to the urge to use others' used works?	☐	☐	☐	☐	☐	☐	☐
3 Imagine that you are home with a loved one, and feeling angry after a fight. You want to make up but at the same time you want to score. You haven't got new equipment. Could you resist the urge to use someone else's used works?	☐	☐	☐	☐	☐	☐	☐
4 Imagine it is late, you cannot sleep and drugs are available in the house. You have no clean equipment. Could you resist the urge to use someone else's old works to help you get to sleep?	☐	☐	☐	☐	☐	☐	☐
5 Imagine that, you are going out with friends and expecting to score. Could you resist the urge to share equipment?	☐	☐	☐	☐	☐	☐	☐
6 Imagine that you are home with your loved one, and very angry after a fight. You are tempted to get back at your partner by getting loaded. You haven't got new equipment. Would you give in to the temptation to use someone else's used works?	☐	☐	☐	☐	☐	☐	☐

	1	2	3	4	5	6	7
7 Imagine that a very important relationship has just ended, and you are very depressed. You haven't got clean equipment. Would you give in to the urge to use someone else's used works?	☐	☐	☐	☐	☐	☐	☐
8 Imagine that you have run into 2 friends who have drugs on them they offer to share. You have no clean equipment on you. Could you resist the urge to join them and share their works?	☐	☐	☐	☐	☐	☐	☐
9 Imagine that you are with others and feeling uptight. Most people seem to be having a good time. You are tempted to use someone else's equipment that is lying around. Would you?	☐	☐	☐	☐	☐	☐	☐
10 Imagine you have been trying to not share equipment but gave in last night when a friend had scored and you didn't have any works. Because of last night you are feeling weak. You haven't got new equipment. Would you use others' used works?	☐	☐	☐	☐	☐	☐	☐
11 Imagine that a good friend has accused you of doing something you didn't do. You haven't got clean equipment. Now you are feeling hurt and tempted to use someone else's used works. Could you resist?	☐	☐	☐	☐	☐	☐	☐
12 Imagine that a good friend is feeling miserable. He/she wants you to join him to score. He/she only has one set of clean works. Could you resist the urge to share his/her works?	☐	☐	☐	☐	☐	☐	☐
13 Imagine that you are home alone; it is a dull weekend with nothing in particular to look forward to. You are bored but have no clean equipment. Would you give in to the urge to use used works?	☐	☐	☐	☐	☐	☐	☐
14 Imagine that you have woken up and you are in withdrawal. You have gear but don't have clean equipment on you. You find used works. Would you use them?	☐	☐	☐	☐	☐	☐	☐

Group Identification Scale

*Participant ID:*_____

Sani, F., Madhok, V., Norbury, M., Dugard, P., & Wakefield, J. R. H. (2015). Greater number of group identifications is associated with healthier behaviour: Evidence from a Scottish community sample. *British Journal of Health Psychology, 20*, 466-481.

1	2	3	4	5	6	7
Strongly Agree	Agree	Slightly Agree	Neither Agree nor Disagree	Slightly Disagree	Disagree	Strongly Disagree

	1	2	3	4	5	6	7
1 I feel a bond with my family.	☐	☐	☐	☐	☐	☐	☐
2 I feel similar to the other members of my family.	☐	☐	☐	☐	☐	☐	☐
3 I have a sense of belonging to my family.	☐	☐	☐	☐	☐	☐	☐
4 I have a lot in common with the members of my family.	☐	☐	☐	☐	☐	☐	☐

	1	2	3	4	5	6	7
1 I feel a bond with my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐
2 I feel similar to the other members of my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐
3 I have a sense of belonging to my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐
4 I have a lot in common with the members of my injecting/drug network.	☐	☐	☐	☐	☐	☐	☐

Brief Illness Perception Questionnaire

Participant ID:_____

For the following questions, please circle the number that best corresponds to your views:
(Broadbent, Petrie, Main & Weinman, 2006)

	1	2	3	4	5	6	7	8	9	10
1 How much does your Hepatitis C affect your life?	☐ No affect at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Severely affects my life
2 How long do you think your illness will continue?	☐ Very short time	☐	☐	☐	☐	☐	☐	☐	☐	☐ Forever
3 How much control do you feel you have over your illness?	☐ Absolutely no control	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extreme amount of control
4 How much do you think your treatment can help your illness?	☐ Not at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely helpful
5 How much do you experience symptoms from your illness?	☐ No symptoms at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Many sever symptoms
6 How concerned are you about your illness?	☐ Not at all concerned	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely concerned
7 How well do you feel you understand your illness?	☐ Don't understand at all	☐	☐	☐	☐	☐	☐	☐	☐	☐ Understand very clearly

8 How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?)	☐ Not at all affected emotionally	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely affected emotionally

9 Please list in rank-order the three most important factors that you believe caused your illness. The most important causes for me:

1. _____
2. _____
3. _____

Appendix 10.2

List of Publications and Outputs during PhD

List of Publications from the PhD Thesis

Malaguti, A., Ciocanel, O., Sani, F., Dillon, J. F., Eriksen, A. & Power, K. (2020). Effectiveness of the use of implementation intentions on reduction of substance use: a meta-analysis. *Drug & Alcohol Dependence, 214*: 1-11. Doi:10.1016/j.drugalcdep.2020.108120

Malaguti, A., Sani, F., Stephens, B. P., Ahmad, F., Dugard, P. & Dillon, J. F. (2019). Change in injecting behaviour among people treated for hepatitis C virus: The role of intimate partnerships. *Journal of Viral Hepatitis*, *26*(1), 65–72. Doi: 10.1111/jvh.13009

List of publications completed throughout the doctorate (not part of thesis) (April 2017 – present)

Publications:

Inglis, S., Beer, L., Byrne, C., Malaguti, A., Robinson, E. M., Sharkey, C., Gillings, K., Stephens, B. S. & Dillon, J. F. (2019). Randomised controlled trial conducted in injecting equipment provision sites to compare the effectiveness of different hepatitis c treatment regiments in people who inject drugs: A Direct observed therapy vs fortNightly CollEction Study for HCV Treatment – ADVANCE HCV Study. *BMJ Open, 9*(8): 1-8. Doi: 10.1136/bmjopen-2019-029516

Caven, M., Malaguti, A., Robinson, E., Fletcher, E. & Dillon, J. F. (2019). Impact of Hepatitis C treatment on behavioural change in relation to drug use in people who inject drugs: A systematic review. *International Journal of Drug Policy*, *72*: 169-176. Doi: 10.1016/j.drugpo.2019.05.011

Malaguti, A**.** (2017). Reflections on the EHPS/DHP conference (Bursary winner – 2016 event review). *Health Psychology Update, 26(1):* 37-38.

Funding awarded throughout the doctorate

Scottish Government (Drug Deaths Taskforce) 2020: Malaguti, A. & Sani, F. + Research team (Jennifer Breen, Fiona Cowden, Emma Fletcher, Ann Eriksen, Donna Thain) – Designing a Behaviour Change Intervention to Reduce the Risk of Overdose: £88,328.00

Partial conference scholarship 2019: INHSU 2019 (International Network for Hepatitis Care in substance Users) – *Montreal, Canada.* €385

PsyPAG Worshop/Training event bursary 2018: Structural Equation Modelling using MPlus (University of Manchester) - £100 (CANCELLED for strike & award returned)

Partial conference scholarship 2017: INHSU 2017 – *Jersey City, New York, USA*. €500

Conference Presentations completed throughout the doctorate (April 2017 – present)

FPH (Faculty of Public Health) Scotland 2019 – *Dunblane, Scotland*:

- Malaguti A, Ciocanel O, Sani F, Dillon JF, Eriksen A & Power K (2019). Effectiveness of the use of implementation intentions on reduction of substance use: a meta-analysis. *(Oral presentation)*

INHSU 2019 (International Network for Hepatitis Care in substance Users) – *Montreal, Canada.* (Partial conference scholarship winner):

- Malaguti A, Sani F, Eriksen A, Power K & Dillon JF. (2019*).* Psychosocial predictors of hepatitis C (HCV) re-infection in people who inject drugs on HCV treatment. *(Poster presentation).*

EHPS 2019 (European Health Psychology Society) – *Dubrovnik, Croatia:*

- Malaguti A, Sani F, Eriksen A, Power K & Dillon JF. (2019). Psychosocial predictors of injecting risk behaviour in people who inject drugs on hepatitis C treatment. *(Invited as speaker for Oral presentation in Symposium: Europe's illicit drug use challenges: are health psychological, social and policy responses fit for purpose?).*

NRS 2018 (NHS Research Scotland) – *Perth, Scotland*:

- Malaguti A, Sani F, Stephens BP, Ahmad F, Dugard P & Dillon JF, on behalf of the ERADICATE-C Study Group (2018). Receiving hepatitis C treatment as a couple: Romantic partners' mutual reduction of injecting behaviour frequency. *(Poster presentation).*

INHSU 2018 (International Network for Hepatitis Care in Substance Users) – *Lisbon, Portugal*:

- Malaguti A, Sani F, Stephens BP, Ahmad F, Dugard P & Dillon JF, on behalf of the ERADICATE-C Study Group (2018). Receiving hepatitis C treatment as a couple: Romantic partners' mutual reduction of injecting behaviour frequency. *(Poster presentation).*

EHPS 2018 (European Health Psychology Society) – *Galway, Ireland*:

- Malaguti A, Sani F, Stephens BP, Ahmad F, Dugard P & Dillon JF, on behalf of the ERADICATE-C Study Group (2018). Evidence of behaviour change in people who inject drugs on treatment for hepatitis C infection. *(Poster presentation).*

<u>Departmental Presentations:</u>

January 2020 - Experience of healthcare provision in Accra, Ghana – a travel diary

February 2018 - Substance Misuse, Hepatitis C and Health Psychology

<u>During PhD but not part of PhD programme:</u>

INHSU 2017 – *Jersey City, New York, USA*. (Partial conference scholarship winner):

- Malaguti A, Power K, Swanson V & Eriksen A. (2017). Staff's attitudes toward injecting drug use and Hepatitis C (HCV). *(Poster presentation).*

- Malaguti A, Kelly D, Eriksen A, Swanson V & Power K (2017). Reducing injecting drug use risks by providing foil to smoke heroin: A service improvement pilot evaluation. *(Poster presentation).*

Chemsex in Scotland 2017 – Glasgow, Scotland.

- Malaguti, A (2017). Chemsex: Building the picture. *(Oral presentation).*

Appendix 10.3

First paper from thesis: Malaguti et al. 2019

MISS AMY MALAGUTI (Orcid ID : 0000-0003-0903-5448)

Article type : Original Paper

Amy Malaguti (Orcid ID: 0000-0003-0903-5448)
Article type: Original article

Corresponding author's email: a.malaguti@dundee.ac.uk

TITLE

Change in injecting behaviour among people treated for hepatitis C virus: the role of intimate partnerships.

SHORT RUNNING TITLE

Change in injecting behaviour during treatment for hepatitis C.

AUTHORS

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ACKNOWLEDGMENTS

We would like to thank Janssen-Cilag and the Scottish Government for funding the Eradicate-C trial, and Roche and Janssen-Cilag for support of the drug costs. Thanks to the Eradicate-C study research team for their essential contributions to the study, in particular to Mrs Linda Johnston and Dr Sarah Inglis. We are also grateful for the services provided by Cair Scotland's IEP staff, helping with recruitment and retention. Finally, thanks to Professor Kevin Power and Mrs Ann Eriksen, for their continued professional and moral support.

CONFLICT OF INTEREST STATEMENT

AM, FS, FA and PD declare no conflict of interest. BPS has received honoraria for lectures from Janssen-Cilag, Merck Sharp & Dohme and Gilead Sciences. JFD has received honoraria for lectures and research grants from Janssen-Cilag, Roche, Merck Sharp & Dohme, AbbVie, Bristol-Myers Squibb and Gilead Sciences.

FUNDING

The Eradicate-C trial was funded by Janssen-Cilag and the Scottish Government, drug treatment was provided by Roche and Janssen-Cilag.

ABSTRACT

Injecting behaviour in people who inject drugs is the main risk factor for hepatitis C virus (HCV) infection. Psychosocial factors such as having a partner who injects drugs and living with other drug users have been associated with increases in injecting risk behaviour. This study aimed to investigate changes in injecting behaviour during treatment for HCV infection whilst exploring the role of psychosocial factors on patients' injecting behaviour. Eradicate-C was a single centred clinical trial (ISRCTN27564683) investigating the effectiveness of HCV treatment within the injecting drug using population between 2012 and 2017. A total of 94 participants completed up to 24 weeks of treatment, with social and behavioural measures taken at different intervals throughout treatment. Data for 84 participants was analysed retrospectively to explore mechanisms of potential behavioural changes which had occurred during treatment.Injecting frequency reduced significantly between baseline (week 1) and every 4-weekly interval until week 26. Not being on Opiate Substitution Therapy (OST) was associated with a statistically significant decrease in injecting frequency, χ^2 (1) = 10.412, p =.001, as was having a partner who also used drugs, in particular when that partner was also on treatment for HCV infection, Z= -2.312, p=.021. Treating a ' hard-to-reach population for HCV infection is not only possible, but also bears health benefits beyond treatment of HCV alone. Enrolling couples on HCV treatment when partners are sero-concordant, has shown enhanced benefits for reduction in injecting behaviour. Implications for practice are discussed.

Keywords

Hepatitis C, People who inject drugs, Injecting behaviour, Partner, Opiate substitution therapy.

Abbreviations

HCC – Hepatocellular Carcinoma; HCV - Hepatitis C Virus; IFN – Interferon; IEP – Injecting Equipment Provision; LARC – Long-Acting Reversible Contraception; OST - Opiate substitution therapy; PEG-INF – Pegylated Interferon; PWID - People who inject drugs; RBV - Ribavirin; SVR – Sustained Virological Response.

MAIN TEXT

Introduction

Over 71 million people worldwide are chronically infected with the hepatitis C virus [1-2]. The disease burden is axiomatic, with an estimated HCV-related mortality of 400,000 people a year [1]. The most common transmission route in Western countries remains injecting drug use, with an estimated 60-80% of the HCV-positive population having acquired the virus via injecting risk behaviour [3-5]. A variety of psychosocial factors have been associated with injecting risk behaviour: injecting frequency, poly-drug use, having a sexual partner who also injects, trust and risk perception to name a few [6-8]. Despite the continued injecting risks carried out by people who inject drugs, many studies have

shown that fears of non-adherence and low sustained-virological response (SVR) rates are unjustified, with people who inject drugs (PWID) showing both successful adherence and high SVR rates [3, 9-10].

Psychosocial factors seem to have conflicting effects on injecting risk behaviour and HCV treatment success. Published literature reports an association between HCV treatment success rates and social support [11]. Peers help to increase motivation, feelings of hope and strength to complete treatment, as well as decreasing internalised stigma and shame related to HCV and substance misuse, reducing use of substances itself [12-13]. Yet, historically, close relationships with other PWID, such as romantic partnerships and living with other drug users, are among the factors most strongly linked to continued injecting risk behaviour [6-8]. A possible explanation of these polar effects could be that in a hostile environment where the behaviours of vulnerable adults are influenced negatively by partners, a positive sense of acceptance, belonging and self-worth can stem from these partnerships [14]. Integrated models of behaviour change attempt to explain how couple dynamics can influence risk and health behaviours [15].

HCV treatment itself seems to have a wider effect on PWID than curing hepatitis C alone. It has been associated with a decrease in ancillary injecting equipment sharing after treatment completion [16], suggesting treatment might impact the injecting behavoiur as well as HCV. Midgard and colleagues [17] investigated changes in behaviour during and after treatment, and reported a decrease in recent injecting drug use, alcohol use and an increase in opiate substitution therapy (OST) uptake throughout HCV treatment and at follow-up. However, they found no changes in daily injecting, use of sterile or shared equipment [17]. Only a few studies have investigated the effects of HCV treatment on risk behaviour [16-17] and no literature to date has investigated the role of psychosocial factors such as romantic partnerships and living situation on risk behaviour during and following HCV treatment.

The Eradicate-C study was carried out to investigate the effectiveness of interferon-based HCV treatment on current PWID, characterised by a strenuous lifestyle and erratic engagement with healthcare services. This study aimed to investigate changes in injecting behaviour during treatment, examining the role of psychosocial factors on hypothesised injecting behaviour change.

Methods

Study design

Eradicate-C was a single centred clinical trial investigating the effectiveness of HCV treatment within the injecting drug using population between 2012 and 2017. Participants were seen on a weekly basis for 26 consecutive weeks for treatment and the additional period of follow-up. The nurses, starting on visit 2 of the study, provided a weekly injection of 180µg pegylated interferon α (PEG-IFNα) and supplied participants with a week's worth take-home daily dose of between 400 – 1400 mg (weight based) of self-administered ribavirin (RBV). Patients presenting with a genotype 1 infection, also received protease inhibitors: telaprevir or simeprevir. The study treatment mirrored the standard of care treatment duration of 24 weeks for genotype 1 infections and of 16 weeks for genotypes 2 and 3 infections. All participants completed behavioural and social measures at different time points during the 26 visits of treatment.

The study was conducted in accordance with the Declaration of Helsinki and the principles of good clinical practice (GCP). The study was co-sponsored by the University of Dundee and NHS Tayside, and was ethically reviewed and approved by the East of Scotland Research Ethics Service REC 2. It was also registered with the National Institute for Health Research (NIHR) on UK Clinical Trials Gateway as ISRCTN27564683.

Outcomes

The primary outcome of the Eradicate-C study was to analyse SVR12 in the PWID population, which resulted in an 81.1% genotype 1 and 82.5% genotype 2 & 3 achieving SVR. The total SVR12 rate for all participants was 81.9%.

In this paper, the outcomes of interest were the behavioural and social measures collected during treatment. The primary outcome was injecting frequency throughout treatment (collected at visit 1, 4, 8, 12, 20, 24 and 26). Independent variables analysed were OST, living situation, living with other drug users, having children, having a partner, having a partner who used drugs/alcohol and the EQ5D scores. These measures were taken at visit 1 and visit 26, with the exception of OST, taken every visit from visit 2 to follow up (visits 27 and 28).

Study participants

A total of 94 participants completed up to 24 weeks of treatment between January 2013 and December 2016 within the largest Injecting Equipment Provision (IEP) service in Dundee (Scotland, UK). Participants were aged between 18 and 70 years, had an active HCV infection and reported current illicit drug use (defined as those who had injected in the past 4 weeks)which was confirmed through injection sites inspection.This study analysed behavioural and social data from visit 1 and visit 8 of treatment. Not all 94 participants who completed treatment provided data for both visits, reducing the pool of participants to 84 for the present analysis.

Analysis

Data was analysed using IBM SPSS Statistics 22. Descriptive analyses were run to obtain characteristics of the sample. If data was missing for one visit (e.g. visit 8) but available for immediately preceding and subsequent weeks (e.g. visits 7 and 9), an average score was used for the required missing visit. If immediately preceding and subsequent visit scores were not available, data was considered missing. Non-parametric testing was selected following data testing for violation of normality, which showed skewed data with kurtosis at all time points. A square root transformation was attempted to normalise distributions and eliminate outliers, but distribution remained skewed. Outliers were included in the analysis as non-parametric use of medians signifies outliers hold less influence over test results. The null hypothesis (no difference in injecting frequency at different time points) was tested with a non-parametric Friedman test, and subsequent post-hoc analyses using Wilcoxon Signed Ranked tests were run to identify where differences lay.

Effect size *r* was calculated with Rosenthal's formula $\square = \frac{\square}{\sqrt{\square}}$ [18], where Z is the post hoc Wilcoxon Signed Rank Test score and N is the number of observations. The coefficient *r* is more commonly used as a correlation coefficient to measure the strength of a relationship; however, it is a versatile coefficient and it is used, especially within non-parametric testing, as a measure of experimental effect [19].

Once identified that the largest injecting frequency difference was observed between week 1 and week 8 of the study, this difference was used to create a new dependent variable of injecting change, used in the analysis both as a categorical variable, to allow for Crosstab explorations using multiple categorical social factors, and as a continuous variable, to allow investigation of significant differences between the most important categorical social factors using Mann-Whitney U tests.

Results

A total of 106 participants consented to treatment. Two never completed baseline measures: 1 participant did not meet inclusion criteria and 1 participant died before starting treatment and completing baseline data. Of the remaining 104 consented, 94 completed treatment, but only 84 had completed behavioural and social data. Ten participants never commenced treatment: 3 spontaneously cleared the infection, 4 were lost to follow-up, 2 were treated on standard pathway after becoming drug-free and 1 was in prison out-with the catchment area. The remaining 10 consented participants who completed treatment had data missing for the visit 8 follow-up and were therefore not included in this sub-study analysis. Characteristics of participants at enrolment are presented in Table 1.

Table 1 shows $\square^2$ for the 2*2 tables, except for Partner uses drugs, where the smallest expected number is too small to be informative. There are 3 variables which make significance on $\square^2$: On OST, Has children and Has partner.

Only 32 of the 84 participants presented a complete set of data on injecting frequency at the 8 time points. A Friedman test for differences in weekly injecting frequency among the time points gave a significant result, $\chi^2_{\square}(7) = 36.44$, $p < .001$. The median for week 1 was 4.5, for week 4 was 2, and thereafter for weeks 8 to 26 the median was 1. The range for the 8 time points was always between 0-14 and 0-30. The results and effect sizes of post hoc analyses are shown in Table 2.

Week 8 was the time point at which the largest decrease in injecting was observed. Figure 1 shows the difference in mean injecting frequency between week 1 and week 8 of treatment among the grouping variables analysed above.

Chi-Square tests were run to explore associations between participant characteristics and injecting behaviour change as judged by the new variable Better or Not Better (Table 3). Odds ratio for the association between having a partner who used drugs and 'Better' was uninformative as one of the 2x2 factors equalled 0, causing the calculation to be impossible. The odds of reducing injecting behaviour were over 5 times as high for participants not on OST on week 2 compared to those who were on OST (OR 5.22; 95% CI 1.83-14.90; p=.002).

A Mann-Whitney U test showed that those who had a partner who used drugs and was also on treatment for HCV (N=22) reduced their injecting frequency significantly more than those whose partner was not on treatment (N=20), Z= -2.312, p=.021, medium effect size r =0.36. The mean weekly injecting difference was M = 5.65 (95% CI: -0.23 to 11.54) (Figure 1). These results were confirmed by analysing the association between the injecting frequency difference between week 1 and week 8 in couple members. Couples were assigned a couple ID. All couples were heterosexual.

The male-female Pearson's correlation coefficient was $r = .629$, $p = .038$, which meant that when males reduced their injecting, so did their female partners and vice versa.

Discussion

The findings of this paper show a significant reduction in injecting frequency between baseline, i.e. before the start of HCV treatment, and every other time point. The largest reduction was recorded between week 1 (baseline) and week 8, with injecting frequency stabilising thereafter whilst on treatment.

Possible mechanisms of behaviour change were explored using baseline social factors.

Benefits for non-OST patients

Firstly, not being on OST on week 2 of treatment (first treatment visit recording this information) was found to be associated with a significant reduction in injecting frequency. It has been widely demonstrated that OST impacts injecting drug use [20-23]. Meta-analysis and pooled analysis of the effect of OST and Needle and Syringe Programmes (NSP) on incidence of HCV infections [22] reported a mean injecting frequency reduction of 20.8 injections per month (95% CI: -27.3 to -14.4), though OST did not reduce lifetime timeframe duration of injecting [23]. So it is possible that the patients who were on treatment for HCV and were already enrolled on OST, had previously reduced their injecting frequency before starting HCV treatment. Previous studies however, have attributed decreases in ancilliary injecting equipment and decrease in recent injecting drug use to enrolment in HCV treatment [16-17]. Enrolment on OST might therefore attenuate the effects of receiving HCV treatment on injecting behaviour.

On the other hand, those who were not on OST on week 2 of Eradicate-C had not experienced the behavioural benefits of OST before their engagement with HCV treatment. It is well recognised that PWID are reluctant to access healthcare services, generally due to a lack of material resources, complicated and lengthy referral pathways, experience of stigma and poor relationship with healthcare providers [24-27]. For these individuals who were not on OST, engagement with HCV nurses might have been the only contact with any healthcare provider. Given the regular and considerate nature of this contact, a therapeutic relationship with the nurses providing the HCV treatment might have functioned as a behaviour change mechanism these patients had not experienced because not enrolled on OST. Therapeutic alliance was not measured in this study, yet previously published literature attests for the importance of this factor on healthcare outcomes relating to this population [28-31]. Meta-analyses have shown positive therapeutic alliance to increase patients' engagement and retention within drug services, as well as motivation, treatment readiness and treatment experience [31]. The results of this study suggest a possible negative correlation between engagement in HCV treatment and injecting behaviour frequency in populations who have mimimum contact with other healthcare services.

Behaviour change in intimate partnerships

The observed reduction in weekly injecting frequency was also linked to drug-using status of romantic partners. Those who had a partner who used drugs were more likely to reduce their injecting frequency, a reduction difference of more than 9 injections a week. This finding was surprising, as previous literature associated having a partner who uses drugs, in particular those injecting, with increased frequency of injecting and of sharing of injecting equipment [6-8, 14]. A variety of papers have been published on the power imbalance and social inequalities that drive injecting risk behaviour in heterosexual couples, in particular in women who inject drugs, who often rely on their male partner to acquire, prepare and inject the drugs [32-34]. Disregard of injecting risk occurs as a consequence of emotional closeness, intimacy, trust and commitment [14, 34-35]. Given the high level of sero-concordance in people who inject drugs in intimate partnerships [14], the study team identified patients in dyadic intimate partnerships who had both been enrolled on the Eradicate-C trial. The trial nurses identified 22 participants in couples. The final study findings confirmed that members of couples both treated for HCV on Eradicate-C were significantly more likely to reduce their injecting than other individuals.This effect was explored through models of behaviour change explaining the influence of partners on each other's health-related behaviour. The Interdependence model of couple communal coping and behaviour change [15], explores couple dynamics and their influence on motivation and health behaviour change.

In the general population, the health benefits of being married or in a committed intimate relationship are well documented [14-15]. People in romantic partnerships tend to be healthier, engage with health care services and show a longer lifespan [15]. The role of intimate partnerships within the drug using population, however, has often been linked to increased risk-taking behaviour and generally has been viewed as a bad influence on health [14, 32-35]. Qualitative studies have shown that HCV management within couples could help consolidate a relationship, introducing sentiments such as feeling valued and cared for [14]. PWID generally experience hostile social environments, and intimate partnerships which involve sentiments such as those above, might represent one of the only types of meaningful social support and care that PWID encounter [14]. Social support is regarded as an essential part of HCV treatment, with many care pathways for PWID involving the role of a peer support worker as integral part of the treatment [36], providing empathy and trustworthiness to patients on treatment. However, it is not simply individualistic social support perception that has to be considered to explain the study findings.

Lewis' couples' interdependence theory [15] explains how motivation transformation can occur when partners experience a health event which is not only significant for the self, but has cognitive and emotional significance for the relationship. The attribution of significance of the health event to the dyad rather than the individual is the result of automatic consideration of partnership roles, subjective norms, commitment, quality of the relationship, and trust [15]. HCV infection is a health threat that has both emotional and cognitive implications on the relationship and on each partner. These implications help transform motivation from 'individual-focused' to 'relationship-focused', adding a layer of complex interplay between intrapersonal and interpersonal behaviour change processes. Once motivation has become 'relationship-focused', couples work together through communal coping to achieve better health through shared action to manage the health threat [15, 37]. Communal coping requires shared beliefs that joint effort is advantageous to combat HCV, communication about HCV infection between partners and cooperation between partners to manage HCV and its treatment. Communal coping

impacts health behaviour through the processes of outcome efficacy and couple efficacy [15, 37]. The couple's belief about the effectiveness of the coping/action strategies, i.e. HCV treatment, coupled with the couple's confidence about engaging in joint coping, i.e. reducing injecting frequency will ensure HCV is less likely to recur in the couple, will influence the behavioural outcome. The responsibility of the couples' (and individual) health therefore lies equally on both partners, enabling the couple to become the unit for risk-reducing behaviour change [14-15]. Associations between changes in self-perception and self-care have been identified before [12, 38]. Often these self-perceptions are intended as the 'self' as an 'addict' becoming the 'self' as a 'patient worthy of HCV treatment' [12, 14]. A similar process of psychological alteration might take place within the couple, with the couple's identity changing from 'drug-using partners' to 'HCV-treated partners, who coped with effects of treatment and achieved SVR as a unit', presenting a shared sense of 'self'.

Reinfection

One of the main challenges of treating patients with ongoing injecting risk behaviour is the risk of reinfection following successful treatment (defined as 12 weeks post-treatment aviremia). Published literature shows that people who have previously been infected (and been treated) are more likely to become infected with HCV once again compared to people who are HCV-naïve [39-42]. In a meta-analysis of 59 studies, Simmons and colleagues [42] report pooled HCV recurrence rates for low-risk, high-risk and HIV co-infected populations after treatment during IFN-era: respectively 1.85/1000 person years of follow-up (PYFU), 22.32/1000 PYFU and 32.02/1000 PYFU. These recurrence rates led to a summary 5-year risk of 0.95%, 10.67% and 15.02% respectively [42].
Reducing injecting risk behaviour is the first step to reduce the risk of HCV reinfection after successful treatment. Reducing injecting behaviour within romantic partnerships could have particular benefits in preventing reinfection, given the widespread injecting equipment sharing practices among sexual partners. The observed injecting frequency reduction within couples during treatment in this study, would seem to suggest a transitive relation between treating couples in a romantic partnership and a reduced risk of reinfection, with the reduced injecting behaviour as the linking factor. This will be investigated in future reinfection studies.

Conclusions

This study shows that treating a hard-to-reach population for HCV infection is not only possible, but also suggests health benefits beyond treatment of HCV alone. A significant reduction in injecting behaviour was observed in people who are not on OST and/or couples on HCV treatment when partners are sero-concordant compared to the rest of the sample A complex interplay of relationship-focused motivation transformation, outcome efficacy, couple efficacy and communal coping might improve patients' injecting risk-avoidance behaviour.

A few limitations are recognised within the study. Firstly, albeit the initial sample size seemed promising, missing data at different time points and the selection of different grouping variables considerably reduced the sample size for some of the analyses (N=42). However, the majority of clinical trials experience missing data [43] and the analyses were performed taking this into consideration. Two social variables did show a significant difference between those retained in the study and those lost, suggesting those who were lost to follow-up were less likely to have romantic or family social connections. This observation gives even more importance to this paper's findings of being on HCV treatment with a romantic partner, as it would suggest important social connections can influence engagement with research and healthcare professionals. Secondly, the effect of the results might not be as large for DAA treatment. IFN-based treatment was notoriously harsh and both therapeutic alliance in non-OST patients and communal coping within the couples might have developed strongly as a consequence of this. With the advent of DAA treatment, relationship-focused motivation and communal coping might become less necessary and prominent. Fewer side effects, significantly shorter treatment times and ease of treatment (oral treatment) will render the development of communal coping somewhat unnecessary, therefore reducing the likelihood of couples influencing each others' health-enhancing behaviour change. Shorter treatment times and ease of treatment might also affect the quality of the therapeutic relationship established between hard-to-reach patients and healthcare provider. Once again, this might impact on the hereby observed injecting behaviour change. However, the notion of HCV treatment alone, rather than the hardship endured or the length of treatment time, might be enough to kick-start the motivational transformation within an intimate partnership and effects on communal coping and risk-behaviour reduction could still be observed in the DAA treatment era. Further research on similar populations being treated with IFN-free DAA is needed in order to shed light on the generalisability of these results.

REFERENCES

1. World Health Organisation. Global Hepatitis Report, 2017. apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf . Accessed April 13, 2018.
2. Blach S and the Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancel Gastroenterol Hepatol. 2017;2:161-76.
3. Aspinall EJ, Corson S, Doyle JS, Grebely J, Hutchinson S, Dore GJ, Goldberg DJ, Hellard ME. Treatment of hepatitis C virus infection among people who are actively injecting drugs: a systematic review and meta-analysis. Clin Inf Dis. 2013;57:s80-9.
4. Mcdonald SA, Hutchinson SJ, Schnier C, McLeod A, Goldberg DJ. Estimating the number of injecting drug users in Scotland's HCV-diagnosed population using capture-recapture methods. Epidem & Inf. 2014;142:200-7.
5. Nelson PK, Mathers B M, Cowie B, Hagan H, Des Jarlais D, Horyniak D, Degenhardt L. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet, 2011;378:571-83.
6. De P, Cox J, Boivin JF, Platt RW, Jolly A M. Social network-related risk factors for bloodborne virus infections among injection drug users receiving syringes through secondary exchange. J Urb Health: Bull NY Acad Med. 2007;85:77-89.
7. Dunn M, Degenhardt L, Bruno R. Transition to and from injecting drug use among regular ecstasy users. Addict Behav. 2010;35:909-12.
8. Shaw SY, Shah L, Jolly AM, Wylie J L. Determinants of injection drug users (IDU) syringe sharing: the relationship between availability of syringes and risk network member characteristics in Winnipeg, Canada. Addiction, 2007;102:1626-35.
9. Hellard M, Sacks-Davis R, Gold J. Hepatitis C treatment for injection drug users: A review of the available evidence. Clin Infect Dis. 2009;49:561-573.
10. Wolfe D, Luhmann N, Harris M, Momenghalibaf A, Albers E, Byrne J, Swan F. Human rights and access to hepatitis C treatment for people who inject drugs. Int J Drug Policy, 2015;26:1072-1080.

11. Janda M, Mergenhagen KA. The Effect of Psychosocial Factors on Success Rates of Hepatitis C Treatment. Psychosomatics, 2017;58:624-663.
12. Batchelder AW, Peyser D, Nahvi S, Arnsten JH, Litwin AH. "Hepatiits C treatment turned me around:" Psychological and behavioural transformation related to hepatitis C treatment. Drug & Alcohol Dependence 2015;153:66-71.
13. Treloar C, Rance J, Backmund M. Understanding barriers to hepatitis C virus care and stigmatization from a social perspective. Clin Infect Dis. 2013;57:S51-S55.
14. Rance J, Treloar C, Fraser S, Bryant J, Rhodes T. "Don't think I'm going to leave you over it": Accounts of changing hepatitis C status among couples who inject drugs. Drug & Alcohol Dependence, 2017;173:78-84.
15. Lewis MA, McBride CM, Pollak KI, Puleo E, Butterfield RM, Emmon KM. Understanding health behavior change among couples: An interdependence and communal coping approach. Soc Sc & Med. 2006;62:1369-1380.
16. Alavi M, Spelman T, Matthews GV, Haber PS, Day C, van Beek I, Walsh N, Yeung B, Bruneau J, Petoumenos K, Dolan K, Kaldor JM., Dore GJ, Hellard M, Grebeley J, on behalf of the ATAHC Study Group. Injecting risk behaviours following treatment for hepatitis C virus infection among people who inject drugs: The Australian Trial in acute hepatitis C. Int J Drug Policy, 2015;26:976-983.
17. Midgard H, Hajarizadeh B, Cunningham EB, Conway B, Backmund M, Bruggmann P, Bruneau J, Bourgeois S, Dunlop A, Foster GR, Hellard M, Robaeys G, Thurnheer M C, Weltman M, Amin J, Mark PS, Quiene S, Dore GJ, Dalgard O, Grebeley J on behalf of the ACTIVATE Study Group. Changes in risk behaviours during and following treatment for hepatitis C virus infection among people who inject drugs: The ACTIVATE study. Int J Drug Policy, 2017;47:230-238.
18. Rosenthal R. Meta-analytic procedures for social research. Newbury Park, CA: Sage, 1991. Revised Edition.
19. Field A. Discovering Statistics Using IBM SPSS Statistics. London: Sage Publications Ltd, 2017. 5th Edition.
20. Kemode M, Crofts N, Kumar MS, Dorabjee J. Opiod substitution therapy in resource-poor settings. Bull of the WHO, 2011;89:243.

21. Gowing L, Farrell M, Bornemann R, Sullivan LE, Ali R. Substitution treatment of injecting opioid users for prevention of HIV. Cochrane Database Syst Rev, 2008;21-85.
22. Turner KME, Hutchinson S, Vickerman P, Hope V, Craine N, Palmateer N, May M, Taylor A, De Angelis D, Cameron S, Parry J, Lyons M, Goldberg D, Allen E, Hickman M. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. Addiction, 2011;106:1978-1988.
23. Kimber J, Copeland L, Hickman M, Macleod J, McKenzie J, De Angelis D, Robertson JR. Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution treatment. BMJ, 2010;341:1-8.
24. Morgan K, Lee J, Sebar B. Community health workers: A bridge to healthcare for people who inject drugs. Int J Drug Pol. 2015;26:380-387.
25. Day C, Islam M, White A, Reid SE, Hayes S, Haber PS. Development of a nurse-led primary healthcare service for injecting drug users in inner-city Sydney. Australian J Primary Health, 2011;17:10-15.
26. Ahern J, Stuber J, Galea S. Stigma, discrimination and the health of illicit drug users. Drug Alcohol Depend. 2007;88:188-196.
27. Neale J, Tompkins C, Shear L. Barriers to accessing generic health and social care services: A qualitative study of injecting drug users. Health and Soc Care in the Community, 2008;16:147-154.
28. Simpson DD, Jow GW, Rowan-Szal GA. Drug abuse treatment retention and process effects on follow-up outcomes. Drug Alcohol Depend. 1997;47:227-235.
29. Haber, PS, Demirkol A, Lange K, Murnion B. Management of injecting drug users admitted to hospital. Lancet, 2009;374:1284-1293.
30. Schneider J, Kaplan SH, Greenfield S, Li W, Wilson IB. Better Physician-Patient Relationships Are Associated with Higher Reported Adherence to Antiretroviral Therapy in Patients with HIV Infection. J Gen Int Med. 2004;19:1096-1103.
31. Meier PS, Barrowclough C, Donmall MC. The role of the therapeutic alliance in the treatment of substance misuse: a critical review of the literature. Addiction, 2005;100:304-316.
32. Harvey E, Strathdee SA, Patrick DM, Ofner M, Archibald CP, Eades G, O'Shaughnessy MV. A qualitative investigation into an HIV outbreak among injecting drug users in Vancouver, British

Columbia. AIDS Care, 1998;10:313-321.

33. Wagner KD, Bloom JJ, Hathazi SD, Sanders B, Lankenau SE. Control over drug acquisition, preparation, and injection: Implication for HIV and HCV risk among young female injection drug users. ISRN Addiction, 2013:1-9.
34. El-Bassel N, Shaw SA, Dasgupta A, Strathdee SA. People Who Inject Drugs in Intimate Relationships: It Takes Two to Combat HIV. Current HIV/AIDS Rep. 2014;11:45-51.
35. Simmons J, Rajan S, McMahon JM. Retrospective accounts of injection initiation in intimate partnerships. Int J Drug Pol. 2012;23:303-311.
36. Bonnington O, Harris M. Tensions in relation: How peer support is experienced and received in a hepatitis C treatment intervention. Int J Drug Pol. 2017;47:221-229.
37. Lyons RF, Michelson KD, Sullivan MJ, Coyne JC. Coping as a communal process. J Soc & Pers Rel. 1998;15:579-605.
38. Jauffret-Roustide M, Cohen J, Poisot-Martin I, Spire B, Gossop M, Carrieri MP, Manif 2000 Study Group. Distributive sharing among HIV-HCV co-infected injecting drug users: the preventive role of trust in one's physician. AIDS Care, 2012;24:232-238.
39. Aitken CK, Lewis J, Tracy SL, Spelman T, Bowden DS, Bharadwaj M, Drummer H, Hellard M. High incidence of Hepatitis C Virus Reinfection in a Cohort of Injecting Drug Users. Hepatology, 2008;48:1746-1752.
40. Martinello M, Grebely J, Petoumenos K, Gane E, Hellard M, Shaw D, Sasadeusz J, Applegate TL, Dore GJ, Matthews GV. HCV reinfection incidence among individuals treated for recent infection. J Viral Hepat, 2017;24:359-370.
41. Page K, Hahn JA, Evans J, Shiboski S, Lum P, Delwart E, Tobler L, Andrews W, Avanesyan L, Cooper S, Busch MP. Acute Hepatitis C Virus Infection in Young Adult Injection Drug Users: A Prospective Study of Incident Infection, Resolution, and Reinfection. J Inf Dis, 2009;200:1216-1226.
42. Simmons B, Saleem J, Hill A, Riley RD, Cooke GS. Risk of Late Relapse or Reinfectoin with Gepatitis C Virus after Achieving a Sustained Virological Response: A Systematic Review and Meta-analysis. Clin Inf Dis, 2016;62:683-694.
43. Dziura JD, Post LA, Zhao Q, Fu Z, Peduzzi P. Strategies for Dealing with Missing Data in Clinical Trials: From Design to Analysis. Yale J Biol Med. 2013;86:343-358.

TABLES

Table 1: Characteristics of participants at enrolment on Eradicate-C study (study population and those lost to follow-up or with missing behavioural data).

Characteristic	Study population (N=84)	Lost to Follow-up or Missing Data (N=20)	□□	Smallest expected
Female Sex (%)	26 (31)	2 (10)	3.60	5.4
Age, median (IQR)	34 (23-45)	33 (25.25-40.75)		
Legal situation: none (%)	49 (58.3)	11 (55)	0.07	8.5
Living situation				
Homeless (%)	16 (19)	6 (30)	1.16	4.2
Living in own or rented accommodation (%)	61 (72.6)	13 (65)	0.46	5.8
Living alone (%)	38 (45.2)	12 (60)	1.41	9.6
Living with partner (%)	25 (29.8)	4 (20)	0.77	5.6
Living with parents (%)	12 (14.3)	1 (5)	1.27	2.5
Living with other drug users (%)	30 (35.7)	5 (25)	0.83	6.7
Romantic relationships				
Has partner (%)	42 (50)	5 (25)	4.08* Fisher p=0.049	9.0
Partner uses drugs (% of Has partner)	34 (81)	4 (80)	Fisher p=1	Too small
Has children (%)	50 (59.5)	7 (35)	3.92* Fisher p=0.08	9.0
Healthcare-related measures				
EQ5D Health state score, median (IQR)	50 (20-80)	45 (20-70)		
On OST (%)	60 (71.4)	4 (20)	4.06* Fisher p=0.07	4.3
Methadone dose, median (IQR)	70 (45-95)	75 (61-89)		
Weekly injecting frequency, Mean (STD)	9.39 (8.87)	11.35 (11.37)		

Table 2: Post Hoc comparisons for weekly injecting frequency between week 1 of treatment and all subsequent repeated measurement every 4 weeks (N=32).

	Z	p *	*r*†
Weeks 1-4	-3.534	< .001*	-.63
Weeks 1-8	-5.459	< .001*	-.97
Weeks 1-12	-5.265	< .001*	-.93
Weeks 1-16	-4.759	< .001*	-.84
Weeks 1-20	-3.768	< .001*	-.67
Weeks 1-24	-3.225	.001*	-.57
Weeks 1-26	-4.495	< .001*	-.80

* **Wilcoxon Signed Rank tests** Significant at p < .007 with Bonferroni correction
† Effect size *r*: Small = .1, Medium = .3, Large= .5

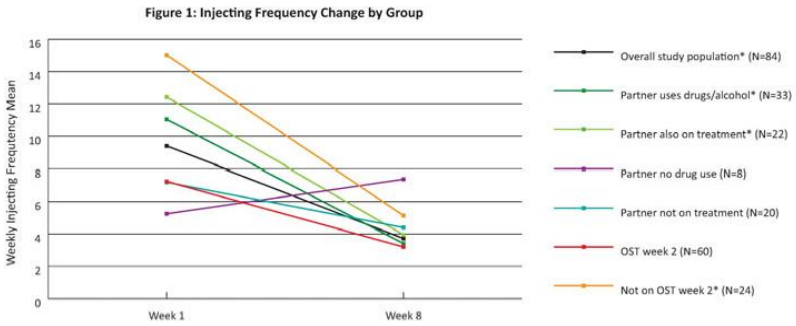
Table 3: Chi Square Tests for association between injecting behaviour change variable (better/not better†) and psychosocial factors.

Characteristic (N)	χ^2 (df)	p *	Fisher's Exact Test *
Legal situation (82)	4.254 (4)	.373	na
Living situation (82)	1.361 (3)	.715	na
Accommodation (82)	.04 (2)	.98	na
Living with other drug users (79)	2.007 (1)	.157	.21
Romantic relationships			
Has partner (42)	.023 (1)	.880	1
Partner uses drugs* (42)	4.43 (1)	.035*	.043*
Has children (82)	.067 (1)	.795	.813
Healthcare-related measures			
EQ5D Mobility (80)	.05 (1)	.823	1
EQ5D Self-care (80)	1.088 (1)	.297	.368
EQ5D Activity (79)	.621 (2)	.733	na
EQ5D Pain (80)	.905 (2)	.636	na
EQ5D Anxiety (80)	1.159 (2)	.56	na
On OST week 2* (82)	10.412 (1)	.001*	.003*

* Significant at p < .05
na: not available
† The difference between week 1 and week 8 injecting frequency was computed and categorised as 'Better' for a difference of ≥ 7or 'Not Better' otherwise

FIGURE LEGENDS

Figure 1: Injecting frequency change by grouping: * Significant at $p < .05$



Appendix 10.4

Second paper from thesis: Malaguti et al. 2020

Effectiveness of the use of implementation intentions on reduction of substance use: a meta-analysis.

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Effectiveness of the use of implementation intentions on reduction of substance use: a meta-analysis.

ABSTRACT

Objective: *Background*: Substance use, such as alcohol drinking, tobacco smoking and illicit drug use, have been associated with severe health conditions and an annual estimated 12% of all deaths worldwide. Implementation intentions are self-regulatory processes which help achieve health-related behaviour change. *Objectives*: To investigate the effectiveness of forming implementation intentions to reduce substance use.

Design: *Data sources*: PsycINFO, MEDLINE, Psychology and Behavioural Science Collection, clinicaltrials.gov, UK Clinical Trials Gateway, Reference lists. *Inclusion criteria*: RCT of substance users forming implementation intentions to reduce consumption (active or passive control condition present). *Study appraisal and synthesis methods*: the SIGN checklist for RCT quality was used for quality appraisal, data was extracted by two reviewers.

Results: Twenty-one studies were included in the meta-analysis. The overall effect size for alcohol use was g=0.31 (95% CI: 0.21, 0.42), p< .001; for tobacco smoking g=0.31 (CI: 0.12, 0.5), p=.002; no studies were retrieved for the use of implementation intentions on illicit drug use.

Conclusion: This review suggests that implementation intention interventions are effective in reducing some forms of substance use (alcohol use and tobacco smoking), albeit revealing small effect sizes, among the general population and students in secondary and higher education. *Review registration number*: CRD42018116170.

Keywords

Implementation intentions, substance use, alcohol, tobacco smoking, behavior change.

1 Background

Commonly consumed psychoactive substances such as alcohol, nicotine and opioids have been associated with a number of health conditions (World Health Organisation - WHO,

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2018a) and an estimated yearly 12% of all deaths worldwide (Hodder et al., 2016), amounting to around 11 million deaths a year.

Alcohol consumption is linked to both acute and chronic poor health outcomes (and related mortality) such as injuries, hepato-gastroenterological diseases, cardiovascular disease, infectious diseases and cancers (Bahorik et al., 2017; Schuckit, 2009; WHO, 2018a).

Smoking of tobacco is the single leading cause of preventable deaths around the world. Cardiovascular disease, cancers, chronic respiratory disease, diabetes have all been linked to tobacco smoking (WHO, 2014a). Illicit drug use disorders have been linked to increased mortality and other poor health outcomes, such as arthritis, chronic pain, bacterial and viral infections (HIV and hepatitis C), cardiovascular disease, poor mental health (e.g. suicidality, anxiety and depression), chronic pulmonary disease, respiratory and other cancers (Bahorik et al., 2017; WHO, 2016).

In the proceeding paragraphs, the association between substance use and health is investigated and categorised by substance.

1.1 Implementation intentions to promote health behaviour

Implementation intentions are self-regulatory processes which take the form of 'if-then' plans and facilitate the attainment of goals and behaviour change (Gollwitzer, 1993). The role of intentions in behaviour change has been explored within a variety of theories and models of behaviour change, e.g. Ajzen's Theory of Planned Behaviour (1991). Previous research shows that action planning interventions (implemented either as a once-off intervention or as repeated sessions) can be helpful in reducing substance use behaviours in both populations with diagnosed addictions (Latka et al., 2008; Robles et al., 2004) and the general population (Bolman et al., 2015).

Implementation intentions have been used to recognise contextual barriers and to plan in detail how to achieve a goal: when, where and how to perform a specific behaviour. They

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take the form of if-then plans: "if Y happens then I will perform Z", which commits individuals to behave in a particular way (Z) when they are presented with a certain situation (Y) (Gollwitzer, 1993). This provides the individual with self-regulatory strategies that create heightened accessibility of environmental cues, allowing individuals to automatically respond to contextual cues by unconsciously initiating their planned behaviour (Aarts et al., 1999; Gollwitzer, 1993). Implementation intentions are specifically mentioned in the Behaviour Change Technique Taxonomy (Michie et al. 2013) as a theoretical framework within action planning. Action planning in the taxonomy is the technique 1.4, part of Group 1: Goals and planning. It requires prompt detailed planning, including context, frequency, duration and/or intensity, of performance of a behaviour, and the context can be environmental or internal (Michie et al. 2013). Implementation intentions interventions can assume a variety of different formats. Type of implementation intentions can be oral or in writing, on paper or on screen (sometimes online), self-generated by people completing the intervention or pre-specified by the researchers or clinicians, or pre-specified situation and self-generated solutions (Armitage 2009; Armitage 2015; Caudwell et al. 2018; Hagger et al. 2012a).

A number of studies have investigated the effects of implementation intentions on health-related behaviours. A medium to large effect size of $d = 0.65$ was reported in a meta-analysis of behaviour change studies (Gollwitzer and Sheeran, 2006). Implementation intentions are a short and inexpensive intervention which could benefit people misusing substances and their effectiveness for such behaviours needs to be examined.

Numerous systematic reviews and meta-analyses have been carried out on the effectiveness of implementations intentions (Adriaanse et al., 2011; Bélanger-Gravel et al., 2013; Gollwitzer and Sheeran, 2006). No reviews to date have been solely focused on substance use and this review aims to rectify the lack of evidence on this topic.

1.2 Objectives

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This review's objective was to investigate the effectiveness of forming implementation intentions to reduce substance use in students and the general population. It aimed, in more detail, to answer the following questions:

1. Does forming implementation intentions reduce alcohol consumption?
2. Does forming implementation intentions reduce tobacco smoking?
3. Does forming implementation intentions reduce illicit drug use?

2 Methods

The methodology and reporting of this review comply with the PRISMA statement checklist for reporting of systematic reviews and meta-analyses (Moher et al., 2009), with the Meta-Analysis Reporting Standards – MARS (American Psychological Association, 2008) and with the Scottish Intercollegiate Guidelines Network (SIGN) checklist 1: systematic reviews and meta analysis (SIGN, 2018). The review protocol with methods and inclusion criteria was registered in advance on the University of York's Centre for Reviews and Dissemination PROSPERO register, as CRD42018116170.

2.1 Eligibility Criteria

Only studies written in English were considered for selection, with no limit on publication dates on the first searches carried out between April and September 2018. An update search was run in January 2019, to which restricted publication dates were applied between 2018 and 2019 only. No geographical restrictions were applied.

2.1.1 Participants

No restrictions were applied to study participant characteristics.

2.1.2 Interventions

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The intervention under review was the formation of implementation intention for the reduction of substance use behaviours, such as tobacco smoking, drinking alcohol, and other drug use. Trials with more than one intervention were selected when the implementation intention was reported independently so that the effect could be measured independently.

2.1.3 Comparisons

All studies had to present a control group. This included passive control groups (not performing any task) and active controls (performing an unrelated time-control task such as filling in an extra questionnaire or creating implementation intentions for an unrelated behaviour).

2.1.4 Outcomes

All studies were required to report on substance use as their main outcome measures.

2.1.5 Study Design

Randomised controlled trials (RCTs) were selected for review. Intervention follow-up length was left unrestricted for selection.

2.2 Information sources

The following databases were searched between April 2018 and September 2018 via EBSCOhost: PsycINFO, MEDLINE and Psychology and Behavioural Science Collection. Reference lists of all selected papers for screening were searched by hand between September and October 2018. The following clinical trial registers were searched in November 2018: Clinicaltrials.gov and UK Clinical Trials Gateway.

2.3 Search and Study selection

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The search strategy was similar across all databases, adjusting for database-specific headings. An example of the search strategy for PsycINFO is provided in Supplementary File 1.[1] Reference lists were searched by hand for relevant titles; whilst research registers were searched with "implementation intentions" in the title or trial description.

One reviewer carried out the full search on the three different databases via EBSCOhost. Searches were saved in an EBSCOhost folder. All selected titles were transferred into the reviewer's EBSCOhost list. Duplicates were removed manually.

2.4 Data collection process and items

Data was extracted by 2 reviewers together, both chartered health psychologists, and inputted into a summary table then transferred into the Comprehensive Meta-Analysis Software v3.3. The data extracted (See Table 1) were study design (including control group format), follow up period, sample characteristics (sample size, age, sex, students or general population), theoretical approach, behavioural goal (reduce alcohol consumption, reduce tobacco smoking or reduce drug use), implementation intentions format (online or pen & paper, pre-specified or self-generated, number of plans), outcome measures of substance use reduction (units/day, binge drinking occasions, cigarettes/day, tobacco smoking quitting status) and effect size (Hedge's g with specified 95% Confidence Intervals, See section 2.7 for effect size calculation). For 10 studies, the authors were contacted for data or data clarification. Eight replied and further information was provided for 5 studies.

2.5 Risk of bias in individual studies

Risk of bias in individual studies was assessed with the SIGN checklist 2 for randomised controlled trials (SIGN, 2018). This checklist assesses selection bias, ascertainment bias, measurement bias, attrition bias and reporting bias. Agreement for assessment of individual

[1] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi: ...

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studies by different reviewers was calculated using Cohen's kappa coefficient of inter-rater reliability (McHugh, 2012).

2.6 Statistical analyses

The Comprehensive Meta-Analysis software (version 3.3) was used to perform all calculations, test for heterogeneity and generate forest plots. Given the assumed heterogeneity in interventions, populations and outcomes, a random-effects model was selected (Hedges and Vevea, 1998).

2.7 Effect size calculations

For *continuous outcomes* (alcohol use and smoking) Hedges' g with 95% confidence intervals (CIs) were calculated as the difference between the intervention group's mean follow up scores and the comparison groups' mean follow up score divided by the pooled standard deviation and adjusted for sample size. Hedges' g corrects for small sample sizes (Borenstein et al., 2009).

For *dichotomous outcomes* (e.g. percentage of people who quit smoking, group differences in abstinence) we calculated the risk ratio (RR) and 95% confidence intervals (CIs) on the basis of the number of events and the number of participants in the intervention and control groups. We then transformed these (using meta-analysis software) to *g* statistics to allow for comparisons across studies (Borenstein et al., 2009).

In studies were the primary outcome was investigated with more than one measure (i.e. alcohol units consumed per week and binge drinking occasions or cigarettes smoked per day and nicotine dependence score) results were combined into a single overall outcome mean effect size (i.e. alcohol use or smoking) using the Comprehensive Meta-Analysis Software v3.3. This allowed for a more comprehensive meta-analysis, and heterogeneity checks were performed during the analysis to ensure validity of outcomes (Puhan et al., 2006).

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Alternative statistics (e.g. F-statistic, odd ratio or p-value and sample size) were used to calculate Hedge's g when studies did not provide means, standard deviations and proportions (Borenstein et al., 2009).

Effect sizes were coded so that positive scores signified favourable intervention effects such as lower alcohol use or smoking, with values of 0.20 considered small effects, 0.50 as medium and 0.80 as large (Cohen, 1988).

2.8 Assessment of heterogeneity

The I^2 and Q statistic tests were used to analyse heterogeneity between studies. I^2 indicates the heterogeneity percentage across the studies (Higgins, 2011). Sensitivity analyses were performed to explore potential sources of heterogeneity.

2.9 Assessment of publication bias

Three techniques were used to determine the extent to which publication bias impacted on the results of the overall sample. Funnel plots were created to explore the presence of publication bias. The Egger regression asymmetry test and the Begg and Mazumdar adjusted rank correlation test (Begg and Mazumdar, 1994) were performed to measure the extent of the funnel plot asymmetry, with $p<0.05$ indicating a statistically significant publication bias. Finally, the Duval and Tweedie's trim-and-fill method (Duval and Tweedie, 2000), in which the studies are 'trimmed' from the right of the funnel plot and entered on the left side to address funnel plot asymmetry, was used to formalise the result of the funnel plot.

2.10 Sensitivity analyses

Sensitivity analyses were performed to determine the robustness of intervention effects by evaluating whether the overall effect size was sensitive to inclusion of any individual study (Higgins and Green, 2011).

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3 Results

3.1 Study selection

AM screened 1756 titles and selected 79 relevant results for abstract selection. Abstracts were again screened by the same reviewer, who selected 29 relevant studies according to the eligibility criteria. Full-texts of 12 studies were excluded with reason and 18 were selected for quality appraisal and inclusion in this study (see supplementary file 2).[2]

A further 9 studies were found via reference lists searches, 2 excluded after abstract screening, 3 excluded after full-text assessment with reason, and 4 selected for quality appraisal. An extra 2 studies were selected for abstract screening after searching Clinicaltrials.gov and UK Clinical Trials Gateway. One was retained for full-text assessment and included in this study.

After re-running the searches in January 2019, an extra 104 studies were screened by title, 8 selected for abstract screening, 4 were removed as duplicates and 3 selected for full-text screening. All 3 were excluded with reason (see supplementary file 2).[3]

Overall, a total of 1906 were identified in the search for this review, 94 were screened through their abstract, 40 selected for full-text assessment, 18 excluded with reason (See supplementary file 2)[4], 22 selected for quality appraisal, and 21 included in the meta-analysis (See Figure 1). One study was included in the qualitative synthesis but excluded from the meta-analysis (Conner and Higgins, 2010). The study presented interval follow-up period of 4 to 48 months; however, the authors, after being contacted for unadjusted 4 months follow-

[2] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi: ...
[3] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi: ...
[4] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi: ...

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up data, suggested the exclusion of their paper on the basis of the multi-level nature of their data.

3.2 Characteristics of the studies

Among the 22 studies selected for the review, 15 studies were RCTs on interventions to reduce alcohol consumption, whilst the remaining 7 RCTs aimed at reducing cigarette smoking (See Table 1). One paper (Armitage and Arden, 2016) reported 2 different studies, which were treated as separate studies for the analysis, whilst another divided results by nationality of the sample (Hagger et al., 2012b) bringing the total number of studies reviewed for the alcohol use outcome to 18. All studies had suitable explanation about the randomisation procedure, albeit details on which online software or website was often missing. All studies reported behavioural outcomes.

The two main outcome analyses were run on studies with a follow-up of between 2 weeks and 3 months (k= 19), with a mean follow-up period of M= 5.68 weeks (SD= 4.8). These were all considered short follow-up timeframes, given healthy habits tend to require around 6 months to become established (Armitage et al., 2011).

The papers selected for the meta-analysis (k=21) reported an initial samples total of N= 6655. The analysed sample total was 2758, with some papers performing an intention-to-treat analysis (k= 13). Some of the studies selected were comparing control conditions to implementation intention groups and other intervention groups, such as Theory of Planned Behaviour messages (Table 1), increasing the difference between total and analysed samples. The participants included in these groups do not feature in this analysis as only the control groups and implementation intention groups were used for the analysis. In total, a sample of 2055 was analysed for the alcohol use outcome and 703 for the smoking outcome.

3.3 Characteristics of the participants

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The two main populations recruited within the selected studies were students (k=11) and the general population (k=10). The total mean age of the sample ranged from 16.6 to 43.7 (M= 26.97, SD= 8.69, k= 20). A slightly higher percentage of women was generally included in the studies, ranging from 43 to 76% (M= 59.03%, SD= 9.95, k= 22).

3.4 Characteristics of substance use outcomes

Most studies measuring alcohol use outcomes used self-reported weekly or daily consumption or binge drinking occasions (k=14). One study (Ehret and Sherman, 2018) used the Daily Drinking Questionnaire (Collins et al., 1985). The studies measuring tobacco smoking outcomes tended to use a mixture of self-report on cigarettes a day and quitting status (k=6), nicotine dependence score (k=3) and objective carbon monoxide (CO) breath tests (Matcham et al., 2014), a non-invasive procedure used for data validation.

3.5 Characteristics of implementation intention interventions

All studies referred to Gollwitzer's (1993) principles of implementation intentions. Implementation intentions were characterised mainly by two features. All implementation intentions were delivered after other questionnaires, such as demographic information or self-affirmation messages. The first feature to characterise the intervention was type of implementation intentions: self-generated (k=10) or pre-specified plans (k=12). The second feature was mode of delivery: delivered online on a computer screen (in person or remotely; k=5) or delivered in person on paper (k=17).

3.6 Risk of bias within studies

Risk of bias in individual studies was assessed with the SIGN checklist 2 for randomised controlled trials (SIGN, 2018). One reviewer (R1) completed the quality appraisal for all studies. A second reviewer (R2) appraised 13 studies whilst a third reviewer (R3) appraised 10 studies (McHugh, 2012). There was a substantial inter-rater agreement between R1 and

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R2, with K=0.64, p<.001 (n=143), and a moderate inter-rater agreement between R1 and R3, with K=0.54, p<.001 (n=110). Disagreement or discrepancies were resolved by discussion (See Table 2).

3.7 Synthesis of results

The effectiveness of implementation intention was analysed by behavioural outcome and described in the paragraphs below. The intervention effectiveness was calculated between-groups at follow-up.

3.7.1 Alcohol consumption

Firstly, data was pooled from 16 studies that reported unadjusted data (Arden and Armitage, 2012; Armitage, 2009; Armitage, 2015; Armitage and Arden, 2012; Armitage and Arden, 2016a; Armitage and Arden, 2016b; Armitage et al., 2011; Armitage et al., 2014; Caudwell et al., 2018; Ehret and Sherman, 2018; Hagger et al., 2012a; Hagger et al., 2012b (3 samples); Murgraff et al., 2007; Rivis et al., 2013) and included 2055 individuals (students and general population). The effect size for alcohol use was g=0.31 (95% CI: 0.21, 0.42), p< .001, indicating that implementation intentions had a small but significant effect in reducing alcohol consumption (Figure 2). The statistical heterogeneity across the studies was not significant ($Q_{statistic}$= 18.39; df=15; I^2 = 18.41%; p= .24).

3.7.2 Tobacco Smoking

Data was pooled from 6 studies (Armitage, 2007; Armitage, 2008; Armitage, 2016; Armitage and Arden, 2008; Matcham et al., 2014; Webb et al., 2009) and included 703 individuals. A small effect size was detected, with g=.31 (95% CI: 0.12, 0.5), p=.002, indicating that implementation intentions had a small effect on reducing tobacco smoking (Figure 3). The homogeneity analysis suggested a moderate, yet non-significant degree of statistical heterogeneity ($Q_{statistic}$= 9.9; df= 5; I^2 = 49.49%; p= .08).

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3.7.3 Illicit drug use

No studies that fitted the inclusion criteria were found in the present systematic search for the use of implementation intentions on reduction of illicit drug use. Literature suggests implementation intentions should be employed to prevent and treat addiction (Prestwich et al., 2006), yet more research is undoubtedly needed in this area. The lack of literature on this topic could also be due to publication bias, favouring publication of significant results.

3.8 Risk of bias across studies

3.8.1 Assessment of publication bias.

Funnel plots for the studies reporting alcohol and tobacco smoking follow-up effect sizes were visually inspected to assess publication bias, with no obvious bias detected (see supplementary file 3)[5]. Eggers regression test (Egger et al., 1997) showed no evidence of publication bias among the studies reporting alcohol use (intercept=0.4; SE=1.25; 95% CI: -2.28, 3.08) and among those reporting tobacco smoking (intercept=-2.33; SE=1.89; 95% CI: -7.57, 2.91). Furthermore, the trim and-fill method (Duval and Tweedie, 2000) suggested that no missing studies were needed to make the plot symmetric for the tobacco smoking outcome. Nevertheless, it suggested the inclusion of an extra 2 studies for greater symmetry for the alcohol outcome. This simply estimates that the addition of 2 unpublished studies would increase the symmetry of funnel plot, showing slight publication bias towards studies with positive medium effect sizes.

3.8.2 Sensitivity analyses

Sensitivity analyses were used to remove individual studies with high relative weight to investigate the robustness of the overall results. For the alcohol outcome, two studies (Armitage et al., 2011; Rivis et al., 2013) were found to influence the meta-analysis results

[5] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi: ..

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more than other studies. When Armitage et al. (2011) was omitted from the analysis, a slight reduction in pooled effect size was observed, g=0.28 (95% CI: 0.18, 0.39), p<.001. When Rivis et al. (2013) was omitted from the analysis, a slight increase in pooled effect size was observed, g=0.33 (95% CI: 0.21, 0.44), p<.001. Opposite effects were observed on the pooled effect size, with one study increasing and the other decreasing such value, confirmed by further analysis in which both studies were omitted and the effect size returned to be similar to the original pooled value, g= 0.3 (95% CI: 0.19, 0.41), p<.001.

For the tobacco smoking outcome, one study (Armitage and Arden 2008) was omitted, providing a slightly smaller effect size, g=0.25 (95% CI: 0.02, 0.48), p=.031.

4 Discussion

This meta-analysis reviewed the evidence of the effectiveness of implementation intention on the reduction of substance use. It found a small, yet significant, effect size for both alcohol use and tobacco smoking. The Hedges' g values reported in this meta-analysis are smaller than the medium effect size of *d* = 0.65 reported in a highly cited meta-analysis of behaviour change studies (Gollwitzer and Sheeran, 2006). The results are, however, similar to other meta-analyses investigating the effectiveness of implementations intentions on specific health behaviour, such as promoting physical activity, SMD= 0.24 (Bélanger-Gravel et al., 2013), and reducing unhealthy eating, d=0.29 (Adriaanse et al., 2011).

The results of this meta-analysis suggest that implementation intentions have been successfully applied to some substance use behaviours such as alcohol consumption and tobacco smoking, implying that the automaticity aspect of implementation intentions could function as the mechanism of behaviour change. The results for the alcohol use outcome were consistent throughout the sensitivity analyses, suggesting a degree of confidence in the

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strength of the findings. The number of studies included for this outcome (k=16) and the general high quality of the studies presented, contributed to the strength of the findings. The strength of the findings on the tobacco smoking outcome was slightly less consistent due to the low number of studies identified for the meta-analysis (k=6). However, the results are in line with previously published literature on effectiveness of implementation intentions (Adriaanse et al., 2011; Bélanger-Gravel et al., 2013; Kwasnicka et al., 2013).

In some of the included studies, implementation intention interventions were coupled or provided alongside other behaviour change techniques (BCTs), such as self-affirmation manipulations, social comparisons and information about social and environmental consequences or mental rehearsal of successful performance . It is possible that the effect sizes reported in the findings of this review might have been influenced by more than one BCT. This is the nature of social and health psychological research, presenting research with possible confounders given 'laboratory' experimental conditions are unnatural and arguably lack ecological validity (Orne, 1962).

Regrettably, this review was unable to analyse whether implementation intentions interventions can reduce illicit drug use. The lack of identifiable studies on this subject is surprising, highlighting a need for this type of research to be conducted. Given the interest this topic had raised in previous years (Brandstätter, Lengfelder & Gollwitzer, 2001; Churchill and Jessop, 2010; Prestwich et al., 2006; Verdejo-García et al., 2008), it is possible studies have been conducted, but have been victim of publication bias, where studies with no significant effects have failed to be published and distributed to the wider scientific community.

4.1 Implications for practice

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The damaging effects on health of substance use, such as alcohol and tobacco smoking, and their related mortality rates, were explored in detail at the start of this paper. Implementation intentions are a brief, one-off and inexpensive intervention that can be provided by primary and secondary care healthcare providers alike. They provide individuals with self-regulatory strategies to automatically initiate action planning after experiencing environmental cues. Given the small significant effect sizes and the characteristics of study participants, it is unclear what the implications from this review may be for clinical practice. Therefore future research on implementation intentions should test them as part of clinical practice with patients in alcohol use and smoking cessation settings.

4.2 Limitations

At a study level, this review did not exclude studies with high risk of bias. Only RCTs were included in the review, in order to minimise risk of bias and increase confidence in the overall findings. However, studies which were found to have low methodological quality were retained in the review, which could have increased the risk of bias at review level. Equally, excluding these studies might have increased the risk of bias at review level by reporting only high-quality studies. A decision was made to keep all studies despite their individual risk of bias, as there was an identified need to translate the findings into real-world clinical application, allowing therefore for some methodological imperfections.

At review level, other limitations were also identified. Only 3 databases were searched for literature, no grey literature was reviewed and only one reviewer conducted the searches and identified the studies for quality appraisal. Grey literature is not peer reviewed and therefore was purposefully not included. Two clinical trial databases were searched for ongoing RCTs, yet only published trials were identified with this search. Reference lists searches were conducted and proved fruitful.

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All populations included in the studies analysed were from Western societies. High-income Western countries may have a very different cultural relationship with substance use compared to low- and middle-income countries in other parts of the world. Further research which elucidates whether the automaticity of action planning initiation following environmental cues can differ between cultures should be conducted.

Lastly, the reviewers observed some heterogeneity with regards to implementation intentions intervention delivery, yet when I^2 and $Q_{statistic}$ tests were run to assess heterogeneity between studies, only the smoking outcome showed a somewhat moderate level of non-significant heterogeneity. All data was checked to be correct and this analysis was reported, as some degree of heterogeneity is to be expected in meta-analysis (Higgins, 2008).

4.3 Conclusions

This meta-analysis suggests that implementation intention interventions show significant small effects in reducing some forms of substance use (alcohol use and tobacco smoking) among the general population and students in secondary and higher education. The evidence of the effectiveness of this intervention could be improved by standardising implementation intention interventions (oral or written, self-generated or pre-specified, implementation intention seen once or with repeated exposure). Generalisability could be improved by conducting interventions in clinical populations and in low- to middle-income countries with different cultural views on substance use. Future research efforts should also be applied on the use of implementation intentions to reduce illicit drug use, whether or not the effect of this intervention is significant, and on the use of implementation intentions in clinical practice.

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Data Availability Statement

Data supporting the findings of this study are available in Open Science Framework at https://osf.io/gta24/?view_only=f78d38ccd2ab4cc99ae0b7d87ff47ec9 .

References

*Articles included in the present systematic review

Aarts, H., Dijksterhuis, A. P. and Midden, C. , 1999. To plan or not to plan? Goal achievement or interrupting the performance of mundane behaviors. Eur. J. Soc. Psychol. 29, 971-979.

Adriaanse, M. A., Vinkers, C. D. W., De Ridder, D. T. D., Hox, J. J. and De Wit J. B. F., 2011. Do implementation intentions help to eat a healthy diet? A systematic review and meta-analysis of the empirical evidence. Appetite, 56, 183-193.

Ajzen, I., 1991. The theory of planned behaviour. Organ. Behav. Hum. Decis. Process. 50: 179-211.

American Psychological Society Publications and Communications Board Working Froup on Kournal Article Reporting Standards (APA), 2008. Reporting standards for research in psychology: Why do we need them? What might they be? Am. Psychol., 63, 848-849.

*Arden, M. A. and Armitage, C. J., 2012. A Volitional help sheet to reduce binge drinking in students: a randomized exploratory trial. Alcohol Alcohol. 47, 156-159.

*Armitage, C. J., 2007. Efficacy of a brief worksite intervention to reduce smoking: the roles of behavioural and implementation intentions. J. Occup. Health Psychol. 12, 376-390.

*Armitage, C. J., 2008. A volitional help sheet to encourage smoking cessation: a randomised exploratory trial. Health Psychol. 27, 557-566.

Doi: https://doi.org/10.1016/j.drugalcdep.2020.108120

*Armitage, C. J., 2009. Effectiveness of experimenter-provided and self-generated implementation intentions to reduce alcohol consumption in a sample of the general populations: a randomized exploratory trial. Health Psychol. 28, 545-553.

*Armitage, C. J., 2015. Evidence that a volitional help sheet reduces alcohol consumption among smokers: a pilot randomized controlled trial. Behav. Ther. 46, 342-349.

*Armitage, C. J., 2016. Evidence that implementation intentions can overcome the effects of smoking habits. Health Psychol., 35, 935-943.

*Armitage, C. J. and Arden, M. A., 2008. How useful are the stages of change for targeting interventions? Randomized test of a brief intervention to reduce smoking. Health Psychol. 27, 789-798.

*Armitage, C. J. and Arden, M. A., 2012. A volitional help sheet to reduce alcohol consumption in the general population: a field experiment. Prev. Sci. 13, 635-643.

*Armitage, C. J. and Arden, M. A., 2016. Enhancing the effectiveness of alcohol warning labels with a self-affirming implementation intention. Health Psychol. 35, 1159-1163.

*Armitage, C. J., Harris, P. R. and Arden, M. A., 2011. Evidence that self-affirmation reduces alcohol consumption: randomized exploratory trial with a new, brief means of self-affirming. Health Psychol. 30, 633-641.

*Armitage, C. J., Rowe, R., Arden, M. A. and Harirs, P. R., 2014. A brief psychological intervention that reduces adolescent alcohol consumption. J. Consult. Clin. Psychol. 82, 546-550.

Doi: https://doi.org/10.1016/j.drugalcdep.2020.108120

Bahorik, A. L., Satre, D. D., Kline-Simon, A. H., Weisner, C. M. and Campbell C. I., 2017. Alcohol, Cannabis, and Opioid Use Disorders, and Disease Burden in an Integrated Healthcare System. J. Addict. Med. 11, 3-9.

Begg, C. B. and Mazumdar, M., 1994. Operating characteristics of a rank correlation test for publication bias. Biometrics, 50, 1088-1101.

Bélanger-Gravel, A., Godin, G. and Amireault, S., 2013. A meta-analytic review of the effect of implementation intentions on physical activity. Health Psychol. Rev. 7, 23-54.

Bolman, C., Eggers, S. M., van Osch, L., Poel, F. T., Candel, M. and de Vries, H., 2015. Is action planning helpgul for smoking cessation? Assessing the effects of action planning in a web-based computer-tailored intervention. Subst. Use Misuse, 50, 1249-1260.

Borenstein, M., Hedges, V., Higgins, J. P. and Rothstein, H. R., 2009. Introduction to meta-analysis. John Wiley & Sons Ltd., Chichester, UK.

Brandstätter, V., Lengfelder, A. and Gollwitzer, P. M., 2001. Implementation intentions and efficient action initiation. J. Pers. Soc. Psychol., 81, 946-960.

*Caudwell, K. M., Mullan, B. A. and Hagger, M. S., 2018. Testing an online, theory-based intervention to reduce pre-drinking alcohol consumption and alcohol-related harm in undergraduates: a randomized controlled trial. Int. J. Behav. Med. 25, 592-604.

Churchill, S. and Jessop, D. C., 2011. Too impulsive for implementation intentions? Evidence that impulsivity moderates the effectiveness of an implementation intention intervention. Psychol. Health, 26, 517-530.

Cohen, J., 1988. Statistical power analysis for the behavioural sciences. Lawrence Earlbaum Associates, Hillside, New Jersey.

Doi: https://doi.org/10.1016/j.drugalcdep.2020.108120

Collins, R. L., Parks, G. A. and Marlatt, G. A., 1985. Social determinants of alcohol consumption: the effects of social interaction and model status on the self-administration of alcohol. J. Consult. Clin. Psychol., 53, 189-200.

*Conner, M. and Higgins, A. R., 2010. Long-term effects of implementation intentions of prevention of smoking uptake among adolescents: a cluster randomized controlled trial. Health Psychol. 29, 529-538.

Cooper, H., Hedges, L. V. and Valentine, J. C., 2009. The Handbook of Research Synthesis and Meta-analysis. Russell Sage Foundation, New York City, USA.

Duval, S. J. and Tweedie, R. L., 2000. A nonparametric "trim and fill" method of accounting for publication bias in meta-analysis. J. Am. Stat. Assoc. 95, 89–98.

Egger, M., Davey-Smith, G., Schneider, M., and Minder, C., 1997. Bias in meta-analysis detected by a simple graphical test. BMJ, 315, 629-35.

*Ehret, P. J. and Sherman, D. K., 2018. Integrating self-affirmation and implementation intentions: effects on college student drinking. Ann. Behav. Med. 52, 633-644.

Gollwitzer, P. M. and Sheeran, P., 2006. Implementation intentions and goal achievement: A meta-analysis of effect and processes. Adv. Exp. Soc. Psychol. 38: 69-119.

*Hagger, M. S., Lonsdale, A. and Chatzisarantis, N. L. D., 2012a. A theory-based intervention to reduce alcohol drinking in excess of guideline limits among undergraduate students. Br. J. Health Psychol. 17, 18-43.

*Hagger, M. S., Lonsdale, A., Koka, A., Hein, V., Pasi, H., Lintunen, T., Chatzisarantis, N. L. D., 2012b. An intervention to reduce alcohol consumption in undergraduate students using

Doi: https://doi.org/10.1016/j.drugalcdep.2020.108120

implementation intentions and mental simulations: a cross-national study. Int. J. Behav. Med. 19, 82-96.

Hedges, L. V. And Vevea, J. L., 1998. Fixed- and random-effects models in meta-analysis. Psychol. Methods, 3, 486-504.

Higgins, J. P. T., 2008. Commentary: heterogeneity in meta-analysis should be expected and appropriately quantified. Int. J. Epidemiol. 37, 1158–1160.

Higgins, J. P. T. and Green, S. (editors), 2011. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Accessed online on 12/11/18 at handbook-5-1.cochrane.org

Hodder, R. K., Freund, M., Bowman, J., Wolfenden, L., Gillham, K., Dray, J. and Wiggers, J., 2016. Association between adolescent tobacco, alcohol and illicit drug use and individual and environmental resilience protective factors. BMJ Open, 6, e012688.

International Alliance for Responsible Drinking – IARD, 2018. Drinking guidelines: General population. Accessed online on 30/11/18 at iard.org/resources/drinking-guidelines-general-population/

Kwasnicka, D., Presseau, J., White, M. and Sniehotta, F. F., 2013. Does planning how to cope with anticipated barriers facilitate health-related behaviour change? A systematic review. Health Psychol. Rev. 7, 129-145.

Landis, J. R. and Koch, G. G., 1977. The measurement of observer agreement for categorical data. Biometrics, 33, 159-174.

Latka, M. H., Hagan, H., Kapadia, F., Golub, E. T., Bonner, S., Campbell, J. V., Coady, M. H., Garfein, R. S., Pu, M., Thomas, D. L., Thiel, T. K. and Strathdee, S. A., 2008. A

Doi: https://doi.org/10.1016/j.drugalcdep.2020.108120

Randomized Intervention Trial to Reduce the Lending of Used Injection Equipment Among Injection Drug Users Infected With Hepatitis C. Am. J. Public Health, 98, 853-861.

*Matcham, F., McNally, L. and Vogt, F., 2014. A pilot randomized controlled trial to increase smoking cessation by maintaining National Health Service Stop Smoking Service attendance. Br. J. Health Psychol. 19, 795-809.

McHugh, M. L., 2012. Inter-rater reliability: The kappa statistic. Biochem. Med. 22, 276-282.

Michie, S., Richardson, M., Johnston, M., Abraham, C., Francis, J., Hardeman, W., Eccles, M. P., Cane, J. and Wood, C. E. 2013. The Behavior Change Technique Taxonomy (v1) of 93 Hierarchically Clustered Techniques: Building an International Consensus for the Reporting of Behavior Change Interventions. Ann Behav Med, 46: 81-95.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G. and The PRISMA Group, 2009. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 6, e1000097.

*Murgraff, V., Abraham, C. and McDermott, M., 2007. Reducing Friday alcohol consumption among moderate, women drinkers: evaluation of a brief evidence-based intervention. Alcohol Alcohol. 42, 37-41.

*Norman, P. and Wrona-Clarke, A., 2016. Combining self-affirmation and implementation intentions to reduce heavy episodic drinking in university students. Psychol. Addict. Behav. 30, 434-441.

*Norman, P., Cameron, D., Epton, T., Webb, T. L., Harris, P. R., Millings, A. and Sheeran, P., 2018. A randomized controlled trial of a brief online intervention to reduce alcohol

Doi: https://doi.org/10.1016/j.drugalcdep.2020.108120

consumption in new university students: Combining self-affirmation, theory of planned behaviour messages, and implementation intentions. Br. J. Health Psychol. 23, 108-127.

Prestwich, A., Conner, M. and Lawton, R. J., 2006. Implementation Intentions: Can they be used to prevent and treat addiction?. In Wiers, R. W. and Stacy, A. W. (Eds). Handbook of Implicit Cognition and Addiction (455-470). SAGE Publications Inc.,Thousand Oaks, California, US.

Puhan, M. A., Soesilo, I., Guyatt, G. H. and Schünemann, H. J., 2006. Combining scores from different patient reported outcome measures in meta-analyses: when is it justified? Health Qual. Life Outcomes, 4, 1-8.

*Rivis, A. and Sheeran, P., 2013. Automatic risk behaviour: direct effects of binge drinkers stereotypes on drinking behaviour. Health Psychol. 32, 571-580.

Robles, R. R., Reyes, J. C., Colón, H. M., Sahai, H., Marrero, A., Mator, T. D., Calderón, J. M. and Shepard, E. W., 2004. Effects of combined counseling and case management to reduce HIV risk behaviors among Hispanic drug injectors in Puerto Rico: A randomized controlled study. J. Subst. Abuse Treat. 27, 145-152.

Ronksley, P. E., Brien, S. E., Turner, B. J., Mukamal, K. J. and Ghali, W. A., 2011. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. BMJ, 342, d671.

Schuckit, M., 2009. Alcohol-use disorders. Lancet, 373, 493-501.

Scottish Intercollegiate Guidelines Network – SIGN, 2018. Critical appraisal notes and checklists. Accessed online on 06/09/2018 at sign.ac.uk/checklists-and-notes.html

Doi: https://doi.org/10.1016/j.drugalcdep.2020.108120

Sheeran, P., 2002. Intention-behaviour relations: A conceptual and empirical review. Eur. Rev. Soc. Psychol. 12, 1-36.

Sheeran, P., Milne, S., Webb, T. L. and Gollwitzer, P. M., 2005. Implementation intentions and health behaviour. In Conner, M. and Norman, P. (Eds): Predicting health behaviour, second edition, 276-323. Open University Press: Maidenhead.

Siu, N. Y. F., Lam, H. H. Y., Le, J. J. Y. and Przepiorka, A. M., 2014. Time perception and time perspective differences between adolescents and adults. Acta Psychol. 151, 222-229.

Steinberg, L., Graham, S., O'Brien, L., Woolard, J., Cauffman, E. and Banich, M., 2009. Age Differences in Future Orientation and Delay Discounting. Child Dev. 80, 28-44.

Sutton, A. J., Abrams, K. R. and Jones, D. R., 2001. An illustrated guide to the methods of meta-analysis. J. Eval. Clin. Pract. 7, 135-148.

Sutton, S., 1998. Predicting and Explaining Intentions and Behavior: How Well Are we Doing? J. Appl. Soc. Psychol. 28, 1317-1338.

Verdejo-García, A., Lawrence, A. J., Clark, L., 2008. Impulsivity as a vulnerability marker for substance-use disorders: Review of findings from high-risk research, problem gamblers and genetic association studies. Neurosci. Biobehav. Rev. 32, 777-810.

*Webb, T. L., Sheeran, P. and Luszczynska, A., 2009. Planning to break unwanted habits: habit strength moderates implementation intention effects on behaviour change. Br. J. Soc. Psychol. 48: 507-523.

World Health Organisation – WHO, 2014a. Global status report on noncommunicable diseases 2014:"Attaining the nine global noncommunicable diseases targets; a shared responsibility". Geneva.

Doi: https://doi.org/10.1016/j.drugalcdep.2020.108120

World Health Organisation – WHO, 2016. Cannabis. The health and social effects of non-medical cannabis use. Accessed online on 30/11/18 at who.int/substance_abuse/publications/en

World Health Organisation –WHO, 2018a. Global status report on alcohol and health 2018. Geneva, Licence: CC BY-NC-SA 3.0 IGO.

Doi: https://doi.org/10.1016/j.drugalcdep.2020.108120

Table 1: Table 1: Summary table of characteristics of studies included in the meta-analysis (*k*=22)

Authors (year)	Study Design (group types)	Follow up period	Sample characteristics	Behavioural goal	Implementation intentions format	Measures of substance use reduction	Effect size (Hedge's g) [95%CI]
Arden & Armitage (2012)	RCT (2x control groups and 1x II)	2 weeks	56 students; Age: 20.57y (1.9); 66.1% ♀; UK	Reduce alcohol consumption	Pen and paper, pre-specified situation and solutions.	Alcohol consumption Units/week, binge drinking occasions	Combined g= 0.64 [0.21; 1.07]
Armitage (2007)	RCT	2 months	90 adults; Age: 33y (13); 45.56% ♀; UK	Reduce tobacco smoking	Pen and paper for one self-generated plan.	Nicotine dependence, N of quitters	Combined g=0.47 [0.08; 0.85]
Armitage (2008)	RCT (2 intervention x2 control)	1 month	193 adults; Age: 37y (14.6); 51.8% ♀; UK	Reduce tobacco smoking	Pen and paper, pre-specified situation and solutions.	Cigarettes/day, nicotine dependence , N of quitters	Combined g=0.57 [0.23; 0.9]
Armitage (2009)	RCT (2 intervention x2 control)	1 month	248 adults; Age: 38.4y (15.46); 50.4% ♀; UK	Reduce alcohol consumption	Pen and paper form. Plans pre-specified/self-generated in the written form	Alcohol consumption Units/day	g= 0.3 [-0.06; 0.66]
Armitage (2015)	RCT (Intervention, Active control)	1 month	65 adults; Age: 33.77y (9.69); 56.9% ♀; UK	Reduce alcohol consumption	Pen and paper form. Control asked to tick pre-specified VHS, intervention to link	Alcohol consumption Units/week	g= 0.13 [-0.35; 0.61]
Armitage (2016)	RCT 4 groups (if-then, when-then, 2 x control)	1 month	168 adults; Age: 33y (12.30), 47.01% ♀; UK	Reduce tobacco smoking	Pen and paper, pre-specified situation and solutions.	Quitting, cigarettes/day	g=-0.01 [-0.43; 0.41]
Armitage & Arden (2008)	RCT (2x control groups and 1x II)	2 months	350 adults; Age: 36.20y (14.3); 50.6% ♀; UK	Reduce tobacco smoking	Pen and paper, self-generated plan	Quitting and nicotine dependence score	Combined g= 0.46 [0.26; 0.67]
Armitage & Arden (2012)	RCT (2 CP (multiple or single) x II x active control	3 months	69 adults; Age: 38.51y (16.34); 52.2% ♀; UK	Reduce alcohol consumption	Pen and paper, pre-specified situation and solutions.	Alcohol consumption in Units	g= 0.54 [-0.13; 1.2]

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Armitage & Arden (2016)	2-study RCT	1 month	Adults & students; UK Study 1: N= 85 Age 23.69y (3.61); 62.38% ♀; Study 2: N= 58 Age: 19.38y (0.9); 75.86% ♀;	Reduce alcohol consumption	Self-affirming pre-specified intention	Alcohol consumption in Units/Week	Study 1 g= 0.59 [0.16; 1.02] Study 2 g= 0.47 [-0.04; 0.99]
Armitage et al. (2011)	RCT (2 experimental, 1 control)	1 month	278 adults; Age Range 16-74; 66.2% ♀; UK	Reduce alcohol consumption	Pen and paper form. Pre-specified plans but participants had to write them down as one sentence (not link them)	Alcohol consumption in Units/Day	g= 0.57 [0.28; 0.86]
Armitage et al. (2014)	RCT (experimental and control group)	2 months	67 adolescents; Age: 17.09y (0.38); 55.22% ♀; UK	Reduce alcohol consumption	Pen and paper form. Pre-specified plans but participants had to write them down as one sentence	Alcohol consumption in Units/Day	g=0.19 [-0.29; 0.66]
Caudwell et al. (2018)	RCT (2 autonomy support x 2 II)	4 weeks	202 students; Age: 20.95y (4.02); 73% ♀ Australia	Reduce alcohol consumption	Online, to use example given or elf-generate plan.	Weekly pre-drinking summed to create monthly score	g=0.07 [-0.43; 0.56]

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Conner & Higgins (2010)	RCT (II, self-efficacy intervention, 2 control conditions)	48 months	1551 adolescents; Mean age NR; 48.9% ♀; UK	Reduce tobacco smoking	Pen and paper, 5 x pre-specified plans	Jarvis (1997) self-report smoking measure or objective carbon monoxide breathalyser. Binary variable.	g=0.24 [-2.64; 3.12]
Ehret & Sherman (2018)	RCT (II, self-aff, control, II+self-aff)	2 weeks	293 college students; Mean age NR; 70% ♀; USA	Reduce alcohol consumption	On screen in lab. Self-generated plans	Typical drinking week measured with Daily Drinking Questionnaire;	g=0.26 [-0.08; 0.59]
Hagger et al. (2012a)	Cluster RCT 2x2 (mental simulation; II)	1 month	238 undergraduate students; Age: 20.35y (2.51); 58% ♀; UK	Reduce alcohol consumption	Online, self-generated plans + self-affirmation manipulation.	Alcohol consumption in Units/Week & binge drinking occasions	Combined g=0.25 [-0.16; 0.66]

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Hagger et al. (2012b)	Multi-centred Full-factorial RCT 2x2 (mental stimulation; impl intentions)	1 month	718 undergraduate students (240 Estonia, 194 Finland, 284 UK); Age: 21.37y (SD range= 2.7-4.28); 74% ♀	Reduce alcohol consumption	Pen and paper, self-generated plans.	Alcohol consumption in Units/week and binge drinking occasions	UK sample Combined g= 0.35 [0.06; 0.65] Estonian sample Combined g= 0.31 [0.02; 0.6] Finnish sample Combined g= -0.16 [-0.49; 0.18]
Matcham et al. 2014	RCT 2x2 (effectiveness booklet and/or/not II)	4 weeks	160 adults; Age: 43.7y (14.2); 54.4% ♀; UK	Reduce tobacco smoking	Pre-specified plans written on paper but repeated orally.	Self-report 4-week quit status (and CO breath test where possible)	g= 0.06 [-0.4; 0.53]
Murgraff et al. (2007)	RCT	8 weeks	347 students; Age: 26y (SD NR) 73.2% ♀; UK	Reduce alcohol consumption	A4 paper sheet with recommended daily units + statements of normative misperceptions + statements to boots self-efficacy + 6 pre-specified plans.	Alcohol consumption on Friday (units)	g=0.44 [0.09; 0.8]

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Norman & Wrona-Clarke (2016)	Cluster RCT 2x2 (mental simulation; II)	1 week	348 undergraduate students; Age: 22.58y (6.31); 64.1% ♀; UK	Reducing alcohol consumption	Online, self-generated plans + self-affirmation manipulation.	Alcohol consumption in Units/Week and binge drinking occasions	Combined g=0.19 [-0.04; 0.42] Adjusted data
Norman et al. (2018)	RCT (2 self-affirmation x 2 TPB messages x 2 II)	6 months	2682 students; Age: 18.76y (1.94); 53.8% ♀; UK	Reduce alcohol consumption	Online, self-generated plans.	Alcohol consumption in Units/week and binge drinking sessions	Combined g= -0.03 [-0.23; 0.17] Adjusted data
Rivis et al. (2013)	RCT (2 II x 2 stereotype evaluation)	1 month	202 pupils; Age: 16.62y (0.68); 55.4% ♀; UK	Reduce alcohol consumption	One pre-specified plan on paper read by participant 3 times	Binge drinking sessions	g=0.2 [-0.08; 0.47]
Webb et al. (2009)	RCT (1 intervention, 1 control)	1 month	172 students; Age: 18.49y (SD NR); 43% ♀; UK	Reduce tobacco smoking	Pen and paper. 4 pre specified situations, subjective solution. Seat belt control group.	Cigarettes/day	g= 0.11 [-0.19; 0.41]

Note: RCT - Randomised Controlled Trial; II - Implementation intentions; VHS - Volitional Help Sheet; NR – Not reported.

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Table 2: Risk of bias

	Randomisation sequence concealment (selection bias)	Allocation concealment (selection bias)	Blinding of subjects and investigators (ascertainment bias)	Similarity in groups at baseline (selection bias)	Relevant, valid and reliable outcomes (measurement bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Overall quality
Arden & Armitage 2012	+	+	?	+	+	+	+	++
Armitage 2007	+	+	+	+	+	+	+	++
Armitage 2008	+	+	+	+	+	+	+	++
Armitage 2009	+	+	+	+	+	+	?	++
Armitage 2015	+	+	+	+	+	+	+	++
Armitage 2016	+	+	+	+	+	+	+	++
Armitage & Arden 2008	+	+	+	-	+	+	+	++
Armitage & Arden 2012	+	+	+	+	+	+	?	++
Armitage & Arden 2016	+	+	?	+	+	?	?	++
Armitage et al. 2011	+	+	+	+	+	+	+	++
Armitage et al. 2014	+	+	+	+	+	+	+	++
Caudwell et al. 2018	+	+	+	+	+	-	+	++
Conner & Higgins, 2010	+	+	-	-	+	-	+	+
Ehret et al. 2018	+	?	?	?	+	+	+	+
Hagger et al. 2012a	+	+	+	-	+	-	?	-
Hagger et al. 2012b	+	+	?	-	+	-	+	+
Matcham et al. 2014	+	-	-	?	+	?	+	+
Murgraff et al. 2007	+	-	?	?	?	-	?	-
Norman & Wrona-Clarke 2016	+	+	+	+	+	+	-	+
Norman et al. 2018	+	-	-	+	+	-	+	+
Rivis & Sheeran, 2013	+	?	?	+	?	-	?	-
Webb et al. 2009	+	+	+	+	+	+	+	++

Note: Quality assessed as: ++ (High quality); + (Acceptable); - (Low quality), ? (Can't say/Does Not Apply)

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