The progression and management of depression and anxiety in chronic hepatitis C patients

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Thesis submitted in fulfilment of the requirements for the combined degree of Doctor of Philosophy with Master of Psychology (Clinical)

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LIST OF ABBREVIATIONS

ACT, Australian Capital Territory

AD, anti-depressant(s)

CALD, culturally and linguistically diverse

CBT, cognitive behavioural therapy

CHC, chronic hepatitis C

CI, confidence interval

C-UP, a Unified Program for people with hepatitis C to manage depression and anxiety

DASS, Depression Anxiety Stress Scales

DSM, Diagnostic and Statistical Manual of Mental Disorders

DSP, disability support pension

GP, general practitioner

HADS, Hospital Anxiety and Depression Scale

HBV, hepatitis B virus

HCV, hepatitis C Virus

HIV, human immunodeficiency virus

ICD, International Classification of Diseases

IDRS, Illicit Drug Reporting System

IDU, injecting drug use(rs)

IFN, interferon

IQR, interquartile range

K10, 10-item Kessler Psychological Distress Scale

M, mean

MDN, median

MOS-SSS, Medical Outcomes Study Social Support Survey

NSMHW, National Surveys of Mental Health and Wellbeing

NSW, New South Wales

NT, Northern Territory

OR, odds ratio

QLD, Queensland

RA, rheumatoid arthritis

RAH, Royal Adelaide Hospital

RCT, randomised controlled trial

RR, risk ratio

SA, South Australia

SCID, Structured Clinical Interview for DSM-IV Axis I Disorders

SCL-90-R, Revised 90 Item Symptom Checklist

SD, standard deviation

SE, standard error

SEIFA, Socio-Economic Index For Areas

SVR, sustained viral response

TAS, Tasmania

US, United States of America

VIC, Victoria

WA, Western Australia

ABSTRACT

In those living with chronic hepatitis C (CHC), co-morbid depression and anxiety are highly prevalent (el-Serag, Kunik, Richardson, & Rabeneck, 2002), leading to diminished quality of life (Häuser, Zimmer, Schiedermaier, & Grandt, 2004), exacerbated physical symptoms (Morasco et al., 2010), increased functional impairment (Dwight et al., 2000), and poorer anti-viral treatment outcomes (Zanini, Covolo, Donato, & Lanzini, 2010). However, there is a dearth of research exploring this co-morbidity and how best to assess and manage it. This body of work aimed to address this gap in the literature in conducting the four studies comprising this thesis.

Study one assessed the acceptability of various mental health treatment options through a postal survey of South Australian CHC outpatients and an online survey of Australians living with CHC in the community. This study found that individual psychotherapy was the most acceptable treatment, followed by bibliotherapy, pharmacotherapy, online therapy, and group psychotherapy. The most important predictor of the acceptability of a treatment was past satisfaction with use of that treatment modality. Study two assessed the progression of depression and anxiety symptoms over a course of between two and five years. This was conducted in a sub-sample of CHC outpatients who responded to the survey used in study one and were also participants of a previous study assessing the prevalence and predictors of depression and anxiety (Stewart et

al., 2012). This study reported a worsening of depression and anxiety over time. Baseline anxiety was the most prominent predictor of future depressive and anxious symptomatology.

Study three examined changes in self-reported rates of mental health problems and service use in regular injecting drug users in the 2006 and 2012 Illicit Drug Reporting System surveys conducted by the National Drug and Alcohol Research Centre, over half of whom reported also having CHC. This study found that while the rates of self-reported problems increased significantly, there was an accompanying decrease in service use (albeit with a proportional increase in the use of psychologists). Study four involved the development of a treatment protocol entitled "C-UP: A Unified Program for people with hepatitis C to manage depression and anxiety." A transdiagnostic cognitive behavioural therapy approach was chosen as it has the promise of treating co-morbid depression and anxiety simultaneously, a clinical presentation which is common in people with CHC (el-Serag et al., 2002; Navinés et al., 2012; Stewart et al., 2012). C-UP involves five components which cover psychoeducation, acceptance of distressing emotions, cognitive restructuring, behavioural activation and graded exposure, and relapse prevention. Informal feedback from clinical psychologists, CHC workers, and those living with CHC was overwhelmingly positive. However, a randomised controlled trial and qualitative research is needed to more rigorously assess the efficacy and acceptability, respectively, of C-UP.

When considering the deleterious effects of co-morbid depression and anxiety, it is apparent that a comprehensive and targeted approach on a policy and practice level is needed. While this approach has been lacking to date, it is anticipated that this thesis will lead to an increased focus on the assessment and management of co-morbid depression and anxiety in research, policy, and clinical practice.

DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree. I give consent to this copy of my thesis when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968. The author acknowledges that copyright of published works contained within this thesis resides with the copyright holder(s) of those works. I also give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

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OVERVIEW

Outline of candidature

The current dissertation was undertaken to fulfil the requirements of a combined Master of Psychology (Clinical) with Doctor of Philosophy program at The University of Adelaide, South Australia, Australia. The studies have combined a full research program for a Doctor of Philosophy (equivalent to three years full time) with a Clinical Masters of Psychology (equivalent to two years full time) within a four year period of candidature. The research component of this program must have a clinical psychological focus to fulfil the requirements of the degree. The Masters component of this program includes a coursework load totalling 21 units with 1 000 hours of clinical internship totalling 12 units. The following thesis is submitted to fulfil the requirements of a Doctor of Philosophy.

Outline of thesis

This thesis examines the progression of co-morbid depression and anxiety in people living with chronic hepatitis C and explored methods for managing this co-morbidity. Chapter I provides a brief overview of the relevant literature surrounding psychiatric co-morbidity associated with chronic hepatitis C

infection. Chapter II provides a summary of the four research studies presented in this thesis. Chapters III through VI include the manuscripts of each of the four studies. Chapter VII provides a discussion of the strengths and limitations of the thesis, a summary of the key findings, and recommendations for further research, policy, and practice.

CHAPTER I: INTRODUCTION

This chapter provides a brief overview of the literature on the psychiatric co-morbidity associated with chronic hepatitis C (CHC) infection while contextualising this with necessary medical information. Particular attention is focussed on: (1) the natural history and pathogenesis of CHC; (2) epidemiology of CHC; (3) testing, diagnosis, and treatment of CHC; (4) depression and anxiety; (5) epidemiology of psychiatric co-morbidity; (6) aetiology of psychiatric co-morbidity; (7) effects of psychiatric co-morbidity; and (8) treatment of psychiatric co-morbidity.

1.1. The natural history and pathogenesis of the hepatitis C virus

Formerly known as non-A, non-B hepatitis, the hepatitis C virus (HCV) was first identified in 1989 (Choo et al., 1989; Kuo et al., 1989). HCV is a member of the flaviviridae family and hepacivirus genus and consists of six viral genotypes and more than 50 subtypes (Hoofnagle, 2002). The virus is transmitted parenterally, usually via direct percutaneous transmission as in injections or transfusions of contaminated blood or blood products or, more rarely, via inadvertent mucous-membrane transmission, such as sexual or perinatal transmission (Liang, Rehermann, Seeff, & Hoofnagle, 2000). The virus then enters hepatocytes and other vulnerable cells within the liver and

replicates, establishing acute HCV infection which is usually either unaccompanied by any overt symptomatology, or coincides with non-specific symptoms such as jaundice, malaise, or nausea - usually within seven to eight weeks (Lauer & Walker, 2001).

The immune system's response is sufficient to clear the viral infection in approximately 25% of those acutely infected with HCV within six to 12 months, while the remaining 75% experience chronic hepatitis C (CHC) infection (Micallef, Kaldor, & Dore, 2006). Several factors are positively associated with the progression to chronicity, including younger age, male gender, African-American ethnicity, lack of jaundice during acute infection, and immune deficiency (Hoofnagle, 2002). In patients with CHC, the failure of the immune system response leads to low level hepatocellular injury and persistent inflammation within the liver, which can, over a period of time, progressively lead to liver fibrosis (formation of scar tissue), cirrhosis (replacement of liver tissue with accumulated scar tissue which compromises liver function), steatosis (accumulation of fat within the liver), and hepatocellular carcinoma (Guidotti & Chisari, 2006; Liang et al., 2000). Similar to the progression from acute to chronic disease, the development of liver cirrhosis also generally occurs without overt symptomatology (Seeff, 2002).

Consequently, it is difficult to follow the natural history of infection and the prognosis can vary widely after two decades of infection have passed (Seeff, 2002). Furthermore, the rate of progression across the disease continuum is non-linear (Thein, Yi, Dore, & Krahn, 2008). Nevertheless, a meta-analysis

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calculated an estimated risk of cirrhosis of 16% at 20 years post- infection and 41% at 30 years post-infection (Thein et al., 2008). Older age at infection, male gender, and higher alcohol consumption increase the rate of progression to cirrhosis (Thein et al., 2008). Once liver disease has progressed to compensated cirrhosis, where the liver can still function reasonably, the risk of developing further complications for each additional year is 3.6-6.0% for developing decompensated cirrhosis, 1.4-3.3% for hepatocellular carcinoma (which can develop independently of cirrhosis), and 2.6-4.0% for death from liver disease (Everson, 2005). Once decompensated liver cirrhosis develops, five year survival is only 50% (Everson, 2005).

To summarise, HCV is a blood-borne viral infection which, once contracted, generally progresses to chronic infection without symptoms. While a quarter of individuals acutely infected will spontaneously clear the virus, in the remaining 75% who are chronically infected, a minority will slowly progress to the potentially fatal sequelae of liver cirrhosis, liver cancer, and liver failure.

1.2. Epidemiology of CHC

According to recent global estimates, there are approximately 160 million chronically infected individuals, constituting 2.35% of the world's population (Lavanchy, 2011). Estimated prevalence rates vary dramatically between various regions of the world; there are approximately 400 000 (1.2%) chronically infected individuals in Australia and Oceania, 14 million (1.5%) in the Americas,

83 million (2.1%) in Asia, 17.5 million (2.3%) in Europe, 28.1 million (3.2%) in Africa, and 16 million (4.7%) in the Middle East. In most developed countries, the predominant mode of viral transmission is injecting drug use (IDU), as the widespread adoption of blood product screening procedures since the early 1990s has virtually eliminated nosocomial infection (Lavanchy, 2009). Conversely, nosocomial transmission is still the predominant form of transmission in many developing nations, although the role of IDU is increasing (Lavanchy, 2009). The global burden of morbidity and mortality resulting from HCV is considerable. It is estimated that 27% of the cases of cirrhosis and 25% of hepatocellular carcinoma worldwide can be attributed to HCV (Perz, Armstrong, Farrington, Hutin, & Bell, 2006).

Recent estimates suggest that, of the 310 000 Australians who have been exposed to HCV, 231 500 are chronically infected and 6 500 are living with HCV-related cirrhosis (The Kirby Institute, 2013). Of those infected with HCV prior to 2005, it is estimated that 82.3% acquired the virus through IDU, 10.9% were migrants from countries with high HCV prevalence, and 6.8% were exposed through other routes of transmission, including blood transfusions occurring before the advent of screening procedures in 1990, as well as peri-natal, sexual, occupational, or household exposure (Razali et al., 2007). However, IDU accounts for just under 90% of the estimated 10 000 newly acquired HCV infections each year (Razali et al., 2007). Men are more likely to be infected with HCV and the male to female ratio for HCV notifications is 1.7:1 (Gidding et al., 2009).

A recently published Australian community-based linkage study revealed markedly increased rates of morbidity due to HCV (Gidding, Amin, Dore, Ward, & Law, 2010). When compared with hospitalisation rates of the general population in New South Wales (NSW), rates of hospitalisation in HCV infected individuals were found to be 1.4 times higher for all causes, 16.1 times higher for illicit drug use, 5.1 times higher for alcohol-related admissions, 9.5 times higher for alcoholic liver disease, 14 times higher for non-alcoholic liver disease, and 16.2 times higher for liver cancer (Gidding et al., 2010). Individuals with HCV were also more likely to be hospitalised for renal failure, diabetes mellitus, blood and immune disorders, atherosclerosis, respiratory diseases, skin and subcutaneous tissue diseases, and injury, poisoning, and other consequences of external causes (Gidding et al., 2010). HCV-related cirrhosis was the most common primary indication for liver transplantation between 1997 and 2006 in Australia, constituting 25% of all cases, with a further 5.5% of cases having HCV-related cirrhosis as a secondary indication, and 50% of cases having an indication of hepatocellular cancer with co-morbid HCV infection (Gidding et al., 2009).

With respect to mortality, another recent linkage study demonstrated that mortality rates due to liver disease were 16.8 times higher in HCV infected individuals when compared with the NSW population, while mortality rates due to drug-induced death were 19.3 times higher (Amin, Law, Bartlett, Kaldor, & Dore, 2006). However, it is estimated that just 6.9% of all deaths amongst individuals infected with HCV between 1960 and 2005 were attributable to HCV

(Razali et al., 2007). Moreover, evidence suggests that in people with HCV, the risk of dying from drug-related causes is significantly higher than the risk of dying from liver-related causes (Amin et al., 2006).

In economic terms, the cost of CHC is considerable (Brown & Crofts, 1998; Shiell & Law, 2001). In 1998 it was estimated that if the rate of 10 000 new HCV infections in Australian IDUs continued for 60 years, the direct healthcare costs alone would be approximately AUD $4 billion during that period (Brown & Crofts, 1998). Shiell and Law (2001) estimate that for every single incidence of HCV infection avoided, AUD $19 100 would be saved in health care costs and lost productivity.

In countries with higher prevalence rates and population sizes, the morbidity, mortality, and economic costs may be even more significant. In the U.S., it is estimated that from 2010 to 2019, 181 300 people will die from HCV-related chronic liver disease, 27 200 will die from HCV-related hepatocellular carcinoma, with the direct medical costs totalling USD $10.7 billion (Wong, McQuillan, McHutchison, & Poynard, 2000). After adding the economic costs of lost quality of life, productivity, and caregiver time, the total economic burden of HCV in the U.S. between 2010 and 2019 is projected to be a staggering USD $184 billion (Shah & Wong, 2006).

In summary, HCV is predominantly transmitted via IDU in Australia and other developed nations, while nosocomial transmission is more prevalent in the developing world. Recent data suggest that morbidity and mortality rates are

significantly elevated in those with HCV infection, yet most individuals with HCV die from drug-related causes. Nevertheless, due to the particularly high prevalence of HCV both globally and, to a lesser extent, within Australia, the number of deaths resulting from HCV and the burden on the health care systems is considerable - and expanding.

1.3. Testing, diagnosis, and treatment of CHC

Due to the lack of specific symptoms indicating the presence or progression of HCV infection until advanced disease with complications present, current guidelines recommend that testing occurs following the identification of any risk factor in individuals (Ghany, Strader, Thomas, & Seeff, 2009; National HCV Testing Policy Expert Reference Committee, 2012). Such individuals may include those who: (1) have injected illicit drugs; (2) have been incarcerated; (3) have received organs, tissues, blood, or blood products before February 1990 in Australia, or at any time overseas; (4) have had skin penetrating procedures such as tattoos performed in settings with poor infection control, such as some countries overseas or custodial settings; (5) were born in countries with a high HCV prevalence rate; (6) are health care workers who have been exposed to blood or bodily fluids which may contain blood, such as through needle stick injuries; (7) are from Aboriginal or Torres Strait Islander backgrounds; (8) were born to HCV-positive mothers; and (9) have had sexual intercourse with a HCV-infected partner (Ghany et al., 2009; National HCV

Testing Policy Expert Reference Committee, 2012). However, it should be noted that the risk of sexual transmission is very low unless there is an exposure to blood, unprotected anal sex, and/or co-infection with human immunodeficiency virus (HIV) in men who have had sex with men.

HCV testing generally involves performing an immunoassay detecting the presence of HCV antibodies in serum or plasma which can identify, but not distinguish between, cases of acute, resolved, or chronic infection, whereas a polymerase chain reaction test can be conducted to detect HCV ribonucleic acid in the blood which confirms current (most likely chronic) infection (Ghany et al., 2009). The current Australian guidelines stipulate that pre- and post-test discussions should take place between the health care provider and the individual being tested (National HCV Testing Policy Expert Reference Committee, 2012). This counselling should ascertain the readiness of the individual for testing, obtain informed consent, and provide information on the testing process, legal requirements regarding disclosure, appropriate infection control practices, medical and complementary management, and support services. These discussions and the testing process should be completed in person and performed in a manner which is sensitive to the individual's gender, culture, knowledge, and practices. There should also be an assessment of the individual's informal and formal support systems and referral for support where required.

Until recently, the standard treatment for CHC has involved a combination therapy of pegylated interferon (IFN) delivered subcutaneously once per week

and orally ingested ribavirin daily (Ghany et al., 2009). Treatment with this regime is required for 24 weeks for those with genotypes 2 and 3, 48 weeks for those with genotypes 1, 4, or 6, and there are no strict guidelines on the duration for those with genotype 5 (Ghany et al., 2009). Response to treatment is typically defined by sustained virological response (SVR), or the inability to detect HCV ribonucleic acid in serum using a polymerase chain reaction test at 24 weeks following the cessation of treatment. SVR rates can vary by genotype and viral load, with SVR rates of patients with genotype 1 ranging from 42-52%, those with genotype 2 or 3 ranging from 76-84%, and those with genotype 4, 5, or 6 achieving rates of 50-82% (Fried et al., 2002; Hadziyannis et al., 2004; Manns et al., 2001). Those with a high baseline viral load achieve SVR rates from 42-53%, while those with lower viral loads achieve SVR rates from 53-78% (Fried et al., 2002; Manns et al., 2001). Those co-infected with HIV have diminished SVR rates of approximately 27% (Carrat et al., 2004; Chung et al., 2004).

Recent therapeutic developments have led to the addition of the protease inhibitors boceprevir or telaprevir to the regimen of IFN and ribavirin in those with genotype 1, leading to increased SVR rates of approximately 70% and cutting treatment times to 24-28 weeks in around 50% of patients (Asselah & Marcellin, 2011; Dore, 2012). IFN-free regimes are also expected to arrive in the near future (Vermehren & Sarrazin, 2011), with several preliminary clinical trials already reported in the recent literature (Kowdley et al., 2014; Lawitz et al., 2014; Sulkowski et al., 2014).

Treatment with pegylated IFN and ribavirin can frequently result in haematologic, dermatologic, neurologic, immunologic, gastrointestinal, pulmonary, cardiovascular, and ocular adverse events (Sulkowski et al., 2011). Approximately 10-14% of patients discontinue therapy due to these adverse events (Sulkowski et al., 2011). The most common physical side effects are similar to those for influenza and include fatigue in 60-90% of patients, headaches in 40-50%, fever in 20-30%, and myalgia in 20-30% (Sulkowski et al., 2011). Common neuropsychiatric side effects include anxiety or irritability in 24-47% of patients, insomnia in 30-40%, depression in 20-30%, dizziness in 14-21%, impaired concentration in 10-17%, and mania in 1-10% (Loftis, Matthews, & Hauser, 2006). A recent meta-analysis reported that at least 25% of patients commencing antiviral treatment develop an IFN-induced major depressive episode (Udina et al., 2012). With the addition of new antiviral drugs, there is an increased risk of toxicity, with telaprevir inducing rash and boceprevir anaemia (Dore, 2012). There is no evidence of increased neuropsychiatric side-effects with the new direct acting antivirals (Sockalingam, Tseng, Giguere, & Wong, 2013). Despite the advent of these new therapies which require less administration of IFN, and the promise of IFN-free treatment in the future, at the present time IFN remains a staple of the anti-viral treatment for CHC and its associated physical and psychiatric side effects will continue to limit patients' ability to access and adhere to therapy, as detailed further in chapter 1.6.

To summarise, a diagnosis of CHC is generally conducted in response to the identification of various risk factors for infection and involves detection of

HCV antibodies and ribonucleic acid in the blood. Guidelines hold that pre- and post-test counselling, in addition to the diagnosis of CHC or lack thereof, should be delivered appropriately and in person. While an effective antiviral treatment is available and can clear the virus in around 70-80% of patients, physical and neuropsychiatric side effects are common.

1.4. A brief description and classification of depression and anxiety

As a primary focus of this research is co-morbid depression and anxiety in those with CHC, the following section will provide a brief description and classification of these co-morbidities. For the purposes of this research, depression refers to depressive disorders described in the recently released fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013, pp. 155-188), while anxiety refers to the anxiety disorders as described in the DSM-5 (American Psychiatric Association, 2013, pp. 189-233). Research has demonstrated that psychiatric symptoms exist on a continuum of severity and chronicity, with diagnosable disorders occurring at a point along that continuum (Klein, 2008; Solomon, Haaga, & Arnow, 2001). Thus, in this thesis, depression and anxiety also refer to the collection of symptoms consistent with these disorders which may be sub-clinical yet lead to significant distress or functional impairment.

The shared features underlying depressive disorders are periods of depressed or sad mood, accompanied by a variety of somatic and cognitive changes, which cause clinically significant distress or functional impairment (American Psychiatric Association, 2013, p. 155). The main distinguishing features of different depressive disorders are the duration, intensity, and causes of depressive episodes (American Psychiatric Association, 2013, p. 155). The two main depressive disorders are major depressive disorder and persistent depressive disorder. Major depressive disorder involves the occurrence of, often recurrent, major depressive episodes, where an individual experiences either depressed mood or diminished pleasure/interest in activities most of the day and nearly every day for a period of at least two weeks (American Psychiatric Association, 2013, p. 160). This is accompanied by other symptoms such as an increase/decrease in weight/appetite, insomnia or hypersomnia, psychomotor agitation/retardation, fatigue or lack of energy, worthlessness or guilt, diminished concentration or indecisiveness, or recurrent thoughts of death or suicidality (American Psychiatric Association, 2013, pp. 160-161). Persistent depressive disorder subsumes the previous diagnoses of dysthymia and chronic major depressive disorder in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text-Revision (DSM-IV-TR; American Psychiatric Association, 2000). This disorder occurs when an individual experiences depressed mood for a period of at least 2 years, accompanied by symptoms such as increased/decreased weight/appetite, insomnia or hypersomnia, fatigue, low self-esteem, poor concentration or indecisiveness, or feelings of hopelessness (American Psychiatric Association, 2013, p. 168).

Anxiety disorders involve the persistent and excessive experience of states of fear and anxiety which cause clinically significant distress and/or functional impairment, often via persistent avoidance of the stimulus which induces this fear/anxiety (American Psychiatric Association, 2013, pp. 189-233). Fear is the emotional response to real or perceived threats and is typically accompanied by autonomic arousal, also known as the fight or flight response, and immediate escape behaviours (American Psychiatric Association, 2013, p. 189). Anxiety involves the anticipation of potential future threats, typically accompanied by muscle tension and checking or avoidant behaviours (American Psychiatric Association, 2013, p. 189). Anxiety disorders often include the presence of panic attacks which involve rapid onset bouts of intense fear, physical sensations, and associated cognitive symptoms (American Psychiatric Association, 2013, pp. 189-190).

The most prominent feature distinguishing anxiety disorders are the objects or situations which provoke the fear/anxiety (American Psychiatric Association, 2013, p. 189). Some of the major anxiety disorders from the DSM-5 (American Psychiatric Association, 2013, pp. 189-233) include: (1) Specific phobias, where individuals experience persistent and excessive fear, anxiety, and/or avoidance of specific objects or situations such as animals, heights, or injections; (2) Social anxiety disorder or social phobia, where individuals are fearful, anxious, and/or avoidant of social interaction and social situations where the possibility of experiencing scrutiny, judgement, and/or embarrassment exists; (3) Panic disorder, where an individual experiences recurrent,

unexpected panic attacks, fear/anxiety about future panic attacks, and avoidance of situations which may induce a panic attack; (4) Agoraphobia, where an individual is fearful or anxious about being in places or situations where escape would be difficult or help would be unavailable in the event of experiencing symptoms of anxiety; (5) Generalised anxiety disorder, where individuals experience persistent, excessive, and seemingly uncontrollable worry about everyday matters such as work, school, finances, and relationships. This is accompanied by symptoms such as restlessness, irritability, fatigue, difficulty concentrating, muscle tension, and sleep impairment.

1.5. The epidemiology of psychiatric co-morbidity

A great wealth of research has demonstrated a significantly elevated incidence of psychiatric co-morbidity in people with CHC (Butt, Evans, Skanderson, & Shakil, 2006; Butt, Khan, McGinnis, Skanderson, & Kent Kwoh, 2007; el-Serag et al., 2002). However, the specific rates of morbidity vary widely, and depend on: (1) the characteristics of the sample investigated, such as country, setting, and inclusion criteria; (2) the type of psychiatric morbidity, such as lifetime or current morbidity; and (3) the methods used to determine psychiatric morbidity, such as self-report scales or diagnostic interviews, and prospective or retrospective data collection. These different methodological characteristics have numerous advantages and disadvantages which may either increase or decrease the prevalence rates found.

The characteristics of the study population may be an important influence on the prevalence rates found. Findings from research using veteran samples may have inflated prevalence rates as veterans have pre-existing higher rates of psychiatric disorders in comparison to the general population (Hankin, Spiro Iii, Miller, & Kazis, 1999). As these samples are predominantly male, they may also not readily generalise to female populations. Research which fails to include strict inclusion criteria relating to the confirmation of chronic infection through polymerase chain reaction testing measures may also be biased as their samples may include patients who are no longer infected. Other studies using samples comprising patients about to commence antiviral therapy also introduce sample and response biases. Firstly, patients who wish to undertake antiviral treatment may be a particularly motivated or functional sub-sample of the wider population. Secondly, patients who are eligible to commence antiviral therapy often have to meet criteria relating to liver histology, alcohol or substance abstinence, or a lack of psychotic or other severe mental illnesses. This may mean the sample is suffering from a comparatively smaller psychological burden, or that the sample is more motivated to 'fake good' in order to receive treatment and may subsequently attempt to underestimate their burden when completing self-report instruments or responding in clinical interviews. Findings from studies using outpatients actively engaged in medical care also may not readily generalise to the community population of people with CHC not engaged in ongoing medical management.

The type of morbidity investigated also influences the results as lifetime rates of morbidity are obviously much higher than current rates. Also, certain categories of disorders are also more or less frequent. For example, substance use disorders are unsurprisingly frequent as IDU is a common risk factor for HCV acquisition. Other disorders follow general trends in the wider population, such as mood or anxiety disorders being more prevalent than psychotic disorders. Finally, whether studies investigate and report rates of specific diagnoses such as generalised anxiety disorder versus broader categories such as any anxiety disorder also have implications for estimating the prevalence of psychiatric disturbance in people with CHC in its various manifestations.

Finally, the methods used to ascertain patients' psychiatric status are also important. Studies using retrospective analysis of medical records data may underestimate the prevalence of morbidity as research has demonstrated that psychiatric disorders can persist undiagnosed in as many as 85% of CHC outpatients (Batista-Neves et al., 2008; Golden, O'Dwyer, & Conroy, 2005). Further, studies which rely on more stringent criteria for demonstrating morbidity such as formal diagnostic interviews may be more reliable and valid than those which use self-report instruments, yet introduce a higher risk for selection bias with respect to people willing to undergo a lengthy diagnostic interview. In addition, in the class of studies using self-report instruments, some scales have higher sensitivity and specificity rates than others. Moreover, even within research using the same instruments, different studies often adopt different cut-off scores for determining 'case-ness.' This breadth of methodological variety

makes reaching a consensus regarding the prevalence of psychiatric morbidity quite difficult. The following section will overview research focussed on the prevalence of current disorders confining itself to data from studies with large sample sizes or smaller samples where a structured clinical interview was used to establish diagnoses. A summary of prevalence rates for mood disorders, anxiety disorders, substance use disorders, and other psychiatric disorders is provided in Tables 1 to 4, respectively.

Three large population-based studies have been conducted to analyse the prevalence of psychiatric co-morbidity in CHC patients. El-Serag and colleagues (2002) retrospectively analysed hospital data for 33,824 HCV-infected veterans hospitalised from 1992-1999. They reported a lifetime prevalence rate of 85% for any psychiatric or substance use disorder and a current (defined as any hospitalisation to psychiatric or drug-rehabilitation bed sections during the study period) rate of 35% (el-Serag et al., 2002). A history of substance use disorders was reported in 80% (current in 35%), while a history of other psychiatric disorders was reported in around 56%, with current rates of 35 and 19% respectively (el-Serag et al., 2002). For specific disorders, lifetime rates were 46% for depression, 38% for anxiety disorders, 23% for post-traumatic stress disorder, 23% for psychotic disorders, 16% for bipolar disorders, and 14% for dementia/delirium (el-Serag et al., 2002). As previously discussed, these rates may be inflated due to their sampling of veterans. Moreover, their reliance on predominantly inpatient data is likely to have inflated

rates of mental illnesses which commonly require hospitalisation, such as substance use disorders, psychotic disorders, and bipolar disorder.

More recently, Butt and colleagues (2007) conducted a similar retrospective analysis of both in- and out-patient data for 126 971 HCV-infected veterans. They reported lifetime rates of 35% for an alcohol use disorder, 30% for a drug use disorder, 19% for mild depression, 11% for major depressive disorder, 13% for post-traumatic stress disorder, 7% for schizophrenia, and 7% for bipolar disorder (Butt et al., 2007). While this study was not as influenced by a reliance on in-patient data, the use of veteran data may have skewed their results, and current rates were not able to be determined. For comparison, Butt et al. (2006) also conducted similar analyses with 5,737 renal dialysis patients, who were approximately 10 years older, on average, than the veteran sample. They reported markedly lower lifetime rates of 17% for drug use disorders, 14% for alcohol use disorders, 14% for mild depression, 8% for major depression, 1.5% for bipolar disorder, 2.5% for schizophrenia, and 0.3% for post-traumatic stress disorder (Butt et al., 2006).

A number of studies have prospectively explored the prevalence of current psychiatric disorders in smaller convenience or consecutively sampled outpatients. Some of these have used structured clinical interviews based on the criteria of the DSM-IV or the International Classification of Diseases, version 10 (ICD-10; World Health Organisation, 1992). Coughlan and colleagues (2002) administered the Schedule for Clinical Assessment in Neuropsychiatry using ICD-10 criteria to 60 CHC Irish female outpatients (out of pool a 182

consecutive attendees, with 33 patients participating but not demonstrating current infection). They reported current rates of 25% for any depressive disorder (15% for mild depressive disorder) and 28% for any anxiety disorder (8% for phobic anxiety disorder, 7% for generalised anxiety disorder, and 8% for panic disorder) for this sample (Coughlan et al., 2002).

Another Irish study (Golden et al., 2005) administered the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) to 90 outpatients from a pool of 101 potential participants (five declined to participate while six were incarcerated and presented too great a security risk to participate). They reported current rates of 28% for any depressive disorder (8% for major depression, 11% for adjustment disorder with depressed mood, and 9% for depressive disorder not otherwise specified or dysthymia), 24% for any anxiety disorder (12% for panic disorder and phobias, 7% for adjustment disorder with anxiety, 2% for obsessive-compulsive disorder, and 3% for anxiety disorder not otherwise specified), 26% for opiate abuse or dependence, and 1% for alcohol abuse or dependence (Golden et al., 2005). Dwight et al. (2000) administered the National Institute of Mental Health Diagnostic Interview Schedule based on DSM-IV criteria to 50 consecutive U.S. CHC outpatients. They reported current rates of 28% for major depression (while 12% also met criteria for dysthymia), 18% for generalised anxiety disorder, 0% for panic disorder, and 4% for both alcohol and substance abuse/dependence (Dwight et al., 2000).

Rowan and others (2005) administered the SCID to 62 consecutive veteran CHC outpatients being considered for anti-viral therapy, reporting

current rates of 10% for depressive disorders, 21% for any substance use disorder, and 5% for psychotic disorders. Batki and colleagues (2011) administered the SCID to 111 consecutive U.S. methadone maintenance patients with CHC being considered for treatment. They found current rates of 56% for substance dependence or abuse, 35% for any mood disorder (22% for major depression, 6% for bipolar I disorder, 3% for bipolar II disorder, and 1% for substance-induced mood disorder), 44% for any anxiety disorder (14% for panic disorder, 13% for social phobia, 17% for post-traumatic stress disorder, and 3% substance-induced anxiety disorder), 9% for any psychotic disorder (1% for schizophrenia, 5% for schizoaffective disorder, 4% for psychotic disorder not otherwise specified, and 3% for major depression with psychotic features), and 40% for antisocial personality disorder (Batki et al., 2011).

An Italian study (Carta et al., 2012) with 135 CHC outpatients without drug and alcohol abuse reported current rates of 33% for major depression, 5% for dysthymia, 10% for generalised anxiety disorder, 9% for panic disorder, and 2% for social phobia using the Composite International Diagnostic based on DSM-IV criteria. A Brazilian study (Fábregas et al., 2013) administered the Mini International Neuropsychiatric Interview (based on DSM-IV criteria) to a convenience sample of 81 CHC outpatients (from 88 who were approached). They found current rates of 32% for depressive disorders (28% for major depression and 4% for dysthymia), 22% for anxiety disorders (11% for specific phobias and 10% for generalised anxiety disorder), 9% for alcohol use disorders, and 9% for drug use disorders (Fábregas et al., 2013). Another study

with 500 consecutive Spanish outpatients referred for anti-viral treatment reported current rates of 18% for any depressive disorder (6% for major depression), 7% for generalised anxiety disorder, and 6% for panic disorder using the SCID (Navinés et al., 2012). Finally, Tavakkoli et al. (2013) gave a convenience sample of 167 CHC outpatients the Patient Health Questionnaire-9, and then utilised psychiatric clinical interviews to confirm diagnoses of major depression, reporting a rate of 31% for current major depressive disorder.

Table 1

Prevalence of mood disorders in people with CHC.

Study	N	Sampling Procedure	Current vs. lifetime	Criteria	Disorder type	Prevalence rate (%)
(Batki et al., 2011)	111	Consecutive HCV+ methadone maintenance patients referred for anti-viral treatment	Current	DSM-IV	Any mood disorder	35
					Major depression	22
					Bipolar I disorder	6
					Bipolar II disorder	3
					Substance-induced mood disorder	1
(Butt et al., 2006)	5 737	Retrospective data for HCV+ haemodialysis patients	Lifetime	ICD-9	Mild depression	14
					Major depression	8
					Bipolar disorder	1.5
(Butt et al., 2007)	126 971	Retrospective data for HCV+ veterans 1999-2003	Lifetime	ICD-9	Mild depression	19
					Major depression	11
					Bipolar disorder	7
(Carta et al., 2012)	135	Convenience sample of outpatients without drug or alcohol abuse	Current	DSM-IV	Major depression	35
					Dysthymia	5
(Coughlan et al., 2002)	60	Consecutive outpatients	Current	ICD-10	Any depressive disorder	25
					Mild depressive disorder	15
(Dwight et al., 2000)	50	Consecutive outpatients	Current	DSM-IV	Major depression	28
					Dysthymia	12
(el-Serag et al., 2002)	33 824	Retrospective data for HCV+ veterans hospitalised 1992-1999	Lifetime	ICD-9-CM	Depression	46
					Bipolar disorders	16

Study	N	Sampling Procedure	Current vs. lifetime	Criteria	Disorder type	Prevalence rate (%)
(Fábregas et al., 2013)	81	Convenience sample of outpatients	Current	DSM-IV	Any depressive disorder	32
					Major depression	28
					Dysthymia	4
(Golden et al., 2005)	90	Consecutive outpatients	Current	DSM-IV	Any depressive disorder	28
					Major depression	8
					Adjustment disorder with depressed mood	11
					Depressive disorder not otherwise specified/dysthymia	9
(Navinés et al., 2012)	500	Consecutive outpatients referred for anti-viral treatment	Current	DSM-IV	Any depressive disorder	18
					Major depression	6
(Rowan et al., 2005)	62	Consecutive outpatients referred for anti-viral treatment	Current	DSM-IV	Any depressive disorder	10
(Tavakkoli et al., 2013)	167	Convenience sample of outpatients	Current	Psychiatric interview	Major depression	31

Table 2

Prevalence of anxiety disorders in people with CHC.

Study	N	Sampling Procedure	Current vs. lifetime	Criteria	Disorder type	Prevalence rate (%)
(Batki et al., 2011)	111	Consecutive HCV+ methadone maintenance patients referred for anti-viral treatment	Current	DSM-IV	Any anxiety disorder	44
					Panic disorder	14
					Social phobia	13
					Post-traumatic stress disorder	17
					Substance-induced anxiety disorder	3
(Carta et al., 2012)	135	Convenience sample of outpatients without drug or alcohol abuse	Current	DSM-IV	Generalised anxiety disorder	10
					Panic disorder	9
					Social phobia	2
(Coughlan et al., 2002)	60	Consecutive outpatients	Current	ICD-10	Any anxiety disorder	28
					Phobic anxiety disorder	8
					Generalised anxiety disorder	7
					Panic disorder	8
(Dwight et al., 2000)	50	Consecutive outpatients	Current	DSM-IV	Generalised anxiety disorder	18
					Panic disorder	0
(el-Serag et al., 2002)	33 824	Retrospective data for HCV+ veterans hospitalised 1992-1999	Lifetime	ICD-9-CM	Anxiety disorders	38
(Fábregas et al., 2013)	81	Convenience sample of outpatients	Current	DSM-IV	Any anxiety disorder	22
					Specific phobia	11
					Generalised anxiety disorder	10

Study	N	Sampling Procedure	Current vs. lifetime	Criteria	Disorder type	Prevalence rate (%)
(Golden et al., 2005)	90	Consecutive outpatients	Current	DSM-IV	Any anxiety disorder	24
					Panic disorder and phobias	12
					Adjustment disorder with anxiety	7
					Obsessive-compulsive disorder	2
					Anxiety disorder not otherwise specified	3
(Navinés et al., 2012)	500	Consecutive outpatients referred for anti-viral treatment	Current	DSM-IV	Generalised anxiety disorder	7
					Panic disorder	6

Table 3

Prevalence of substance use disorders in people with CHC.

Study	N	Sampling Procedure	Current vs. lifetime	Criteria	Disorder type	Prevalence rate (%)
(Butt et al., 2006)	5 737	Retrospective data for HCV+ haemodialysis patients	Lifetime	ICD-9	Alcohol use disorder	14
					Drug use disorder	17
(Butt et al., 2007)	126 971	Retrospective data for HCV+ veterans 1999-2003	Lifetime	ICD-9	Alcohol use disorder	35
					Drug use disorder	30
(Dwight et al., 2000)	50	Consecutive outpatients	Current	DSM-IV	Alcohol abuse or dependence	4
					Substance abuse or dependence	4
(el-Serag et al., 2002)	33 824	Retrospective data for HCV+ veterans hospitalised 1992-1999	Lifetime	ICD-9-CM	Any substance use disorder	80
(Fábregas et al., 2013)	81	Convenience sample of outpatients	Current	DSM-IV	Alcohol use disorder	9
					Drug use disorder	9
(Golden et al., 2005)	90	Consecutive outpatients	Current	DSM-IV	Opiate abuse or dependence	26
					Alcohol abuse or dependence	1
(Rowan et al., 2005)	62	Consecutive outpatients referred for anti-viral treatment	Current	DSM-IV	Any substance use disorder	21

Table 4

Prevalence of other psychiatric disorders in people with CHC.

Study	N	Sampling Procedure	Current vs. lifetime	Criteria	Disorder type	Prevalence rate (%)
(Batki et al., 2011)	111	Consecutive HCV+ methadone maintenance patients referred for anti-viral treatment	Current	DSM-IV	Any psychotic disorder	9
					Schizophrenia	1
					Schizoaffective disorder	5
					Psychotic disorder not otherwise specified	4
					Anti-social personality disorder	40
					Any psychotic disorder	9
(Butt et al., 2006)	5 737	Retrospective data for HCV+ haemodialysis patients	Lifetime	ICD-9	Post-traumatic stress disorder	0.3
					Schizophrenia	2.5
(Butt et al., 2007)	126 971	Retrospective data for HCV+ veterans 1999-2003	Lifetime	ICD-9	Post-traumatic stress disorder	13
					Schizophrenia	7
(el-Serag et al., 2002)	33 824	Retrospective data for HCV+ veterans hospitalised 1992-1999	Lifetime	ICD-9-CM	Post-traumatic stress disorder	23
					Psychotic disorders	23
(Rowan et al., 2005)	62	Consecutive outpatients referred for anti-viral treatment	Current	DSM-IV	Any psychotic disorder	5

Australian research on the prevalence of psychiatric co-morbidity is lacking, however, as shown in Table 5. Alavi and colleagues (Alavi et al., 2012) assessed major depression in 34 consecutive, Australian, and recently infected outpatients using the Mini International Neuropsychiatric Interview, reporting that 26% met the criteria. McDonald and colleagues (2002) administered the revised 90 item symptom checklist (SCL-90-R) to 115 consecutive CHC outpatients, finding that 53% exceeded the cut-off for depression, 45% for anxiety, and 50% for somatization. Mikocka-Walus et al. (2008) found that in 36 CHC outpatients (around 32% of patients invited to participate) given the Hospital Anxiety and Depression Scale (HADS), 44% exceeded the cut-off of ≥ 8 recommended in the literature (Bjelland, Dahl, Haug, & Neckelmann, 2002; Fábregas et al., 2012) for anxiety while 33% exceeded the cut-off of 8 for depression. The largest Australian study to date (Stewart, Mikocka-Walus, Morgan, et al., 2012) examined HADS scores in 395 CHC outpatients on referral for tertiary care, finding that the cut-offs of ≥ 8 were exceeded by 41% for anxiety and 27% for depression. Studies from other countries using slightly higher cut-off scores with the HADS reported comparable rates of 15-25% for depression and 24-50% for anxiety (Coughlan et al., 2002; Erim et al., 2010; Grassi et al., 2001).

Table 5

Prevalence of psychiatric co-morbidity in Australian people with CHC.

Study	N	Sampling Procedure	Current vs. lifetime	Criteria	Disorder type	Prevalence rate (%)
(Alavi et al., 2012)	34	Consecutive recently infected outpatients	Current	DSM-IV	Major depression	26
(McDonald et al., 2002)	115	Consecutive outpatients	Current	SCL-90-R score > cut-off	Depression	53
					Anxiety	45
					Somatization	50
(Mikocka-Walus, Turnbull, Andrews, et al., 2008)	36	Convenience sample of outpatients	Current	HADS score > cut-off	Depression	33
					Anxiety	44
(Stewart, Mikocka-Walus, Morgan, et al., 2012)	395	Consecutive outpatients	Current	HADS score > cut-off	Depression	27
					Anxiety	41

While the significant variance in study methodologies preclude definitive conclusions regarding the prevalence of psychiatric disorders, it is clear infection with CHC increases the risk of this co-morbidity. For example, El-Serag and colleagues (2002) compared 22,341 HCV+ Vietnam veterans with matched case controls without HCV and found that the former were more likely to have all psychiatric and substance use disorders for which data were available for. This finding was replicated in another national sample of veterans (Butt et al., 2007) as well as haemodialysis patients (Butt et al., 2006) when compared with matched controls. An Australian study (Stewart, Mikocka-Walus, Morgan, et al., 2012) compared HADS scores for 395 CHC outpatients with British community norms and found that rates based on established cut-off scores were 1.2 and 2.4 times higher in CHC patients for anxiety and depression respectively.

The presence of multiple co-morbid psychiatric disorders in people with CHC is also common. El-Serag and colleagues (2002) found that, of the 29 202 HCV+ veterans with at least one psychiatric disorder, the average number of lifetime psychiatric diagnoses (including substance use disorders) per patient was 3.6. In those without substance use disorders but with at least one psychiatric disorder, 64% had two or more lifetime diagnoses. In those with substance use disorders, 86% had two or more non-substance use psychiatric disorders. Research with smaller samples using structured clinical interviews to demonstrate psychiatric morbidity have had similar findings, with 21-64% of those with at least one psychiatric disorder meeting criteria for two or more

diagnoses (Dwight et al., 2000; Golden et al., 2005; Navinés et al., 2012; Rowan et al., 2005). The only Australian study to explore co-morbid psychiatric diagnoses in CHC found that, of the 179 outpatients exceeding the cut-off score for depression or anxiety on the HADS, 50% demonstrated both depressive and anxiety case-ness (Stewart, Mikocka-Walus, Morgan, et al., 2012).

To summarise, people with CHC are at high risk of experiencing psychiatric co-morbidity. Methodological limitations preclude definitive estimates of prevalence rates. Large population based studies relied on retrospective analysis of hospital data which were likely skewed by reliance on data from veterans and inpatients and were limited to lifetime rates. Prospective research using structured clinical interviews to establish diagnoses has been limited by smaller sample sizes and vary according to their sampling frames of outpatients, methadone maintenance patients, or veterans once again. Nonetheless, research which has compared people with CHC with matched controls has established that this population experiences increased psychiatric morbidity. Of those who do experience psychiatric co-morbidity, a significant proportion suffer from multiple disorders. Notably for the purposes of the present research, no studies were identified which systematically addressed the prognosis or progression of psychiatric morbidity in this population.

1.6. Aetiology of psychiatric co-morbidity in CHC

Three main factors contribute to the increased risk of psychiatric morbidity in people with CHC: (1) the high rate of substance use; (2) the biological effect of the virus on the nervous system; and (3) the psychosocial impact of CHC.

Firstly, IDU is the transmission route for 80% of Australians living with CHC and 90% of new infections each year (Razali et al., 2007). Research has demonstrated that injecting drug users have an elevated risk of psychiatric morbidity (Brienza et al., 2000; Brooner, King, Kidorf, Schmidt, & Bigelow, 1997; Callaly, Trauer, Munro, & Whelan, 2001; Kidorf et al., 2004; Lieb et al., 2010; Mackesy-Amiti, Donenberg, & Ouellet, 2012; Rodríguez-Llera et al., 2006; Savant et al., 2013; Teesson et al., 2005). The relationship between substance use and psychiatric morbidity may be due, in part, to three factors: (1) a shared diathesis, such as a common genetic vulnerability, life stressors, or early childhood experiences; (2) substance use leading to psychiatric disorders, such as losses/stressors brought about through substance misuse; and (3) psychiatric disorders leading to substance use, such as through self-medication (Jané-Llopis & Matytsina, 2006; Merikangas et al., 1998).

Thus, it is possible that many people with CHC will have co-morbid psychiatric disorders due to their current or former IDU. One retrospective study of hospital data for 306 veterans found that 95% of psychiatric diagnoses preceded the diagnosis of CHC (Yovtcheva, Rifai, Moles, & Van der Linden, 2001). Butt and colleagues (2007) found that the odds of HCV+ veterans having

psychiatric disorders, compared to HCV- matched controls, was greatly reduced after statistically controlling for substance abuse. Research has also shown that the severity of psychiatric and substance use disorders increases as a function of increasing co-morbidity (Merikangas et al., 1998).

However, it is likely there are factors associated with merely being infected with CHC which may contribute to the psychiatric morbidity seen in this population. Lee et al. (2013) found that CHC was independently associated with depression even after controlling for history of drug use, while other chronic liver diseases failed to demonstrate this association. A growing body of research has demonstrated the potential biological impact of HCV on the brain, as reviewed by Weissenborn and colleagues (2009). Many people with CHC complain of fatigue, cognitive impairment, and psychiatric symptoms such as depression, irrespective of the stage of liver disease and these complaints persist after successful antiviral treatment (Weissenborn et al., 2009).

Brain imaging studies have revealed changes in the concentrations of various metabolites in multiple areas of the brain and alterations of serotonin and dopamine transporter binding systems (Weissenborn et al., 2009). Other research has also detected HCV in brain samples and cerebro-spinal fluid, leading to the conclusion that HCV may invade and replicate inside the brain, causing if not contributing to cognitive as well as neuropsychiatric symptoms such as depression (Forton, Taylor-Robinson, & Thomas, 2006; Weissenborn et al., 2009). In addition, research has shown an increased production of proinflammatory cytokines in those with HCV infection, with levels correlating

with increased depressive symptoms (Loftis, Huckans, Ruimy, Hinrichs, & Hauser, 2008).

Secondly, the psychosocial effect of living with CHC cannot be underestimated. A seminal study with recently infected Australians found that those who were aware of their infection demonstrated significantly poorer health-related quality of life compared to those who were unaware (Rodger, Jolley, Thompson, Lanigan, & Crofts, 1999). This led to increased research attempting to identify the psychosocial determinants of psychiatric co-morbidity and reduced quality of life in people with CHC. The most studied factor is that of CHC-related stigmatisation, brought about due to associations with IDU and fears of contracting HCV themselves (Butt, Paterson, & McGuinness, 2008; Stewart, Mikocka-Walus, Harley, & Andrews, 2012; Zickmund, Ho, Masuda, Ippolito, & LaBrecque, 2003).

Studies have reported rates of stigma from 52-85% (Golden, Conroy, O'Dwyer, Golden, & Hardouin, 2006; Moore, Hawley, & Bradley, 2008; Zickmund et al., 2003) and this been associated with anxiety, depression, quality of life, social/occupational impairment, and poorer adjustment to illness (Golden et al., 2006; Zickmund et al., 2003). Qualitative research has highlighted how stigma may also be a barrier to patients seeking social support and mental health treatment (Stewart, Mikocka-Walus, Harley, et al., 2012). Other psychosocial factors which may contribute to psychiatric morbidity include the shock and stress of diagnosis (Gill, Atiq, Sattar, & Khokhar, 2005; Sgorbini, O'Brien, & Jackson, 2009; Stewart, Mikocka-Walus, Harley, et al., 2012),

internalised feelings of contamination (Conrad, Garrett, Cooksley, Dunne, & Macdonald, 2006; Fraser & Treloar, 2006; Stewart, Mikocka-Walus, Harley, et al., 2012), and fears regarding disease progression, premature death, and the transmission of infection to others (Groessl et al., 2008; Minuk, Gutkin, Wong, & Kaita, 2005; Stewart, Mikocka-Walus, Harley, et al., 2012).

To summarise, the elevated risk of psychiatric co-morbidity associated with CHC can in part be explained by the pre-existing high rates of morbidity seen in the IDU population – a population which 80-90% of people with CHC have belonged to at some stage during their lives. However, living with CHC also leads to biopsychosocial effects which contribute to this co-morbidity.

1.7. Effects of psychiatric co-morbidity in CHC

The quality of life of people with CHC has been shown to be significantly diminished compared with population controls in a large body of research (Balfour et al., 2006; Bayliss et al., 1998; Björnsson et al., 2009; Bonkovsky et al., 2007; Bonkovsky & Wolley, 1999; Carithers Jr, Sugano, & Bayliss, 1996; Chong et al., 2003; Coughlan et al., 2002; Foster, Goldin, & Thomas, 1998; Gallegos-Orozco et al., 2003; Helbling et al., 2008; Kwan et al., 2008; Lim, Cronkite, Goldstein, & Cheung, 2006; Rowan et al., 2005; Spiegel et al., 2005; Von Wagner et al., 2006; Ware Jr, Bayliss, Mannocchia, & Davis, 1999). This finding has also been replicated in Australians with CHC (Gunasekera, Fraser, & Alexander, 2008; Miller, Hiller, & Shaw, 2001; Rodger et al., 1999). Moreover,

the quality of life of patients with CHC is worse than those with hypertension (Bayliss et al., 1998; Carithers Jr et al., 1996), and more impaired on particular scales compared to those with the hepatitis B virus (Foster et al., 1998), patients with other forms of liver disease (Tillmann et al., 2011), and patients with diabetes (Bayliss et al., 1998; Carithers Jr et al., 1996).

The presence of psychiatric morbidity or increased psychiatric symptomatology is associated with poorer quality of life (Balfour et al., 2006; Batista-Neves et al., 2009; Bonkovsky et al., 2007; Gallegos-Orozco et al., 2003; Gutteling et al., 2006; Gutteling, Duivenvoorden, Busschbach, De Man, & Darlington, 2010; Häuser et al., 2004; Kwan et al., 2008; Lim et al., 2006; Rowan et al., 2005; Von Wagner et al., 2006). Furthermore, several studies have demonstrated that psychiatric co-morbidity is a stronger predictor of quality of life than many other measures of disease severity (Balfour et al., 2006; Batista-Neves et al., 2009; Bonkovsky et al., 2007; Gutteling et al., 2010; Häuser et al., 2004; Rowan et al., 2005).

Dwight and colleagues (2000) reported that depression in people with CHC is associated with increased fatigue, functional disability, and somatisation, irrespective of stage of liver disease, other medical co-morbidities, and antiviral treatment status. Another study found that depression in CHC patients was associated with higher levels of subjective physical symptoms (Golden et al., 2005). An Australian study demonstrated a strong association between psychiatric symptoms, particularly depression, and fatigue – which was only weakly correlated with liver fibrosis (McDonald et al., 2002). Morasco and

colleagues (2010) also reported that depressive symptoms were a significant independent predictor of pain intensity. Other research also found that depression is correlated with poor social and physical functioning (Hilsabeck, Hassanein, & Perry, 2005).

Another concerning consequence of psychiatric morbidity is its potential to diminish treatment outcomes through a number of pathways. For example, research has found that those with a history of psychiatric disorders (Castellvi et al., 2009; Castera et al., 2006; Fransen van de Putte, Fischer, Posthouwer, Van Erpecum, & Mauser-Bunschoten, 2009) and those with higher baseline depressive symptoms (Castellvi et al., 2009; Castera et al., 2006; Hauser et al., 2002; Leutscher et al., 2010; Martín-Santos et al., 2008; Raison, Borisov, et al., 2005) at the commencement of antiviral therapy are more likely to experience IFN-induced depression during treatment. Similarly, Dieperink and colleagues (2003) found that patients with a personal, or even familial, history of psychiatric disorders were more likely to require psychiatric treatment during antiviral therapy. Another study found a higher rate of mental adverse events during treatment in patients with psychiatric co-morbidity compared to those without (Lang et al., 2010). Evon and colleagues (2009) found that patients with higher baseline depression are more likely to have adverse psychiatric events and more likely to require antidepressant prescription during treatment.

Patients who experience this IFN-induced depression are more likely to subsequently discontinue treatment (Leutscher et al., 2010). Furthermore, research has also directly linked psychiatric or substance use problems with

diminished treatment compliance or completion, including patients: (1) with anxiety or depression (Martín-Santos et al., 2008); (2) who have been deferred from treatment in the past for psychiatric illness or substance use (Evon et al., 2007); (3) with a history of depression who are not taking antidepressants (Alvarez-Uria, Day, Nasir, Russell, & Vilar, 2009); (4) who have higher baseline depressive (Evon et al., 2009) or other psychiatric symptomatology (Kraus et al., 2001); and (5) who are active IDUs (Alvarez-Uria et al., 2009), former IDUs or methadone-substituted patients (Schaefer et al., 2007), or former substance abusers (Schaefer et al., 2003). Although the exacerbation of existing psychiatric symptoms by the neurotoxic agent IFN may become a non-factor in the future with the advent of IFN-free treatment (Vermehren & Sarrazin, 2011), psychiatric co-morbidity will still remain relevant as meta-analytic research has demonstrated the deleterious impact of depression, for instance, on medication adherence across a range of somatic conditions (DiMatteo, Lepper, & Croghan, 2000).

Psychiatric morbidity or substance use may also reduce SVR rates. Two studies have demonstrated that patients who experience increased depressive symptomatology during treatment are less likely to clear the virus, even after controlling for other factors influencing SVR (Leutscher et al., 2010; Raison, Broadwell, et al., 2005). A meta-analysis of treatment outcomes in current IDUs found that in the three trials which included ongoing drug users, the SVR rates were significantly lower than in the remaining trials which required a period of abstinence before treatment (Zanini et al., 2010). Alvarez-Uria and colleagues

(2009) found that patients with a history of depression who were not receiving antidepressants, or patients who were active IDUs, were less likely to achieve an SVR. Another study found that patients initially deferred from treatment for reasons involving psychiatric illness or substance use had lower SVR rates when subsequently treated than patients not deferred for these reasons (Evon et al., 2007). As a consequence of these associations between psychiatric morbidity and decreased treatment outcomes, patients with psychiatric or substance use issues are often delayed or excluded from treatment (Chainuvati et al., 2006; Evon et al., 2010; Evon et al., 2007; Rowan et al., 2005). These decisions to delay or not commence treatment may be of the patients' own volition but can also be the choice of their treating physician based on their clinic policy.

However, research in this area is conflicting, with other studies failing to find an association between a history of depression or substance use (Hauser et al., 2002) or baseline depressive symptomatology (Fontana et al., 2008) with an increased risk of IFN-induced depression during antiviral treatment. Schaefer and colleagues (2003) found that there was no difference between patients with psychiatric disorders, methadone substitution patients, former drug addicts, or controls with respect to the development of depression during IFN therapy. Other research has found no association between completion rates and baseline depressive symptoms (Guadagnino, Trotta, Carioti, Caroleo, & Antinori, 2006), IDU status (Zanini et al., 2010), or the presence of psychiatric

disorders or substance abuse (Chainuvati et al., 2006; Dollarhide et al., 2007; Hauser et al., 2009; Huckans, Mitchell, Ruimy, Loftis, & Hauser, 2010).

Other studies have failed to find a relationship between treatment compliance and the presence of psychiatric disorders (Jakiche et al., 2007; Lang et al., 2010) and baseline depressive symptomatology (Guadagnino et al., 2006). Finally, a larger body of research has found no association between SVR rates and the development of depression or other adverse psychiatric events during treatment (Castera et al., 2006; Evon et al., 2009; Schäfer, Scheurlen, Weissbrich, Schöttker, & Kraus, 2007), the presence of psychiatric disorders or substance abuse (Chainuvati et al., 2006; Hauser et al., 2009; Huckans et al., 2010; Jakiche et al., 2007; Lang et al., 2010; Schaefer et al., 2007; Schaefer et al., 2003), IDU status (Zanini et al., 2010), or former drug addiction or methadone maintenance status (Schaefer et al., 2007; Schaefer et al., 2003).

However, in many of these conflicting studies, specialist mental health care was provided in an integrated, multi-disciplinary setting, with targeted assessments, monitoring, management, and treatment by mental health professionals throughout the anti-viral treatment process (Castera et al., 2006; Chainuvati et al., 2006; Dollarhide et al., 2007; Evon et al., 2009; Guadagnino et al., 2006; Hauser et al., 2002; Hauser et al., 2009; Jakiche et al., 2007; Schaefer et al., 2007; Schaefer et al., 2003). Consequently, there may be selection biases, whereby patients more suited to therapy are included in the research, patients may receive efficacious mental health treatment quickly (which may prevent or partially obscure potential disparities between patients in

the development of neuropsychiatric side-effects during IFN therapy), and patients may be more equipped to deal with the antiviral therapy process and have increased treatment adherence (Chainuvati et al., 2006; Dollarhide et al., 2007; Guadagnino et al., 2006; Zanini et al., 2010).

In summary, psychiatric co-morbidity in people with CHC leads to decreased quality of life, increased perceived physical symptoms such as fatigue and pain, and significant functional impairment. Active psychiatric or substance use problems may induce or exacerbate psychiatric symptoms in some patients during IFN treatment, thereby increasing the risk of requiring dose reduction or cessation, and ultimately reducing the chance of viral clearance – although this risk can be mitigated through integration of mental health services in the treatment setting. Treatment may be postponed or withheld from many others with CHC due to fears of a worsening of psychiatric symptoms.

1.8. Treatment of psychiatric co-morbidity

The majority of the literature on the treatment of psychiatric symptoms in people with CHC has been limited to the management of IFN-induced depression. Within this literature, there has been a focus on research investigating the pharmacological, rather than psychological, treatment of these symptoms. Initial open-label and uncontrolled trials demonstrated that anti-depressants were effective in reducing IFN-induced depression (Hauser et al.,

2002; Kraus, Schäfer, Faller, Csef, & Scheurlen, 2002). A recent meta-analysis of seven randomised, placebo-controlled trials demonstrated that prophylactic anti-depressant use was tolerable in patients and significantly reduced their risk of depression, although their rates of treatment completion and SVR were similar to those who did not receive anti-depressant prophylaxis (Jiang et al., 2013). Apart from the treatment of IFN-induced symptoms, little research has been conducted in the treatment of psychiatric symptoms in people with CHC. Gleason and colleagues (2002; 2005) conducted two open-label trials with antidepressants for CHC patients with major depression, finding that symptoms of depression dropped and quality of life improved significantly. Evidence for pharmacological treatment of other IFN-induced neuropsychiatric symptoms in CHC is also limited to a single case-series which reported good responses to benzodiazepines for anxiety and insomnia (Maddock et al., 2004).

There are a number of challenges in the pharmacological treatment of psychiatric co-morbidity in people with CHC including: (1) the two to six week therapeutic transition period before antidepressants take effect and where patients may be vulnerable; (2) the need for sustained antidepressant treatment after the cessation of antiviral treatment to prevent relapse of depression (which can be problematic if there is insufficient communication between the patient's specialist and their primary care physician in this period); (3) the variation in antidepressant effect and tolerability due to impaired liver function (which is rare unless the patient has severe end-stage liver disease); and (4) the numerous physical and psychiatric side effects of psychiatric drugs, particularly when

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considering drug-drug interactions with IFN, ribavirin, and increasingly the new direct acting antivirals (Asnis & De La Garza, 2006; Neri et al., 2010; Sockalingam et al., 2013).

Meta-analytic research has also shown that combining psychotherapy with pharmacotherapy is slightly more effective in treating depression in the chronically ill (Rizzo, Creed, Goldberg, Meader, & Pilling, 2011). Another meta-analysis found that combined treatment was more effective for panic disorder and reported preliminary support for combined therapy in social anxiety disorder (Bandelow, Seidler-Brandler, Becker, Wedekind, & Rüther, 2007). Thus, psychotherapy may be useful as an adjunct or alternative treatment for some patients. One of the more promising types of psychotherapy is cognitive behavioural therapy (CBT; Beck, 1976).

According to the CBT model, the way in which people think about or appraise themselves, others, their environment, and the situations they encounter in their lives both affects, and in turn is affected by, their emotions and behaviours (Beck & Dozois, 2011). CBT is a structured, collaborative, and time-limited therapy which aims to help individuals become more functional and adaptive by training them to intentionally modify their cognitive and behavioural responses to internal and external experiences (Beck & Dozois, 2011). Cognitive responses are altered through a systematic, critical, and evidence-based examination of thoughts, attitudes, and beliefs with a focus on testing alternative interpretations, known as cognitive restructuring (Beck & Dozois, 2011). This is brought about via a number of processes, including self-

monitoring with diaries, Socratic questioning, and behavioural experiments (Beck & Dozois, 2011). Behavioural strategies are used to habituate to feared stimuli (exposure), elicit pleasure or mastery and shift reinforcement schedules to promote increased activity (behavioural activation), and increase relaxation (breathing retraining and progressive muscle relaxation; Beck & Dozois, 2011).

An abundance of evidence supports the efficacy of CBT in treating a wide range of psychiatric disorders (Butler, Chapman, Forman, & Beck, 2006). More pertinently to CHC, meta-analyses of randomised controlled trials (RCTs) have also demonstrated the efficacy of CBT for treating depression in people with somatic disease (Beltman, Oude Voshaar, & Speckens, 2010), depression, anxiety, anger, and stress in patients with HIV (Crepaz et al., 2008), and alcohol or illicit drug use disorders in adults (Magill & Ray, 2009). However, to date there has been very little research on psychological therapy in people with CHC specifically. One recent open-label, RCT of psychotherapy by Neri and colleagues (2010) examined 211 CHC patients undergoing a 48 week course of antiviral therapy. The patients were randomised to two groups. The first was interviewed by a team of gastroenterologists, psychiatrists, and psychologists and treated with psychotherapy consisting of CBT and interpersonal psychotherapy, once a month. Psychotherapy was individually structured based on the needs of each patient. The second group received treatment as usual and were monitored once a month but did not receive psychotherapy. The psychotherapy group had a clinically importantly lower rate of onset of severe psychiatric manifestations during treatment (4.7% vs 16.1%, p<0.01). Patients

in the psychotherapy group were also less likely to require antidepressant or benzodiazepine prescription (15 vs. 39 participants, $p<0.05$).

While this preliminary evidence suggests that psychotherapeutic options, such as CBT, may be an effective alternative or adjunct therapy to the traditional pharmacological approach in people with CHC, it is clear that more evidence is needed. Moreover, the acceptability of different treatment approaches to people with CHC is unknown. This is important as research has shown that patients offered a treatment they find more acceptable are more likely to take up that treatment (Dwight-Johnson, Unutzer, Sherbourne, Tang, & Wells, 2001; Jorm et al., 2000), are more likely to adhere to the treatment, and are more likely to demonstrate a better treatment response (Swift & Callahan, 2009; Swift, Callahan, & Vollmer, 2011). Furthermore, very little is known about patterns of mental health service utilisation in those living with CHC. One recent qualitative study (Stewart, Mikocka-Walus, Harley, et al., 2012) highlighted a range of barriers to service uptake, including stigma, fears regarding confidentiality, time and financial pressures, and structural issues such as gaps in services, under-resourced services, and flawed referral processes.

1.9. Aims

The overarching aim of this research program was to improve the management of psychiatric co-morbidities, particularly depression and anxiety, in those living with CHC. The specific aims of this research have evolved as

new knowledge from both within this program itself and in the wider literature became available. These aims are as follows:

1. Examine the acceptability of various pharmacological and psychological treatments for psychiatric co-morbidity, and determine the predictors of finding these treatments acceptable.

2. Explore the course of depression and anxiety in people with CHC over time and determine the predictors of symptom change.

3. Assess rates of mental health problems and uptake of mental health services in people with CHC and explore changes in these rates over time.

4. Synthesise prior knowledge in this research program and in the broader literature in order to create a resource to be used in the treatment of depression and anxiety in those living with CHC.

CHAPTER II: EXEGESIS

This chapter provides an overview of the four sequentially completed studies conducted in this research program and describes the links between them. The literature review presented in chapter one highlighted the lack of evidence in four key areas of CHC research: (1) the acceptability of various mental health treatments; (2) the course of depression and anxiety over time; (3) the patterns of mental health problem rates and service utilisation in the CHC population over time; and (4) the efficacy of psychological interventions. This review identified the need to examine four research questions which will be addressed in Chapters III through VI, after being briefly discussed below.

2.1. Study one - Chapter III: Acceptability of psychological and psychiatric therapies

The aim of study one was to examine the acceptability of different psychological and psychiatric treatments for mental health disorders in people with CHC. The study also aimed to examine predictors of treatment acceptability in order to provide information regarding potential factors to be addressed in treatment settings to maximise acceptability. This was achieved using a postal survey of 89 outpatients and online survey of 67 Australians living with CHC. This study found that individual psychotherapy was the most acceptable support type, being endorsed by 83% of participants, followed by

bibliotherapy (61%), pharmacotherapy (56%), online therapy (45%), and group psychotherapy (37%). The most consistent predictor of acceptability of a given treatment was satisfaction with past use of that treatment, highlighting the importance of providing a treatment which is tailored to the patient's context and which takes into account their preferences and expectations of treatment. This study also found that the majority of patients receiving anti-depressants still reported severe depressive and anxious symptoms, providing evidence for a possible therapeutic gap where combined psycho- and pharmacotherapy could be beneficial. These findings were used to inform study four in the design of a CHC specific treatment protocol.

2.2. Study two - Chapter IV: Course of depression and anxiety

The aim of study two was to examine the course of depression and anxiety over time in a single cohort of CHC patients. The study also aimed to identify predictors of a worsening in symptoms in order to identify risk factors for a poor prognosis which might proactively be addressed in treatment settings. These aims were achieved by collating data for participants who participated in two separate studies. Baseline data were taken from a previous investigation of the prevalence and predictors of depression and anxiety in 395 CHC outpatients (Stewart, Mikocka-Walus, Morgan, et al., 2012). The endpoint data were taken from a sub-sample of 61 outpatients with CHC who participated both in the original study and the postal survey component of study one. This data

revealed that symptoms of depression and anxiety became significantly worse over the time assessed, which varied from 21 to 62 months between patients. The most important predictor of worsening depressive and anxiety symptoms was the level of baseline anxiety.

2.3. Study three - Chapter V: Mental health problems and service use 2006-2012

The aim of study three was to examine changes over time in the CHC+/-IDU population with respect to mental health problems and service utilisation. This was achieved by comparing data for the 2006 and 2012 Illicit Drug Reporting System surveys of regular injecting drug users, of which approximately half reported having CHC (O'Brien et al., 2007; Stafford & Burns, 2012). The results indicated that self-reported mental health problem rates increased significantly, while rates of service utilisation dropped. Positive findings were that service utilisation, despite the decline, remained comparable to the general community, and that there was a proportional increase in access to psychologists who are specifically trained in the treatment of psychiatric disorders. It was hypothesised that these changes were due to a number of factors including genuine increases in anxiety over time, increased reporting due to reduced stigma coupled with increased mental health literacy, and structural changes in mental health service provision such as the introduction of the Better Access to Psychiatrists, Psychologists and General Practitioners

through the Medicare Benefits Schedule reform (Better Access; see Chapter 5.3 for a detailed description of Better Access) in late 2006 – particularly with regard to the increase in the use of psychologists which was the primary goal of the reform process.

2.4. Study four - Chapter VI: Development of C-UP protocol

Studies three and four highlighted the need for changes in mental health services as the available data indicated that depression and anxiety typically had a poor trajectory for this population and that there had been a decrease in overall service use over time. Thus, the aim of study four was to develop a CHC specific treatment protocol which could be used to treat co-morbid depression and anxiety. This protocol was primarily informed by recent research in the field of general psychological treatment, CHC specific psychological treatment, as well as the findings of study one. Research has demonstrated the efficacy of CBT in treating depression and anxiety in similar populations such as those with HIV (Crepaz et al., 2008). Recent developments in both theoretical and applied clinical psychology have led to the proposition that the multiple mood and anxiety disorders share more commonalities than differences and that treating these disorders simultaneously using a transdiagnostic CBT approach could be more parsimonious and effective than targeting single disorders (Barlow, Allen, & Choate, 2004; Wilamowska et al., 2010). This consideration is especially relevant given that multiple co-occurring mood and anxiety disorders are

common in people living with CHC (Dwight et al., 2000; el-Serag et al., 2002; Golden et al., 2005; Navinés et al., 2012; Rowan et al., 2005; Stewart, Mikocka-Walus, Morgan, et al., 2012).

Study one demonstrated the high acceptability of individual psychotherapy and, to a somewhat lesser extent, bibliotherapy. When combined with the increased cost-effectiveness of the latter (Vos, Corry, Haby, Carter, & Andrews, 2005), it was hypothesised that the resource developed should be amenable to both self-administration and administration by a therapist. Past research has shown that matching treatments with patient preferences maximises the uptake (Dwight-Johnson et al., 2001; Jorm et al., 2000), adherence, and success of that treatment (Swift & Callahan, 2009; Swift et al., 2011). Moreover, study one demonstrated that satisfaction with past treatment use predicted acceptability for future use of that treatment, highlighting the importance of tailoring the treatment to the patients' context and to meet their expectations. Thus, it was also evident that a CHC specific resource which combined proven therapeutic principles from CBT with CHC specific examples, case illustrations, and information would resonate more with this population and maximise the uptake, adherence, and success of the resource. The resulting treatment protocol entitled "C-UP: A Unified Program for people with hepatitis C to manage depression and anxiety," is a CBT-inspired booklet containing five sections of information, activities, and resources to be completed over six weeks, either under the guidance of a therapist or in a self-directed manner. Preliminary feedback from key experts, including clinical psychologists, CHC specific

counsellors and workers, and people living with CHC was highly positive, with

only minor changes suggested to the wording of some concepts. Future

research should more rigorously and systematically test the efficacy and

acceptability of C-UP.

2.5. Contribution to knowledge

These studies make an important contribution to the body of knowledge on the assessment and management of depression and anxiety in people living with CHC. This research has breached a number of important gaps in knowledge, such as the mental health treatment preferences of those with CHC, the course of depressive and anxiety symptoms over time, and trends in mental health problem and service utilisation rates over time. This culminated in the development of a unique treatment resource which can be used by clinicians and patients to better manage co-morbid depression and anxiety. This was achieved despite the known difficulties in accessing and engaging people with CHC in research (Hope et al., 2011; National Institute on Drug Abuse, 1991; Paterson, Backmund, Hirsch, & Yim, 2007). The use of a combination of research designs contributed to this success, including postal and online surveys in study one, the novel merging of previous datasets used in the current authors' research in study two, the use of pre-existing datasets from other research centres in study three, and the use of the broader clinical psychological literature in developing the C-UP treatment protocol in study four.

Future research can extend and replicate the findings of these studies in order to further improve the assessment and management of co-morbid depression and anxiety. For instance, study one could be expanded upon by exploring the acceptability of particular psychological and psychiatric treatments. The findings of study two could be replicated with a

methodologically stronger design where patients are followed prospectively from diagnosis with multiple assessments and consideration of moderating factors such as mental health treatment and disease progression. Study three could similarly be extended by introducing regular and comprehensive assessment of psychological outcomes on a broader level in the IDU and CHC populations, thereby permitting population level analysis of psychiatric co-morbidity, service utilisation, and the impact of structural changes such as mental health reforms, service restructuring, and public mental health campaigns. Finally, study four can be extended through a pilot trial of the C-UP protocol to provide a preliminary illustration of the acceptability and efficacy of this intervention.

CHAPTER III: STUDY ONE - ACCEPTABILITY OF PSYCHOLOGICAL AND PSYCHIATRIC THERAPIES

3.1. Statement of authorship

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Author contributions:

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

Name of Principal Author (Candidate): Benjamin J.R. Stewart

Contribution to the Paper: Collected, analysed, and interpreted the data, wrote the manuscript, and acted as corresponding author.

Signature: Date: 09 / 09 / 2014

Name of Co-Author: Deborah Turnbull

Contribution to the Paper: Supervised the development of the work, assisted in the data interpretation, and helped evaluate and edit the manuscript.

Signature: Date: 09 / 09 / 2014

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Contribution to the Paper: Supervised the development of the work, assisted in the data interpretation, and helped evaluate and edit the manuscript.

Signature: Date: 09 / 09 / 2014

3.2. Abstract

Despite the prevalence of psychiatric co-morbidity in chronic hepatitis C (CHC), treatment is under-researched. Patient preferences are likely to affect treatment uptake, adherence, and success. Thus, the acceptability of psychological supports was explored. A postal survey of Australian CHC outpatients of the Royal Adelaide Hospital and online survey of Australians living with CHC was conducted, assessing demographic and disease-related variables, psychosocial characteristics including Depression Anxiety Stress Scales and Medical Outcomes Study Social Support Scale scores, past experience with psychological support, and psychological support acceptability. The final sample of 156 patients (58% male) had a mean age of 50 years and mean time since diagnosis of 13 years. They exhibited significantly worse depression, anxiety, stress, and social support than norms. The most acceptable support type was individual psychotherapy (83%), followed by bibliotherapy (61%), pharmacotherapy (56%), online therapy (45%), and group psychotherapy (37%). The most prominent predictor of support acceptability was satisfaction with past use. While individual psychotherapy acceptability was encouragingly high, potentially less costly modalities including group psychotherapy or online therapy may be hampered by low acceptability, the reasons for which need to be further explored.

3.3. Introduction

3.3.1. A brief background to chronic hepatitis C

The hepatitis C virus (HCV) is a blood-borne virus affecting the liver. Of those exposed to HCV, approximately 15-25% spontaneously clear the virus within 6 months, while the remainder experience chronic hepatitis C (CHC) infection (Thomas & Seeff, 2005). CHC is estimated to affect approximately 221,000 Australians, comprising around 1% of the population (The Kirby Institute, 2011). Comparatively, CHC is estimated to affect around 5.4 million (1.8%) people in the U.S. and 160 million (2.4%) globally (Lavanchy, 2011). Over a number of decades, between 15 and 20% of those infected may progress to end-stage liver disease (Liang et al., 2000).

Although the majority of sufferers do not experience this level of disease progression, CHC represents a major public health problem due to its high prevalence and was estimated to have caused 366,000 deaths worldwide in 2002 (Perz et al., 2006). The current anti-viral treatment regime includes pegylated interferon and ribavirin, with the recent addition of the protease inhibitors boceprevir and telaprevir for patients with genotype 1, facilitating a sustained viral response (SVR), whereby HCV is undetectable in blood 6 months post-treatment, in around 65-80% of patients (Ghany, Nelson, Strader, Thomas, & Seeff, 2011). However, neuropsychiatric side-effects are common, with approximately one third of patients experiencing depression or anxiety during treatment (Loftis et al., 2006).

3.3.2. Psychological co-morbidity

CHC can also be characterised as a major public psychological health problem due to the pervasiveness of co-morbid psychiatric disorders, particularly depression and anxiety (el-Serag et al., 2002). Psychiatric co-morbidity has a detrimental impact on the quality of life (Gutteling et al., 2010) and increases patients' experience of physical symptoms, independent of disease status, such as fatigue (Dwight et al., 2000; McDonald et al., 2002) and pain (Morasco et al., 2010). Furthermore, the presence of psychological symptoms can be exacerbated by the neuropsychiatric side-effects of anti-viral treatment with interferon (Castera et al., 2006; Leutscher et al., 2010; Martín-Santos et al., 2008). This can necessitate the need for dose reduction or treatment cessation, subsequently leading to decreased treatment success rates (Leutscher et al., 2010; Raison, Broadwell, et al., 2005). As a consequence, many patients with psychiatric co-morbidity are delayed or excluded from treatment (Chainuvati et al., 2006; Evon et al., 2010; Evon et al., 2007).

3.3.3. Alleviating psychological co-morbidity

Most research regarding mental health treatment in CHC patients has focussed on the use of anti-depressants to prevent or treat depression secondary to anti-viral treatment with interferon. This evidence has demonstrated the efficacy of anti-depressants in treating interferon-induced depression (Hauser et al., 2002; Kraus et al., 2002). The evidence for

prophylactic use of anti-depressants is controversial but appears to be beneficial in 'at-risk' groups such as patients with a history of psychiatric disorders (Schaefer et al., 2005), those with elevated baseline depressive symptomatology (Raison et al., 2007), and patients being retreated after unsuccessful treatment due to interferon-induced depression (Kraus, Schäfer, Al-Taie, & Scheurlen, 2005).

However, the efficacy of psychotropic medications for other disorders such as anxiety, or for depression not induced by interferon, is still unknown. Furthermore, Neri and colleagues (2010) note a number of potential disadvantages to pharmacotherapy in CHC patients, including altered drug kinetics in patients with impaired liver function and physical or neuropsychiatric side-effects. Psychotherapy could therefore be a useful alternative treatment for psychiatric co-morbidity in CHC patients. Recent meta-analyses have demonstrated the efficacy of cognitive behavioural therapy (CBT) in treating depression in people with somatic disease (Beltman et al., 2010), depression, anxiety, anger, and stress in human immunodeficiency virus (HIV) patients (Crepaz et al., 2008), and alcohol or illicit drug use disorders in adults (Magill & Ray, 2009).

Furthermore, combining psychotherapy and pharmacotherapy may prove beneficial, with a recent systematic review reporting that combining pharmacological and psychosocial treatments is more effective in treating depressive disorders in the chronically ill (Rizzo et al., 2011). Evidence for anxiety disorders has been contradictory, although one recent meta-analysis

reported that combined treatment is more effective for panic disorder and could be more effective for social anxiety disorder (Bandelow et al., 2007). Other systematic reviews and meta-analyses (Cuijpers et al., 2011; den Boer, Wiersma, & Van den Bosch, 2004; Lewis, Pearce, & Bisson, 2012) have demonstrated the efficacy of self-help treatments without therapist input, such as self-directed book- or booklet-based treatment (bibliotherapy) and online therapy (E-therapy).

However, there has been very little research on psychotherapy or self-directed therapy in CHC patients specifically. One open-label, randomised, controlled trial of psychotherapy (Neri et al., 2010) was conducted with 211 Italian CHC patients undergoing anti-viral therapy, with half receiving cognitive behavioural and interpersonal psychotherapy. The psychotherapy group had a lower rate of onset of severe psychiatric manifestations during treatment and were less likely to require antidepressant or benzodiazepine prescription. Another multi-centre, clinician-blinded, randomised, controlled trial of a counselling and case-management service (Evon et al., 2011) found that those receiving the intervention were more likely to become eligible for anti-viral treatment.

3.3.4. Acceptability

Patient preferences and the acceptability of psychological treatments is an important factor in assessing the value of a treatment. A randomised controlled trial exploring depression treatment in primary care found that educating

patients about treatment choices and incorporating their preferences into treatment decisions increased patients' uptake of the treatment (Dwight-Johnson et al., 2001). An Australian study found that belief in the efficacy of anti-depressants predicted future use of anti-depressants in those experiencing depression (Jorm et al., 2000). Finally, two recent meta-analyses of randomised controlled psychological treatment trials found that patients randomised to their preferred treatment had significantly lower drop-out rates and significantly greater improvements in treatment outcomes (Swift & Callahan, 2009; Swift et al., 2011).

Thus, while treatment options for psychiatric co-morbidity may be efficacious, this efficacy can be constrained by the acceptability of the therapy type. However, no research to date has explored the acceptability of psychological supports in CHC patients, despite the fact that this patient group is anecdotally known to be difficult to keep in treatment programs due to issues with compliance and adherence. Thus, the primary aim of the present study was to assess the acceptability of different forms of psychological support for CHC patients, including pharmacotherapy. The secondary aim was to assess factors associated with acceptability for the different forms of support.

3.4. Method

3.4.1. Design

This study adopted a cross-sectional design, comprising postal and online surveys using a non-purposive sampling frame. The postal survey was sent to CHC liver clinic outpatients of the Royal Adelaide Hospital (RAH), the largest public teaching hospital in South Australia. An equivalent online survey was conducted with Australians living with CHC in the community. Exclusion criteria were age under 18 years and co-morbid HIV or hepatitis B virus (HBV) infection.

3.4.2. Measures

The survey consisted of six components, the first four of which were designed by the investigators. The first section assessed demographic characteristics, including age, gender, educational history, employment status, marital status, country of birth, number of dependents, and internet access. Postcodes were converted into a proxy measure of socio-economic status using the Socio-Economic Index For Areas (SEIFA) Index of Relative Socio-economic Advantage and Disadvantage Index which has a mean of 1000 and standard deviation of 100 (Australian Bureau of Statistics, 2008).

The second section assessed the acceptability of mental health support, including formal, structured treatments usually offered as part of standard care (pharmacotherapy, individual psychotherapy, and group psychotherapy) and

informal, self-directed treatments which may be offered or sought out by patients themselves (bibliotherapy and E-therapy). Acceptability was measured through presenting statements "I would be willing to use [support type]" and assessing agreement using a 5 point Likert scale ranging from strongly disagree to strongly agree. This section also assessed respondents' perceptions of the ideal length of a hypothetical course of psychological support.

The third section assessed respondents' past history of access to various psychological supports, including: (1) pharmacotherapy from a GP, psychiatrist, or other medical doctor; (2) psychotherapy from a psychologist, psychiatrist, GP, or other non-medical provider (including counsellor, therapist, social worker, or other support worker); (3) self-directed booklet-based psychological support (bibliotherapy); and (4) internet-based psychological support or counselling (E-therapy). Respondents were also asked to state how satisfied they were with various types of support if they had used them, on a 5 point Likert scale ranging from very dissatisfied to very satisfied. GP's were included in the questions on past use of, and satisfaction with, psychotherapy as they are common providers of psychotherapy in Australia, where there are structured training programs for GPs to provide "Focussed Psychological Strategies" using CBT and interpersonal psychotherapy, which can be claimed under GP specific items under Medicare.

The fourth section assessed disease and other medical characteristics, including: (1) estimated time since infection and diagnosis; (2) risk factors for HCV acquisition; (3) current disease-related worries and concerns; (4) viral

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genotype; (5) current and past history of anti-viral treatment; (6) other medical co-morbidities; and (7) current medications.

The fifth section comprised the 21-item version of the Depression Anxiety Stress Scales (DASS; Lovibond & Lovibond, 1995). This self-administered instrument consists of three sets of seven items each measuring symptoms of depression, anxiety, and stress. Participants are asked to indicate how much they experienced these symptoms in the previous week and their answers are scored from 0 to 3, tallied with respect to the three constructs, and doubled in order to scale to the original 42 item version of the DASS. Each sub-scale score ranges from 0 to 42, with higher scores indicating greater symptom severity.

The sixth section comprised the 19-item Medical Outcomes Study Social Support Survey (MOS-SSS; Sherbourne & Stewart, 1991). Participants are asked how often someone who can give a specific type of support is available to them if they need it and responses are scored from 1 to 5. A total social support index was calculated via the average of all 19 items. This was transformed to a scale ranging from 0-100, with higher scores indicating a higher level of social support.

3.4.3. Procedure

Recipients of the postal version of the survey were identified through databases of the RAH liver clinic as people who were diagnosed with CHC. Patient demographic and medical data, where available, were obtained in order

to assess the extent of response bias following the completion of the postal survey by comparing responders and non-responders on these variables.

The postal survey was conducted in accordance with the Dillman method (Dillman, 1991). Eligible patients were sent an advanced notification in November 2011, providing information about the research and an opportunity to opt out of the study via mail, telephone, or e-mail. Recipients who opted out in the following three weeks or whose mailing address was incorrect (as indicated by the postage being returned) were excluded from the mailing list. The survey was sent in December 2011 and over the next two months, recipients who returned a survey, opted out, or whose mailing address was revealed to be incorrect were removed from the mailing list. A reminder letter and replacement survey was sent out in February 2012. Data collection concluded in April 2012.

The adapted online survey was uploaded in December 2011 and promoted via state and local area newspapers in South Australia, the websites and newsletters of various state and territory based CHC councils or organisations, and online community forums for Australians living with CHC. The online survey was deactivated in April 2012.

3.4.4. Data analysis

Normality of continuous variables used was confirmed through Q-Q plots. To assess response bias, differences between postal survey responders and non-responders were assessed using chi square tests for categorical variables and t-tests for continuous variables. Using t-tests, DASS and MOS-SSS scores

were compared, respectively, to Australian community norms (Lovibond & Lovibond, 1995) and U.S. chronically ill patient norms (Sherbourne & Stewart, 1991), with Cohen's *d* calculations using the average standard deviation. Acceptability rates for different treatment options were compared using McNemar's test with alpha adjustments for multiple comparisons using Holm's correction (Holm, 1979). Univariate associations with acceptability rates were assessed using t-tests for continuous variables and chi square tests for categorical variables. Multivariate associations with acceptability rates were assessed using binomial logistic regression models, with forced entry of variables with univariate associations of $p < 0.05$.

3.4.5. Ethics

The Human Research Ethics Committees of the RAH and University of Adelaide approved this study. All participants provided informed consent.

3.5. Results

3.5.1. Postal survey response rate

The contact details of 533 CHC outpatients who had attended the RAH liver clinic were obtained from the hospital database. Ninety four letters were returned due to the person no longer residing at that address, while 127 recipients opted out, 90 returned a survey, and 222 did not respond to any correspondence. One respondent was excluded due to missing data and was

treated as an invalid recipient, leaving a total sample of 89 respondents out of 439 valid potential respondents – yielding a response rate of 20.3%.

To assess the extent of response bias in this postal survey, the 89 respondents were compared with the 350 valid non-respondents based on the data obtained from the hospital database, which included age, gender, marital status, socioeconomic status, Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) scores, nationality, liver fibrosis METAVIR scores (Bedossa et al., 1994), and previous injecting drug use (IDU). As shown in Table 6, those who had received antiviral treatment in the past had a significantly lower response rate. There were no other statistically significant differences between postal responders and non-responders.

Table 6

Comparison of responders and non-responders to postal survey on categorical

variables

Categorical variables		n	Response rate %	χ^2	p
Gender	Females	115	21.7	0.21	0.649
	Males	324	19.8		
Marital status	In relationship	125	20.8	0.02	0.901
	Single	267	21.3		
Country of birth	Born in Australia	202	20.3	0.74	0.390
	Born outside Australia	63	25.4		
Past IDU	Yes	174	21.8	1.88	0.170
	No	55	30.9		
Fibrosis stage	0	22	31.8	3.52	0.475
	1	65	18.5		
	2	47	21.3		
	3	28	32.1		
	4	23	30.4		
Antiviral treatment history	Previously treated	217	15.7	5.63	0.018
	Previously untreated	222	24.8		

Continuous variables	Non-Responder		Responder			
	M	SD	M	SD	t (df)	p
Age	48.23	11.78	50.46	9.49	-1.65 (437)	0.099
SEIFA	952.09	73.66	953.73	80.47	-0.18 (434)	0.855
HADS Anxiety	7.07	4.51	7.42	4.64	-0.53 (293)	0.594
HADS Depression	5.19	4.25	5.29	4.03	-0.16 (293)	0.872

Note. IDU = Injecting drug use. Fibrosis stage is based on METAVIR scores. SEIFA = Socio-Economic Index For Areas – Advantage/Disadvantage Index. HADS = Hospital Anxiety and Depression Scale.

3.5.2. Descriptive statistics

3.5.2.1 Demographic and disease characteristics

Overall, there were 156 respondents. As shown in table 7, 89 (57.1%) were postal responders, males comprised 57.7% (90) of the respondents, and the age ranged from 26 to 79 (M=50.29, SD=9.13). One hundred and thirty nine

(80.1%) respondents reported at least one disease-related worry or concern. These concerns included the fear of disease progression (70.5%), transmitting the virus to others (46.1%), becoming too sick to work (49.4%), becoming too sick to take care of family (32.0%), experiencing stigma from friends or family (37.8%), experiencing stigma from work colleagues (38.5%), experiencing stigma from healthcare workers (30.8%), antiviral treatment side effects (59.6%), other treatment concerns (40.4%), and other non-treatment concerns (9.0%). Eighty three (53.2%) were concerned about experiencing stigma from at least one source.

Table 7

Descriptive statistics for demographic and disease characteristics

Categorical variables		*n*	%
Respondent source	Postal	89	57.1
	Online	67	42.9
Gender	Male	90	57.7
	Female	66	42.3
Education	Year 10	55	35.5
	Year 11	16	10.3
	Year 12	17	11.0
	VET	37	23.9
	University	30	19.4
Employment	Full time	46	29.5
	Part time	20	12.8
	Casual	15	9.6
	Unemployed	15	9.6
	Student	5	3.2
	Home duties	6	3.8
	Disability Support Pension	53	34.0
	Age pension	3	1.9
	Other	2	2.2
Dependents	No	104	66.7
	Yes	52	33.3
Relationship status	Married/de facto	72	46.2
	Separated/divorced/widowed	31	19.9
	Single	53	34.0
Nationality	Born in Australia	114	74.0
	Born overseas	40	26.0
Internet access	No	32	20.8
	Yes	122	79.2
Risk factors for HCV acquisition	Unknown	27	17.3
	IDU	76	48.7
	Tattoos	19	12.2
	Iatrogenic	34	21.8
	Other	11	7.1
Viral genotype	Unknown	62	41.3
	1	46	30.7
	2	19	12.7
	3	18	12.0
	4	1	0.7
	6	4	2.7
Anti-viral treatment	Current	15	9.8
	Past	91	59.5
	Never	47	30.7
SVR	No	46	52.9
	Yes	34	39.1
	Results pending	7	8.0
Other health problems	No	50	32.7
	Yes	69	45.1

Categorical variables			*n*	%
Current medications	All type		103	67.3
	Psychotropic		56	36.6
	Anti-depressant		36	64.3
	Anxiolytic		11	19.6
	Other psychotropic		35	62.5
Continuous variables	Range		*M*	*SD*
Age (years)	26 - 79		50.3	9.1
SEIFA	788 - 1180		978.2	82.7
Years since infection	1 - 44		23.3	10.5
Years since diagnosis	0.02 - 40		13.1	7.8

Note. VET = Vocational education and training. HCV = Hepatitis C virus. IDU = Injecting drug use. SVR = Sustained viral response (HCV clearance) in those who had previously undergone anti-viral treatment. SEIFA = Socio-Economic Index For Areas – Advantage/Disadvantage Index, which has a mean of 1000 (SD = 100) in Australia.

3.5.2.2 Psychosocial characteristics

Table 8 displays the descriptive statistics for the psychosocial characteristics and the comparisons with 2914 community-dwelling Australians (Lovibond & Lovibond, 1995) for depression, anxiety, and stress, and with 2987 U.S. chronically ill patients (Sherbourne & Stewart, 1991) for overall social support. The CHC sample had significantly higher psychological symptoms and lower social support than both comparator groups. In those taking anti-depressants, the rate of severe or extremely severe symptoms was significantly higher for both depression (57.1 vs. 19.8%; *RR*: 2.88 [95% *CI*: 1.81-4.59]) and anxiety (54.3% vs. 18.97%; *RR*: 2.86 [95% *CI*: 1.76-4.64]).

Table 8

Descriptive statistics for psychosocial characteristics and comparisons with norms

| Variable | CHC sample | | Norms† | | | | Cohen's d | Percentage in each Depression Anxiety Stress Scales‡ category | | | | |
	M	SD	M	SD	df	t		Normal (0-78)	Mild (78-87)	Moderate (87-95)	Severe (95-98)	Extremely severe (98-100)
Depression	14.42	12.67	6.34	6.97	3063	13.17*	0.82	42.4	15.9	13.2	7.9	20.5
Anxiety	10.68	9.92	4.70	4.91	3063	13.60*	0.81	44.4	7.9	20.5	6.6	20.5
Stress	15.54	11.93	10.11	7.91	3063	7.98*	0.55	54.3	9.9	9.9	15.2	10.6
Social support	51.10	27.32	70.1	24.2	3135	9.32*	0.74	-	-	-	-	-

Note. † Norms for depression, anxiety, and stress refer to 2914 community-dwelling Australians (Lovibond & Lovibond, 1995). Norms for social support refer to 2987 U.S. chronically ill patients (Sherbourne & Stewart, 1991) ‡ Depression Anxiety Stress Scales categories are based off percentile cut-off points using distributional differences in the standardisation sample (Lovibond & Lovibond, 1995). * $p<0.001$

3.5.3. Psychological support acceptability ratings

The acceptability of various psychological supports was then assessed. As shown in Figure 1, the most acceptable form of support was individual psychotherapy (83.3%; 95% *CI*: 76.3-88.6), followed by bibliotherapy (61.0%; 95% *CI*: 52.8-68.7%), pharmacotherapy (55.8%; 95% *CI*: 47.6-63.6%), E-therapy (45.1%; 95% *CI*: 37.1-53.3%), and group psychotherapy (36.8%; 95% *CI*: 29.3-44.9%).

The rates of acceptability for combinations of formal supports, including
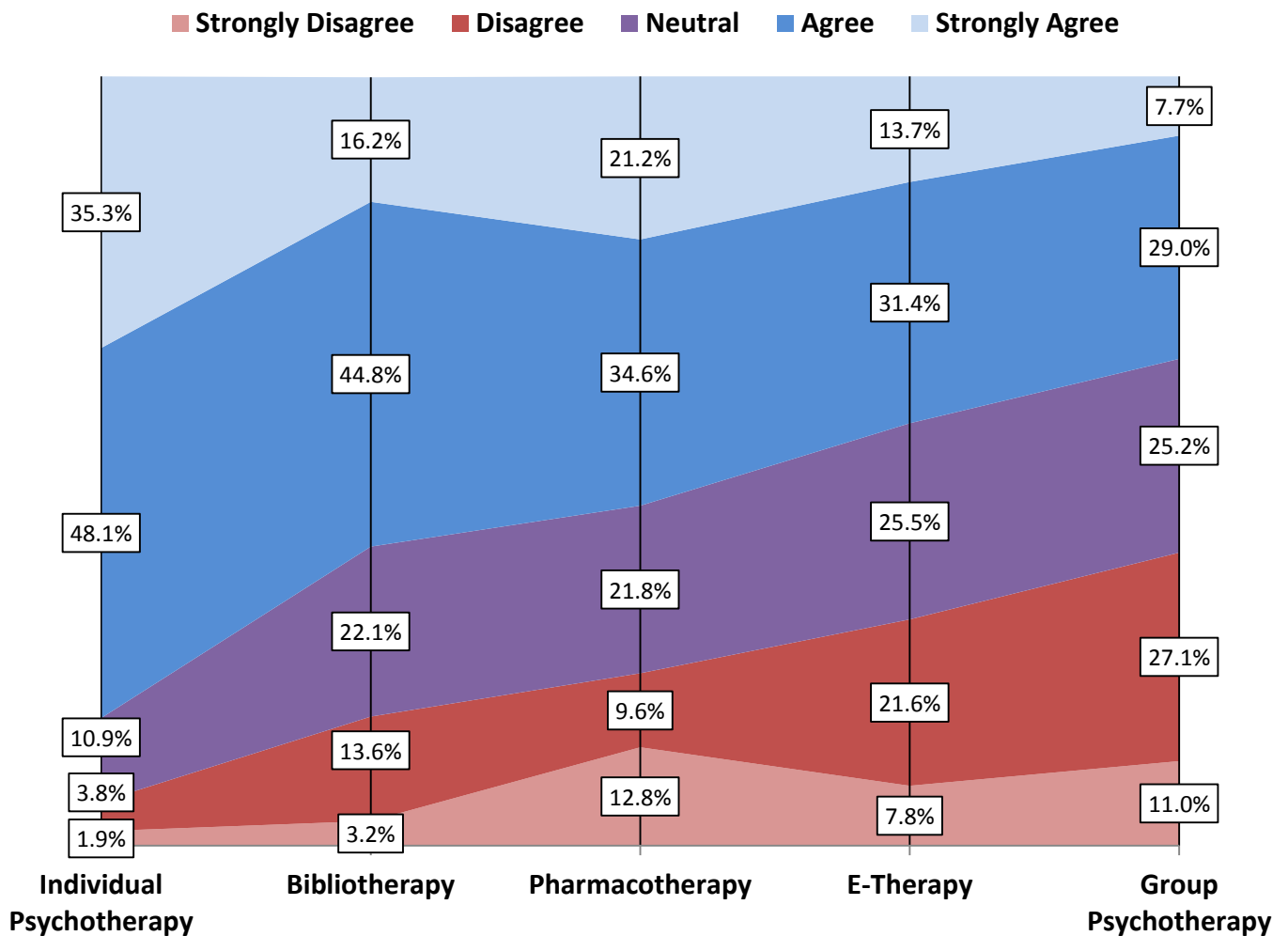
including individual group psychotherapy, was also explored.

Figure 1. Rates of acceptability of psychological supports.

One hundred and forty two (91.0%) respondents found at least one formal source of support acceptable. As shown in Figure 2, of the participants desiring formal support, there was a large overlap in the acceptability of the different treatments, of which individual psychotherapy was the most dominant. Less than 10% endorsed pharmacotherapy or group psychotherapy but not individual psychotherapy. Conversely, nearly a quarter of the participants endorsed individual psychotherapy but not pharmacotherapy or group psychotherapy. A large portion found both individual psychotherapy and pharmacotherapy acceptable.

Group psychotherapy [GP]
40.4%

1.4% [GP]

[Ph] [GP] 1.4%

[Ph] 5.7%

[Ph] [GP] [IP] 23.4%

Pharmacotherapy [Ph]
61.0%

[Ph] [IP] 30.5%

14.2% [GP] [IP]

23.4% [IP]

Individual psychotherapy [IP]
91.5%
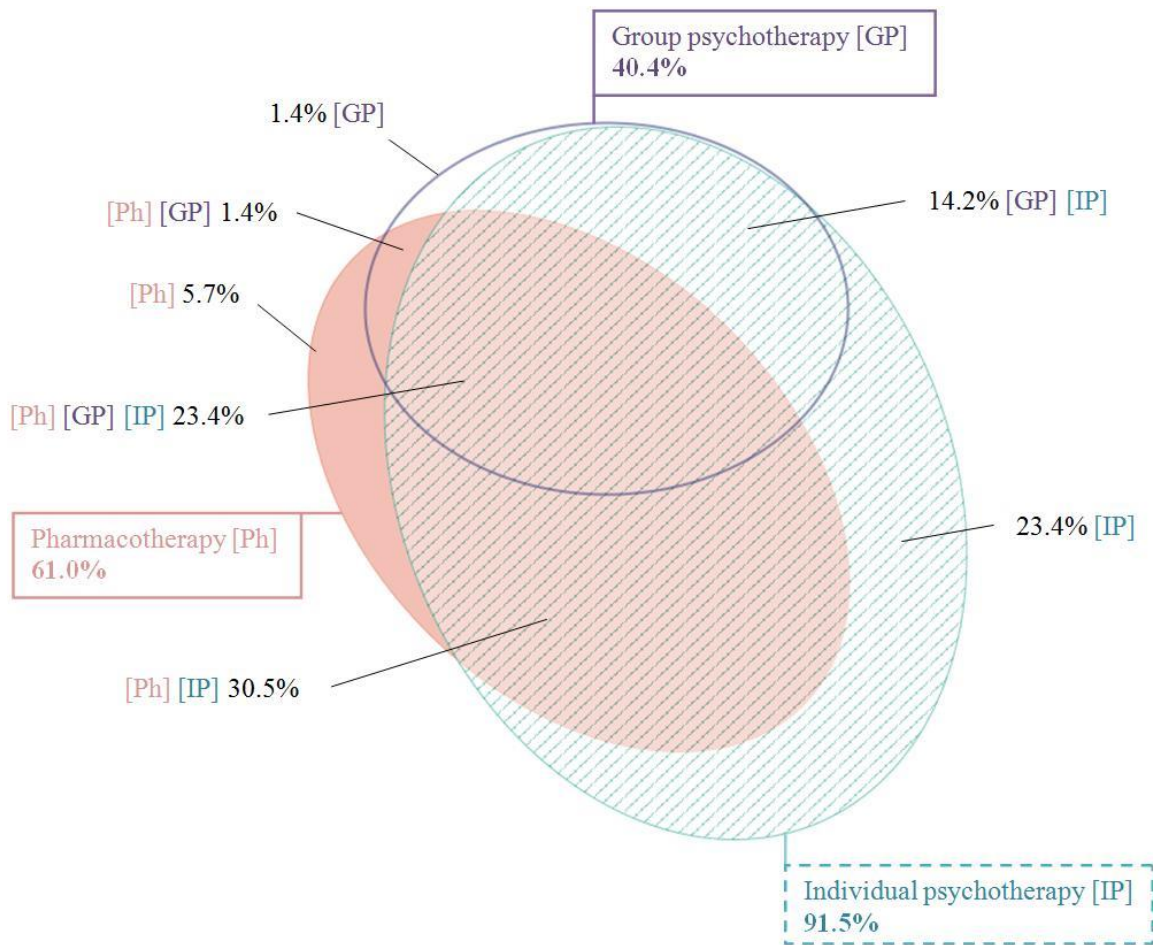
Figure 2. Exclusive and co-occurring acceptability for formal psychological supports. Generated using EulerAPE: http://www.eulerdiagrams.org/eulerAPE/

As shown in Table 9 row 1, individual psychotherapy was significantly more acceptable than all support types. As shown in row 2, pharmacotherapy was significantly more acceptable than group psychotherapy. As per rows 3 and 4, bibliotherapy was significantly more acceptable than group psychotherapy and E-therapy. When asked how long they would want a course of support to last if they did access it, the length of support desired ranged from 1 to 52 weeks (*MDN*=10, *IQR*=6-12) and the total commitment in hours ranged from 1 to 208 hours (*MDN*=12, *IQR*=8-24).

Table 9

Comparison of rates of acceptability across support types

	Individual psychotherapy			Group psychotherapy			Bibliotherapy			E-therapy		
	p	*OR*	*95% CI*	*p*	*OR*	*95% CI*	*p*	*OR*	*95% CI*	*p*	*OR*	*95% CI*
Pharmacotherapy	<0.001	0.19	0.10-0.37	0.001	2.32	1.41-3.82	0.298	0.74	0.44-1.23	0.105	1.50	0.95-2.38
Individual psychotherapy	-			<0.001	19.0	6.95-51.93	<0.001	4.78	2.33-9.80	<0.001	12.6	5.07-31.32
Group psychotherapy	-			-			<0.001	0.34	0.20-0.57	0.124	0.65	0.39-1.08
Bibliotherapy	-			-			-			0.001	2.56	1.44-4.57

Note. The support type found in the left column is the reference group for that row of comparisons. Comparisons were made using McNemar's test, comparing the number of persons finding support type A acceptable but not support type B, with the number who find support B acceptable but not support A. Alpha adjustment was performed using Holm's correction for ten comparisons (Holm, 1979).

Table 10

Rates of prior uptake of, and satisfaction with, psychological supports

Support type		Used support		Satisfaction ratings (%)				
		n	%	Very dissatisfied	Dissatisfied	Neutral	Satisfied	Very satisfied
Pharmacotherapy	GP	67	50.4	9.0	17.9	20.9	41.8	10.4
	Psychiatrist	38	28.6	7.9	26.3	18.4	39.5	7.9
	Other †	27	20.3	14.8	22.2	22.2	33.3	7.4
Psychotherapy	Other ‡	63	47.4	6.3	7.9	17.5	46.0	22.2
	Psychologist	61	45.9	4.9	9.8	21.3	45.9	18.0
	GP	51	38.3	3.9	13.7	29.4	37.3	15.7
	Psychiatrist	45	33.8	13.3	13.3	28.9	35.6	8.9
Bibliotherapy		55	41.4	5.5	9.1	34.5	49.1	1.8
E-therapy		23	17.3	4.3	13.0	47.8	21.7	13.0

Note. GP = General practitioner. † Refers to other medical practitioners. ‡ Refers to counsellors, therapists, social workers, or other support workers

3.5.4. Psychological treatment history

The rates of uptake of, and satisfaction with, psychological supports are displayed in Table 10. Overall, 73 (54.9%) had received any form of pharmacotherapy and 87 (65.4%) had received any form of psychotherapy, while 43 (58.9%) were satisfied with at least one source of pharmacotherapy and 65 (74.7%) were satisfied with at least one source of psychotherapy received. In general, psychotherapy was used more frequently than pharmacotherapy, with the odds of having used one form of psychotherapy but not pharmacotherapy being 3.00 times higher than the reverse (95% *CI*: 1.28-7.06, *p*=0.013). Moreover, the odds of being satisfied with at least one source of psychotherapy but not satisfied with any source of pharmacotherapy was 3.60 times higher than the reverse (95% *CI*: 1.34-9.70, *p*=0.011).

3.5.5. Univariate and multivariate associations with acceptability

In the univariate analysis, higher pharmacotherapy acceptability was associated with: lack of internet access; past use of pharmacotherapy; satisfaction with past pharmacotherapy; and current anti-depressant treatment. Higher Individual psychotherapy acceptability was associated with: higher anxiety; higher stress; being unemployed, casually employed, or in receipt of a disability pension; having no dependents; being single; having used psychotherapy previously; and being satisfied with past psychotherapy. Group psychotherapy acceptability was not significantly associated with any variables investigated. Higher bibliotherapy acceptability was found in those who were satisfied with past bibliotherapy use (85.7% vs. 40.7%, χ^2=12.01, *p*<0.01).

Finally, E-therapy acceptability was associated with: higher SEIFA scores; being an online survey respondent; being female; and having internet access. Predictors which were non-significant at the univariate level for all treatments included: age; years since diagnosis; depression; social support; high school completion; Australian nationality; past IDU; disease-related concerns; stigma-related concerns; current anti-viral treatment; past anti-viral treatment; past SVR; and the presence of other major illnesses.

The variables which were significant at the univariate level were then entered in to a multivariate model in order to determine the independent predictors of acceptability for pharmacotherapy, individual psychotherapy, and E-therapy, as shown in Table 11. As there were no significant univariate predictors for group psychotherapy and, given that only satisfaction with past use predicted bibliotherapy acceptability, no multivariate analysis was performed for these treatments. Satisfaction with past pharmacotherapy and current anti-depressant use remained as significant predictors of pharmacotherapy acceptability, individual psychotherapy acceptability was predicted by past psychotherapy satisfaction, and higher SEIFA scores predicted higher E-therapy acceptability.

Table 11

Multivariate analysis of support acceptability

	Pharmacotherapy			Individual psychotherapy			E-therapy		
Variable	*OR*	*p*	95% *CI*	*OR*	*p*	95% *CI*	*OR*	*p*	95% *CI*
Demographic variables									
Respondent source									
Postal	-	-	-	-	-	-	1.00	-	-
Online	-	-	-	-	-	-	1.43	0.366	0.66-3.09
Gender									
Male	-	-	-	-	-	-	1.00	-	-
Female	-	-	-	-	-	-	1.57	0.217	0.77-3.24
SEIFA	-	-	-	-	-	-	1.01	0.029	1.00-1.01
Employment									
Casually employed, unemployed, DSP	-	-	-	1.00	-	-	-	-	-
Full or part time employed, student, home duties, age pension	-	-	-	0.31	0.272	0.04-2.52	-	-	-
Dependents									
None	-	-	-	1.00	-	-	-	-	-
One or more	-	-	-	0.36	0.234	0.07-1.93	-	-	-
Relationship status									
Single	-	-	-	1.00	-	-	-	-	-
In relationship	-	-	-	0.50	0.453	0.08-3.02	-	-	-
Internet access									
No	1.00	-	-	-	-	-	1.00	-	-
Yes	0.38	0.232	0.08-1.85	-	-	-	2.30	0.126	0.79-6.66

	Pharmacotherapy			Individual psychotherapy			E-therapy		
Variable	*OR*	*p*	*95% CI*	*OR*	*p*	*95% CI*	*OR*	*p*	*95% CI*
Service variables									
Service satisfaction									
Dissatisfied/Neutral	1.00	-	-	1.00	-	-	-	-	-
Satisfied	3.67	0.031	1.13-11.94	9.60	0.009	1.76-52.21	-	-	-
Current AD treatment									
No	1.00	-	-	-	-	-	-	-	-
Yes	20.13	0.006	2.39-169.76	-	-	-	-	-	-
Psychosocial variables									
Anxiety	-	-	-	0.97	0.731	0.82-1.15	-	-	-
Stress	-	-	-	1.03	0.641	0.91-1.17	-	-	-

Note. No multivariate data is presented for bibliotherapy as there was only one variable showing a significant univariate association. Similarly, no data is presented for group psychotherapy as there were no significant univariate associations with this treatment type. Variables without statistics presented were not entered in the multivariate model for that treatment type as they were not significant at the univariate level. SEIFA = Socio-Economic Index For Areas – Advantage/Disadvantage Index. DSP = Disability support pension. AD = Anti-depressant.

3.6. Discussion

The most important finding of this study is the encouragingly high rate of formal treatment acceptability in these patients with CHC who experience markedly increased psychological symptoms compared to Australian community controls and significantly diminished social support compared to U.S. chronically ill patient controls. When asked how long they would want a course of psychological support to last if they were to use it, the average response was 10 sessions of care. This corresponds exactly with the current limitations of reimbursable psychotherapeutic support in Australia under the Better Access to Mental Health Care program, whereby patients are eligible for 10 sessions of psychotherapy per calendar year.

Somewhat more problematic however, was the extremely low acceptability of group psychotherapy (37%). Under the Better Access program in Australia, individuals are also eligible for reimbursement for an additional 10 sessions of group therapy each calendar year – yet if this is not acceptable to patients, it is likely to be an underutilised resource.

While this study was not designed to fully elucidate the reasons behind group therapy's low acceptability, recent qualitative research has found that stigma and fears regarding breaches of privacy are significant potential barriers to CHC patients seeking mental health treatment in general (Stewart, Mikocka-Walus, Harley, et al., 2012). The discrepancy between the acceptability of

individual versus group treatment suggests that these fears may be stronger

with regard to other group members as opposed to the mental health clinicians

facilitating group therapy. Unfortunately, the assessment of stigma was limited

to social, occupational, or general healthcare providers in the present study and

did not specify mental health care providers or other mental health patients in a

group therapy context. Future research may explore whether group

psychotherapy is acceptable if participation is restricted to people living with

CHC.

Overall, individual psychotherapy (83%) was considered by the

respondents to be the most acceptable, followed by bibliotherapy (61%),

pharmacotherapy (56%), E-therapy (45%), and group psychotherapy (37%).

These findings generally correspond with those found in the general Australian

public. A recent national survey of over 6000 Australian adults presented

participants with case vignettes of depression, schizophrenia, post-traumatic

stress disorder, and social phobia (Reavley & Jorm, 2011). Compared with

psychotherapy or CBT, anti-depressants were rated as helpful more frequently

for depression and were rated as helpful at a similar frequency for

schizophrenia, post-traumatic stress disorder and social phobia. However, anti-

depressants were rated as harmful significantly more frequently than

psychotherapy or CBT for all disorder types. Compared with psychotherapy or

CBT, antipsychotics, tranquilisers, and sleeping pills were rated as helpful much

less frequently, and were rated as harmful much more frequently.

This trend appears to translate across countries, with a systematic review of thirteen studies exploring patient preferences in depressed primary care patients and the general public reporting that the majority preferred psychotherapy or counselling over anti-depressants in the treatment of depression (Van Schaik et al., 2004). Psychotherapy appears to be preferred due to the increased opportunity for personal contact and the perception that it addresses the root cause for mental health problems, while fears of side-effects and addiction are common in people's perceptions of psychotropic drugs (Van Schaik et al., 2004). The sparse research comparing the acceptability of group versus individual psychotherapy has reported that individual treatment is generally the preferred option (McDermut, Miller, & Brown, 2001; Sharp, Power, & Swanson, 2004).

As found in the present study, bibliotherapy also appears to be very acceptable to the general Australian public; in a 1995 national survey of over 2000 Australians, when comparing the likely helpfulness of interventions for case vignettes for depression and schizophrenia, respondents gave a higher rating for self-help books than psychotherapy or pharmacotherapy (Jorm et al., 1997), although ratings for these formal treatments have increased markedly in the time since (Reavley & Jorm, 2012a). Similar again to the present findings, while internet-based therapies are acceptable to the general Australian public, the vast majority believe face-to-face treatment is preferable (Gun, Titov, & Andrews, 2011).

Importantly, the rates of previous uptake and satisfaction with psychological supports largely followed the trends found in acceptability. In particular, all-type psychotherapy was used more frequently in the past (65%) and psychotherapy users were more satisfied (75%), compared with pharmacotherapy (55% and 59% had accessed and were satisfied respectively). Satisfaction with previous use of the respective support type was a strong predictor of acceptability for pharmacotherapy, individual psychotherapy, and self-directed bibliotherapy. Also taking into account the high prevalence of CHC and the pervasiveness of psychiatric co-morbidity within this population, the development of a mental health treatment protocol specific to the needs of CHC patients is therefore justifiable.

Considering that a very small proportion endorsed other formal treatments but did not find individual psychotherapy acceptable (just 8.5%) and, given that individual psychotherapy was significantly more acceptable than any other support type, this treatment type appears to be an ideal candidate for a treatment protocol in this population. However, this decision also needs to be made in conjunction with a consideration of both efficacy and cost, or cost-effectiveness. While cost-effectiveness will vary across regions, an Australian economic modelling study reported that bibliotherapy is the most cost-effective treatment for depression due to its very low cost, followed by CBT from a public psychologist, tricyclic prescription, CBT from a private psychologist or psychiatrist, and serotonin selective reuptake inhibitor prescription (Vos et al.,

2005). Also, CBT provided in group settings is much more cost-effective than individual treatment (Vos et al., 2005).

Costs to the patient will similarly vary across regions, yet while both psychotherapy and pharmacotherapy involve a consultation fee which may or may not be subsidised by public or private health-care schemes, pharmacotherapy necessitates the added cost of purchasing the medication. The individual costs of self-directed treatments such as bibliotherapy or E-therapy would depend on the funding in place for these interventions and the level of therapeutic guidance but would presumably involve minor costs to the patient. Equity of access to services is also an important factor, such as in those living in rural or remote areas, where self-directed options such as bibliotherapy and E-therapy may help fill gaps in access to mental health professionals.

A sizeable proportion of patients found both psychotherapy and pharmacotherapy acceptable (54%). Furthermore, of the patients currently taking an anti-depressant, 59% were still experiencing severe to extremely severe depression and 56% were still experiencing severe to extremely severe anxiety. Although the relationship between current use of psychotherapy and continuing psychological symptoms was not explored, it is arguable that a similar result may be found. Nelligan and colleagues (2008) similarly found that 48% of a large sample of U.S. veterans with CHC who were prescribed an anti-depressant were still experiencing moderate to severe depression. These findings collectively provide evidence of a significant therapeutic gap and thus

the potential for greater benefit with the combined use of pharmaco- and psycho-therapies.

In contrast to individual psychotherapy, pharmacotherapy, and bibliotherapy, there was no association between group psychotherapy acceptability and satisfaction with past use, which may reflect the fact that the satisfaction question did not distinguish between uptake of individual versus group forms of psychotherapy. It is probable, given the low acceptability of group psychotherapy, that most respondents who had used psychotherapy in the past were referring to individual therapy - producing the significant relationship between satisfaction and individual but not group psychotherapy acceptability. With regard to E-therapy acceptability, the lack of a relationship with satisfaction with past use could be due to power restrictions based on the low proportion of respondents who had previously used E-therapy.

In the multivariate analysis of E-therapy acceptability, higher SEIFA scores remained a significant predictor while internet access and response source did not. While SEIFA is only a proxy measure, this suggests that those from a more disadvantaged socio-economic background may be less likely to use E-therapy services. The lack of any relationship between the acceptability of any support type and postal versus online respondent source support the generalisability of the findings across tertiary outpatients and community respondents.

3.6.1. Limitations

The main limitation of this study is the modest sample size and low response rate of 20% for the postal survey sample, introducing the risk of response bias. However, postal responders and non-responders did not differ with respect to demographic, disease, or psychological characteristics, with the exception of a slightly higher response rate in those who had not received past anti-viral treatment. However, this may have actually reduced sample bias as the rate of antiviral treatment uptake in Australia is very low (Gidding et al., 2009). The extent of response bias in the online survey is unknown, although it was advertised through a wide range of sources.

Secondly, while this study attempted to exclude patients known to have previously cleared the virus through past treatment from receiving the survey, 34 patients still returned surveys with responses stating they had achieved a SVR. This data was retained as: (1) many patients may need ongoing management for monitoring of pre-existing liver damage and/or follow-up tests to detect any viral relapse; (2) a SVR was not significantly associated with the primary outcome of acceptability for any support type; and (3) patients with a SVR did not significantly differ with regard to depression, anxiety, stress, or social support (results not shown but available on request). This may explain the higher rate of response in the postal sample in those who had not undergone anti-viral treatment, due to some non-postal responders having cleared the virus and not seeing the need to complete the survey.

A third limitation of the study was the relative heterogeneity in the current and past history of having received anti-viral therapy, which is known to affect psychosocial outcomes. However, given that these factors did not predict acceptability, this heterogeneity may increase confidence in the generalisability of the acceptability ratings found across different patient experiences of anti-viral therapy.

An additional limitation was the lack of data regarding the acceptability of different types of psychotherapy (e.g. CBT, interpersonal psychotherapy, or mindfulness-based therapies) or pharmacotherapy (such as anti-depressants, anxiolytics, and anti-psychotics). This data was not obtained due to concerns with explaining these concepts in a way which would be comprehensible to those with low mental health literacy, while keeping the survey brief enough to promote participation. Future research should explore the acceptability of more specific types of psycho- and pharmaco-therapy.

3.6.2. Conclusion

Individual psychotherapy appears to be the most acceptable form of psychological support for Australians living with CHC. It also seems to be the most frequently used support type with the highest satisfaction rating. Given the high rate of psychiatric co-morbidity in this patient group and the clinical benefits of alleviating this co-morbidity, the next step is to develop and evaluate a mental health treatment protocol tailored specifically to CHC patients - potentially

based on individual psychotherapy but with consideration of efficacy, cost, equity in access, and the practicality of alternative treatment modalities.

The sole study in the literature to date found that combined CBT and interpersonal psychotherapy provided in an individual format was effective in preventing the onset of severe psychiatric events during anti-viral treatment and reducing the need for psychotropic prescription (Neri et al., 2010). Further research is necessary to explore the treatment of psychiatric symptoms outside of the anti-viral treatment context. Given the higher cost involved with individual psychotherapy and the limited number of mental health care providers, it is important to further explore the barriers to less costly alternatives such as group psychotherapy and E-therapy which have very low acceptability in this patient group. Bibliotherapy had a reasonably high rate of acceptability and may prove to be a beneficial option in CHC patients if proven to be efficacious and adhered to. Although pharmacotherapy had moderate acceptability, as a common first-line treatment for many patients the reasons for the lower acceptability of pharmacotherapy in comparison to individual psychotherapy also needs to be further explored.

CHAPTER IV: STUDY TWO – COURSE OF DEPRESSION AND ANXIETY

4.1. Statement of authorship

Title: An aggravated trajectory of depression and anxiety co-morbid with hepatitis C: A within-groups study of 61 Australian outpatients.

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Author contributions:

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

Name of Principal Author (Candidate): Benjamin J.R. Stewart

Contribution to the Paper: Collected, analysed, and interpreted the data, wrote the manuscript, and acted as corresponding author.

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Name of Co-Author: Deborah Turnbull

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Signature: Date: 09 / 09 / 2014

Name of Co-Author: Antonina A. Mikocka-Walus

Contribution to the Paper: Supervised the development of the work, assisted in the data interpretation, and helped evaluate and edit the manuscript.

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Contribution to the Paper: Assisted in the data interpretation and helped to evaluate and edit the manuscript.

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Contribution to the Paper: Supervised the development of the work, assisted in the data interpretation, and helped evaluate and edit the manuscript.

Signature: Date: 09 / 09 / 2014

4.2. Abstract

This study aimed to explore the course of depression and anxiety in chronic hepatitis C (CHC) patients. Data were combined from two studies: (1) Hospital Anxiety and Depression Scale (HADS) scores in 395 consecutive Australian outpatients from 2006 to 2010 formed the baseline measurement; and (2) Depression Anxiety Stress Scales (DASS) scores in a survey of a sub-sample of these patients in 2011 formed the follow-up measurement. After converting DASS to HADS scores, changes in symptom scores and rates of case-ness (≥ 8), and predictors of follow-up symptoms were assessed. Follow-up data were available for 61 patients (70.5% male) whose age ranged from 24.5 to 74.6 years (M=45.6) and had been diagnosed with CHC for an average of 12.5 years. The time to follow-up ranged from 20.7 to 61.9 months (M=43.8). Baseline rates of depression (32.8%) and anxiety (44.3%) increased to 62.3% and 67.2%, respectively. These findings were confirmed, independent of the conversion, by comparing baseline HADS and follow-up DASS scores with British community norms. Baseline anxiety and younger age predicted depression, while baseline anxiety, high school non-completion, and single relationship status predicted anxiety. This study demonstrated a worsening trajectory of depression and anxiety. Further controlled and prospective research in a larger sample is required to confirm these findings.

4.3. Introduction

Psychiatric co-morbidity is prevalent in chronic hepatitis C (CHC; el-Serag et al., 2002) and results in diminished quality of life (Gutteling et al., 2010), increased fatigue (Dwight et al., 2000; McDonald et al., 2002) and pain (Morasco et al., 2010), and impaired anti-viral treatment outcomes (Leutscher et al., 2010). Psychosocial stressors are a contributing factor to this morbidity, and include the adverse effect of diagnosis, anti-viral treatment, stigma, and fears regarding disease progression or viral transmission (Stewart, Mikocka-Walus, Harley, et al., 2012). Research has demonstrated poorer quality of life in people aware of their CHC infection compared with those unaware (Dalgard, Egeland, Skaug, Vilimas, & Steen, 2004; Rodger et al., 1999). Thus, the ability of patients to adjust to, and cope with, psychosocial stressors accompanying and following the diagnosis of CHC may be critical in determining the longitudinal course of psychiatric disorders. However, little is known about the course of psychiatric co-morbidity in this cohort. This study aimed to assess the course of depression and anxiety symptoms in a cohort of South Australian CHC outpatients of the Royal Adelaide Hospital (RAH) liver clinic.

4.4. Method

4.4.1. Design and participants

This within-subjects study combined and compared data collected on a sub-set of CHC outpatients from two previous studies. In the first (Stewart, Mikocka-Walus, Morgan, et al., 2012), Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) scores, collected as part of standard clinical care at appointments at the RAH liver clinic from 2006, were analysed to explore the prevalence and predictors of depression and anxiety in 395 consecutive CHC outpatients from 2006-2010. In the second (Stewart, Turnbull, Mikocka-Walus, Harley, & Andrews, 2013), CHC outpatients from this clinic completed a postal survey in late 2011 and early 2012 exploring mental health treatment acceptability, including a measurement with the Depression Anxiety Stress Scales (Lovibond & Lovibond, 1995). Data available for participants of both studies (*n*=61) were collated to assess the level of depression and anxiety at the two time points of assessment.

4.4.2. Procedure

A recent study facilitated a method of converting scores between the HADS and DASS. Covic and colleagues (2012) measured depression and anxiety in British and Australian Rheumatoid Arthritis (RA) patients using the HADS and the DASS. Through use of Rasch Analysis, they were able to calibrate the two scales by mapping scores on to a common underlying metric

of psychopathology. The present study applied this metric to convert DASS scores at follow-up in 2011 to HADS scores. A cut-off score ≥ 8 on the HADS was used to determine depression or anxiety, in accordance with recommendations (Bjelland, Dahl, Haug, & Neckelmann, 2002; Fábregas et al., 2012). The ethics committees of the RAH and University of Adelaide provided approval for the two studies comprising the data for this paper.

4.4.3. Analysis

The normality of continuous variables used was confirmed through Q-Q plots. Differences between HADS scores at baseline (T1) and converted HADS scores at follow-up (T2) were compared using repeated samples t-tests. Rates of case-ness at T1 and T2 were compared using McNemar's test. Levels of depression and anxiety were compared against British norms for T1 HADS scores (Crawford, Henry, Crombie, & Taylor, 2001) and T2 DASS scores (Henry & Crawford, 2005), and the discrepancy between effect sizes analysed, in order to provide an assessment of change independent of DASS conversion. Univariate associations with T2 HADS scores were conducted using Pearson's correlation for continuous predictors and independent samples t-tests for categorical predictors. Multivariate associations were tested using linear regression models with hierarchical entry of predictors with a univariate association of $p<0.05$, with baseline depression and anxiety scores entered at Step 1, and all other predictors at Step 2.

4.5. Results

Socio-demographic and medical data is presented in Table 12. Of the 61
participants for whom T1 and T2 data was available, 43 (70.5%) were male.
Their age ranged from 24.49 to 74.61 years (M=45.61, SD=10.08) and the time
between T1 and T2 assessments ranged from 20.64 to 61.92 months
(M=43.80, SD=12.24).

Table 12

Socio-demographic and medical characteristics of patients

Categorical variables		n	%
Gender	Male	43	70.5
	Female	18	29.5
Education	Non-high school completer	28	45.9
	High school completer	33	54.1
Relationship status	Not partnered	42	73.7
	Partnered	19	26.3
Nationality	Born in Australia	44	72.1
	Born overseas	17	27.9
Previous IDU	No	20	32.8
	Yes	41	67.2
Anti-viral treatment from T1 to T2	No	30	49.2
	Yes	31	50.8
SVR from T1 to T2	No	43	70.5
	Yes	18	29.5
Continuous variables	Range	M	SD
Age (years)	24.49 – 74.61	45.61	10.08
SEIFA	807 – 1098	952.48	77.52
Time since diagnosis (years)	1 – 40	12.51	8.07
T1 to T2 interval (months)	20.70 – 61.93	43.78	12.21

IDU=Injecting drug use, SEIFA=Socio-Economic Index For Areas Index of Advantage /
Disadvantage, based on post-code areas.

As shown in Table 13, depression and anxiety rates increased by T2. The
odds of developing new depressive case-ness by T2 was 10 times higher than
the odds of T1 cases going into remission from depression (p<0.001, 95%

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CI:2.34-42.78). Similarly, the odds of developing anxiety case-ness by T2 was

4.5 times higher than the odds of remission from anxiety by T2 (*p*=0.004, 95%

CI: 1.52-13.30). Finally, the odds of developing co-morbidity by T2 was 4 times

higher than the odds of remission from co-morbidity by T2 (*p*=0.004, 95% *CI*:

1.50-10.66).

Table 13

Depression and anxiety case-ness rates at T1 and T2

	Number of cases † (%)	
Case-ness type	Baseline	Follow-up
Depression‡	20 (32.8)	38 (62.3)
Depression alone	2 (3.3)	5 (8.2)
Anxiety‡	27 (44.3)	41 (67.2)
Anxiety alone	9 (14.8)	8 (13.1)
Any disorder	29 (47.5)	46 (75.4)
One disorder	11 (18.0)	13 (21.3)
Co-morbid disorders	18 (29.5)	33 (54.1)

† Cases are based on HADS subscale scores ≥ 8 ‡ Cases with 'Depression' or 'Anxiety' may also exhibit case-ness of the other disorder type, as compared with 'Depression alone' or 'Anxiety alone' wherein these cases only exhibit case-ness of that disorder type.

As shown in Figure 3, the sample as a whole experienced a significant

increase in both depression (*t*(60)=6.41, *p*<0.001, *d*=0.82) and anxiety

(*t*(60)=4.08, *p*<0.001, *d*=0.52) from T1-T2. When analysed based on case-ness

at T1, depression scores increased significantly in patients without baseline

case-ness (*t*(31)=6.28, *p*<0.001, *d*=1.15) and with one baseline disorder

(*t*(10)=2.87, *p*=0.017, *d*=0.88) but not in those with T1 co-morbidity (*t*(17)=1.64,

p=0.120, *d*=0.39). Anxiety scores increased significantly in those without

baseline case-ness (*t*(31)=5.24, *p*<0.001, *d*=1.01) and remained stable in those

with one baseline disorder (*t*(10)=0.75, *p*=0.473, *d*=0.23) or T1 co-morbidity

(*t*(17)=0.53, *p*=0.605, *d*=0.13).
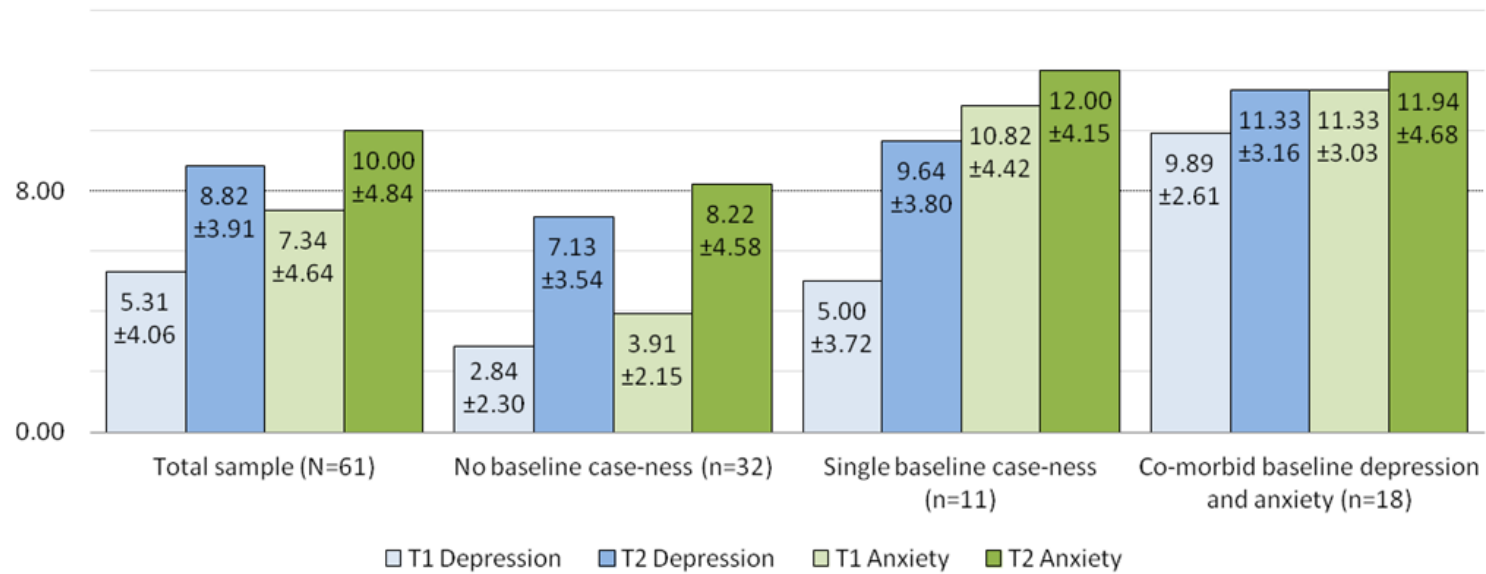
Figure 3. T1 and T2 depression and anxiety ordered by case-ness at T1
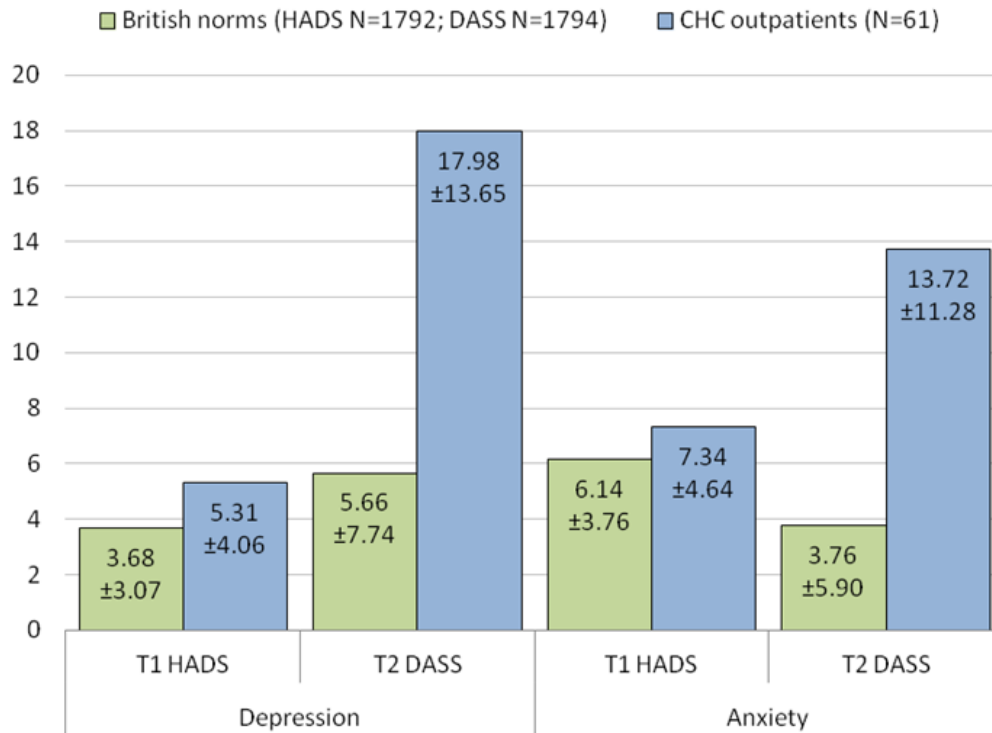
Figure 4. Comparison of T1 HADS and T2 DASS depression and anxiety with British community norms.

As shown in Figure 4, at T1 the present sample was significantly disadvantaged compared to British community HADS norms with respect to both depression ($t(1851)=4.03$, $p<0.001$, Cohen's $d=0.46$) and anxiety ($t(1851)=2.43$, $p=0.015$, Cohen's $d=0.29$). When DASS scores were compared to British norms at T2, this discrepancy had widened markedly for both depression ($t(1853)=11.83$, $p<0.001$, Cohen's $d=1.15$) and anxiety ($t(1853)=12.44$, $p<0.001$, Cohen's $d=1.16$).

Univariate predictors of depression and anxiety at T2 were then assessed, including age at T1, gender, nationality, education, the Socio-Economic Index

For Areas (SEIFA) relative socio-economic advantage and disadvantage index based on post-code areas at T1 (Australian Bureau of Statistics, 2008), relationship status at T1, previous injecting drug use (IDU), years since diagnosis at T2, the time between T1 and T2 assessments, anti-viral treatment between T1 and T2, achieving an SVR between T1 and T2, and T1 anxiety and depression. Depression and anxiety at T1 were significantly and positively correlated with both depression and anxiety scores at T2, while age at T1 was negatively correlated with depression scores at T2. Those who had completed high school and those who were in a relationship at T1 had significantly lower depression and anxiety scores at T2.

Significant univariate predictors were then entered into the multivariate analysis, as shown in Table 14. On step 1, T1 depression and anxiety scores were entered. Only anxiety at T1 independently predicted both depression and anxiety scores at T2. At step 2, education and relationship status were entered into both models and age was added to the depression model. Age remained significant and explained an additional 11% of the variance in depression scores at T2, while education and relationship status remained significant and explained an additional 17% of the variance in anxiety at T2.

Table 14

Multivariate analyses of T2 depression and anxiety

			T2 Depression				T2 Anxiety	
	Variable	*b*	*SE b*	*β*		*b*	*SE b*	*β*
Step 1	*Constant*	*5.64*	*0.87*			*6.61*	*1.10*	
	T1 Depression	0.15	0.15	0.16		0.03	0.19	0.03
	T1 Anxiety	0.32	0.13	0.38*		0.41	0.16	0.40*
Step 2	*Constant*	*10.10*	*3.42*			*6.52*	*3.07*	
	T1 Depression	0.11	0.14	0.11		-0.10	0.17	-0.08
	T1 Anxiety	0.29	0.12	0.35*		0.42	0.15	0.42**
	Age	-0.09	0.04	-0.23*		-	-	-
	High school completion	-1.59	0.90	-0.20		-2.90	1.10	-0.30*
	Relationship status	1.56	1.01	0.18		3.03	1.23	0.28*

For T2 depression, Step 1 Adjusted R^2=0.22, Step 2 ΔR^2=0.11 (ps<0.05). For T2 anxiety, Step 1 Adjusted R^2=0.15, Step 3 ΔR^2=0.17 (ps<0.01). * p<0.05, ** p<0.01.

4.6. Discussion

This study demonstrated a poor trajectory of depression and anxiety in which four groups could be identified: (1) those who were non-cases at both baseline and follow-up (23.0%); (2) those who were non-cases at baseline, but whose symptoms increased to case-ness thresholds by follow-up (29.5%); (3) those who were cases at baseline and follow-up (45.9%); and (4) the sole individual who was a case at baseline and recovered by follow-up (1.6%). Two studies have also reported worsening in symptoms over time in Crohn's disease (Loftus Jr et al., 2011) and cardiovascular patients (Lane, Carroll, Ring, Beevers, & Lip, 2002). However, these findings contradict the stability reported over one year in two smaller studies with CHC (Kraus, Schäfer, Faller, Csef, & Scheurlen, 2003; Mikocka-Walus, Turnbull, Moulding, et al., 2008). Moreover,

research in other populations have reported stability over time, including in the general population (Bjerkeset, Nordahl, Larsson, Dahl, & Linaker, 2008) and those with HIV (Ickovics et al., 2001; Lyketsos et al., 1996), irritable bowel syndrome and inflammatory bowel disease (Banovic, Gilibert, & Cosnes, 2010; Mikocka-Walus, Turnbull, Moulding, et al., 2008), cardiovascular disease (Kaptein, De Jonge, Van Den Brink, & Korf, 2006; Smolderen et al., 2008), and RA (Norton, Sacker, Young, & Done, 2011; Smedstad, Vaglum, Moum, & Kvien, 1997).

It is possible that the aggravated course observed here can be explained by the differential nature of CHC and the psychosocial stressors it poses and/or the nature of the populations who typically acquire CHC – comprising mostly current or former IDUs (67% in this cohort). CHC-specific psychosocial factors include the common experience of stigma (Golden et al., 2006; Zickmund et al., 2003), the stress of diagnosis (Gill, Atiq, Sattar, & Khokhar, 2005; Sgorbini, O'Brien, & Jackson, 2009; Stewart, Mikocka-Walus, Harley, et al., 2012), internalised feelings of contamination (Conrad, Garrett, Cooksley, Dunne, & Macdonald, 2006; Fraser & Treloar, 2006; Stewart, Mikocka-Walus, Harley, et al., 2012), and fears regarding illness-related disability or death and the transmission of CHC to loved ones (Groessl et al., 2008; Minuk, Gutkin, Wong, & Kaita, 2005; Stewart, Mikocka-Walus, Harley, et al., 2012).

Also, previous research has reported a worse prognosis for those with co-morbid depression and anxiety (Fichter, Quadflieg, Fischer, & Kohlboeck, 2010; Richards, 2011), which is common in people with CHC (el-Serag et al., 2002)

and, particularly, in the cohort from which this sample was drawn (Stewart, Mikocka-Walus, Morgan, et al., 2012).

However, this does not account for the aggravation in those without morbidity at baseline - the group in which the main symptom increase occurred. The correlation between depression and anxiety scores at baseline provides insight into the general level of co-morbid symptomatology in the sample regardless of case-ness. In the British community (Crawford et al., 2001), the correlation between HADS anxiety and depression scores is moderate (r=0.53, p<0.001). In the cohort from which the present sample was drawn (Stewart, Mikocka-Walus, Morgan, et al., 2012), the correlation is significantly larger (r=0.66, Z=3.63, p<0.001), indicating a higher degree of co-morbid symptoms in this patient group.

Interestingly, time since diagnosis was not related to depression or anxiety at follow-up. There was also no association between the change in psychopathology and the variable time difference between the baseline and follow-up assessments across patients. This suggests that the aggravation in symptoms observed may not be stemming from a failure to adjust to the diagnosis of CHC per se or from the mere passage of time. It is possible that the progression observed reflects a difficulty in adjusting to new psychosocial stressors, such as disease progression and treatment considerations. These stressors do not occur at predictable time points following diagnosis, as CHC can progress quite slowly and patients may present for specialist treatment at different times following diagnosis.

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In the multivariate analysis, baseline anxiety, but not depression, remained an independent predictor of both increased depression and anxiety at follow-up. This is supported by longitudinal community-based studies which have found that anxiety tends to lead to depression more often than the reverse (Fichter et al., 2010; Wetherell, Gatz, & Pedersen, 2001). After accounting for baseline depression and anxiety, age remained a significant predictor of decreased depression at follow-up, while education and relationship status remained independent predictors of decreased anxiety - consistent with other research (Bjerkeset et al., 2008; Grace et al., 2005).

This study has a number of limitations. Firstly, there were no control comparison subjects and the length of follow-up varied, due to this studies post-hoc use of routinely collected clinical data as the baseline measurement. Secondly, the sample was small and the participants of the second study who provided follow-up data were self-selected (Stewart et al., 2013), introducing the possibility of sample biases. However, excluding a slightly lower response rate in previous recipients of anti-viral treatment (16% vs. 25%), there were no differences between survey responders and non-responders (Stewart et al., 2013). Critically, there were no differences in HADS scores. Thus, both non-responders and responders to the survey experienced comparable mental health at baseline. However, it is possible those who experienced a worse course of depression and anxiety after that baseline measurement were more inclined to respond at follow-up because the issue was more personally salient.

Thirdly, the procedure of converting DASS scores at follow-up to HADS scores to compare symptoms relies on the assumption that the calibration of DASS and HADS scores by Covic and colleagues (2012) is robust and equivalent between RA and CHC patients. To verify the findings independent of this conversion and its assumptions, baseline HADS and follow-up DASS scores were compared separately to British norms for the HADS (Crawford et al., 2001) and DASS (Henry & Crawford, 2005), respectively. At baseline, the present sample had significantly worse HADS scores than British norms. However, by follow-up this disadvantage, in comparison to British norms for the DASS, had inflated by a factor of 2.5 for depression and 4 for anxiety.

Finally, subjects who achieved a SVR between baseline and follow-up assessments were included, as many receive ongoing care to assess for viral relapse and manage existing liver damage. If the SVR rates of the sample that provided follow-up data were lower than normal, this could explain their poorer mental health. However, of the 31 patients who received anti-viral treatment, 58% achieved a SVR, consistent with rates in those treated with interferon and ribavirin (Ghany et al., 2011). Moreover, SVR was not associated with follow-up depression or anxiety in this study.

4.7. Conclusions

This study found a high rate of co-morbid depression and anxiety which increased markedly over a period of up to five years in a small sample of

Australian CHC outpatients. Future research would benefit from a controlled, prospective analysis in a larger sample, involving multiple assessments of symptoms and a focus on potential intervening variables such as psychiatric treatment, social support, and changes in CHC-related psychosocial stressors.

CHAPTER V: STUDY THREE – MENTAL HEALTH PROBLEMS AND SERVICE USE 2006-2012

5.1. Statement of authorship

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Author contributions:

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

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Contribution to the Paper: Analysed and interpreted the data, wrote the manuscript, and acted as corresponding author.

Signature: Date: 09 / 09 / 2014

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Contribution to the Paper: Supervised the collection of the data and helped

evaluate and edit the manuscript.

Signature: Date: 09 / 09 / 2014

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Contribution to the Paper: Supervised the development of the work, assisted in

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Signature: Date: 09 / 09 / 2014

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Signature: Date: 09 / 09 / 2014

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Contribution to the Paper: Supervised the development of the work, assisted in

the data interpretation, and helped evaluate and edit the manuscript.

Signature: Date: 09 / 09 / 2014

5.2. Abstract

This paper aimed to assess changes in rates of mental health problems and service utilisation for Australian regular injecting drug users (IDUs) from 2006-2012. Data were taken from Illicit Drug Reporting System national surveys with 914 regular IDUs in 2006 and 883 in 2012. Changes in rates of self-reported mental health problems and service use were assessed. Rates of self-reported mental health problems increased from 38.3% in 2006 to 43.7% in 2012 - mainly due to increases in anxiety rates. Conversely, there was a decrease in mental health service use from 70.2% to 58.4% by 2012. However, there was a proportional increase in the use of psychologists. These trends remained after controlling for socio-demographic and medical differences between the 2006/2012 samples. K10 scores for 2012 participants validated the use of the self-report measures. Reductions in stigma, improvements in mental health literacy, and modest increases in anxiety may explain increases in self-report of mental health problems. Stagnant service utilisation rates in an expanding population willing to self-report may explain decreasing service use. The introduction of key mental health reforms also may have contributed, particularly with the increase in psychologist access. This paper highlights the need for improved population monitoring of mental health in disadvantaged groups such as IDUs. This paper is the first to assess changes in mental health outcomes over time in Australian IDUs. This examination covered a critical era

in the mental health landscape, with significant increases in public awareness campaigns and major mental health reforms.

5.3. Introduction

A substantial body of evidence has demonstrated high rates of psychiatric morbidity experienced by injecting drug users (IDUs) amongst those in primary treatment (Lieb et al., 2010; Savant et al., 2013), in tertiary treatment (Brienza et al., 2000; Brooner et al., 1997; Callaly et al., 2001; Teesson et al., 2005), and in the community (Kidorf et al., 2004; Mackesy-Amiti et al., 2012; Rodríguez-Llera et al., 2006). Furthermore, the presence of psychiatric co-morbidity (Carpentier et al., 2009) and increased psychological distress (De Maeyer et al., 2011) have been shown to significantly diminish quality of life in IDUs. A meta-analysis also found that depression in IDUs was modestly but significantly associated with higher current drug and alcohol use and impairment, and also with needle sharing (Conner, Pinquart, & Duberstein, 2008). It is estimated that there were 214,700 IDUs in Australia in 2005 (Razali et al., 2007). Thus, IDUs are an important sentinel population in the design, delivery, and evaluation of mental health policy and practice.

Australia has undergone numerous changes in mental health policy and practice over the last decade. In November 2006, the Better Access to Psychiatrists, Psychologists and General Practitioners through the Medicare Benefits Schedule (Better Access) initiative was introduced in Australia to

increase uptake of mental health services (Pirkis, Harris, Hall, & Ftanou, 2011).

Better Access involved addition of new items to the Medicare (Australia's public

funding provider for health care) Benefits Schedule to allow rebates for mental

health services provided by GPs, psychiatrists, psychologists, social workers,

and occupational therapists to people with a mental disorder.

The formal evaluation of Better Access (Pirkis, Harris, et al., 2011) was

positive, noting that it had high uptake across the community, serviced a large

proportion of people who have not previously accessed services, has been

accessed by patients with severe psychiatric symptoms, resulted in significant

improvements in treatment outcomes, and had led to an increase in service use

in those with a disorder.

The evaluation also reported that while the greatest improvements in

uptake occurred in areas of socio-economic disadvantage, uptake in this group

still remained 10% lower than those living in areas of socio-economic

advantage (Pirkis, Harris, et al., 2011). Critically, IDU is associated with both

individual and neighbourhood indices of socio-economic disadvantage

(Boardman, Finch, Ellison, Williams, & Jackson, 2001; Friedman et al., 2004;

Nandi et al., 2010; Ompad et al., 2012; Rhodes et al., 2003; Topp, Iversen,

Baldry, & Maher, 2012; Williams & Latkin, 2007). However, no research to date

has explored the effect of Better Access on IDUs. While Better Access was

broad-based and not designed to target specific groups, its influence on

populations such as IDUs is critical due to their elevated need for mental health

services.

There has also been a marked increase in public awareness campaigns surrounding mental health issues, particularly since 2000 with the formation of Beyond Blue (a national, independent, not-for-profit organisation which, amongst other things, aims to raise mental health awareness and reduce stigma in the community). Studies have shown that these campaigns may have resulted in reducing stigma around mental health issues (Reavley & Jorm, 2012a) in addition to improving mental health literacy (Reavley & Jorm, 2012b) in the general population. However, the effect on IDUs, like that of Better Access, is unknown. This study aimed to assess changes in self-reported mental health problems and mental health service utilisation in current and regular IDUs in the context of these recent mental health reforms and the increasing public dissemination of mental health information.

5.4. Method

5.4.1. Design

The current study utilised cross-sectional data, collected from current, regular IDUs who participated in the 2006 or 2012 Illicit Drug Reporting System (IDRS) studies, described below.

5.4.2. IDRS

The IDRS is an annual national monitoring system coordinated by the National Drug and Alcohol Research Centre, University of New South Wales,

which is designed to monitor trends in illicit drug price, purity, availability, use and related harms. The IDRS has been run nation-wide since 2000 and a comprehensive account of the methodology can be found elsewhere (Stafford & Burns, 2012). One of the three main components of the IDRS involves a face-to-face interview with current, regular IDUs. The present study utilised the data from these interviews for 2006 (O'Brien et al., 2007) and 2012 (Stafford & Burns, 2012).

5.4.3. Participants

IDRS participants had to be 16 years of age or older, have a minimum six month history of at least monthly injecting, and have been residing in the city where the interview took place for 12 months. At least 100 participants were recruited from each capital city of Australia using convenience sampling through advertisements in street press, newspapers, treatment services, and needle and syringe programs, as well as through peer referral.

5.4.4. Materials

The 2006 IDRS structured interview schedule assessed: (1) Demographics; (2) Personal drug use; (3) Knowledge regarding drug trends; (4) Personal criminal behaviour; (5) Personal drug-related risk-taking behaviour; (6) Blood-borne virus testing and treatment history; (7) Drug-related health and mental health problems and associated help-seeking; and (8) General trends regarding illicit drug use.

For the purposes of this research study, data were taken from sections 1, 2, 4, 6, and 7 for 2006 as well as 2012 where they were repeated. The demographic variables assessed included sex, age, postcodes (to analyse Socio-Economic Index For Areas (SEIFA) scores; Australian Bureau of Statistics, 2008), primary spoken language or indigenous heritage (as demonstrating culturally and linguistically diverse or CALD status), education, and employment. The personal drug use variables used included recent drug treatment, age at first IDU, and frequency of recent injecting. The personal criminal variables explored included lifetime imprisonment history. Data on blood-borne virus history was also utilised, comprising history of testing for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV), and treatment for HCV.

Finally, data were also used for self-reported six-month history of mental health problems and subsequent uptake of mental health services, as well as the type(s) of mental health problems experienced and mental health professionals accessed for support. In addition to the 2006 questions carried over, the 2012 IDRS interview also included the 10-item Kessler Psychological Distress Scale (K10; Kessler et al., 2002). Past research has found the K10 to be a valid and accurate screening tool for affective disorders in IDUs and has indicated that a cut-off score of ≥ 27 can accurately identify clinical cases (Hides et al., 2007).

5.4.5. Procedure

Interviews were conducted in locations convenient to the participants such as treatment services, needle and syringe programs, or other public locations. The interviews were administered by trained research staff in each state or territory from June to August in both 2006 and 2012. Interviews lasted approximately 30 to 50 minutes and participants were reimbursed up to $40 for their time and expenses incurred.

5.4.6. Analysis

Prior to analysis, twenty two cases were removed from the 2012 cohort as they reported participating in the 2006 IDRS, to avoid cross-sample contamination. An additional 19 cases were removed from the 2012 cohort for missing data on the outcome variables of mental health problems and service use. The data were analysed using IBM SPSS 19. Normality of continuous variables was confirmed using Q-Q plots. Differences between the 2006 and 2012 cohorts were assessed using independent groups t-tests for continuous variables and chi-square tests for categorical variables. Differences in self-reported rates of mental health problems and service uptake were assessed using chi-square tests. Two hierarchical logistic regression models were run for mental health problems and service use, entering demographic/medical variables which differed between the 2006 and 2012 samples on the first step, while the variable differentiating the 2006/2012 samples was entered on the second step. The accuracy of self-report for mental health problems and service

use was assessed using chi-square tests to compare proportions of 2012 participants reporting a mental health problem in those above and below the K10 cut-off.

5.4.6. Ethics

Ethics approval was granted by the appropriate Human Research Ethics Committees in each state and territory of Australia for both the 2006 and 2012 IDRS surveys. This research was conducted in accordance with the provisions of the Declaration of Helsinki (World Medical Association, 2008).

5.5. Results

Socio-demographic and medical characteristics of the 2006 and 2012 cohorts are shown in Table 15. The 2012 cohort had higher rates of unemployment and HCV treatment, had a lower rate of HCV positivity, were older, and began injecting at a later age. Self-reported mental health problem rates increased significantly from 2006 to 2012, mainly due to a large increase in the rate of anxiety, as shown in Table 16.

Table 15

Socio-demographic and medical characteristics for the 2006 vs. 2012 cohort

Variable		n (%)		χ^2	p
		2006 (*N*=914)	2012 (*N*=883)		
Gender	Male	584 (64.4)	584 (66.4)	0.83	0.362
	Female	323 (35.6)	295 (33.6)		
State or territory of interview	ACT	100 (10.9)	95 (10.8)	4.44	0.728
	NSW	152 (16.6)	148 (16.8)		
	NT	100 (10.9)	121 (13.7)		
	QLD	112 (12.3)	96 (10.9)		
	SA	100 (10.9)	87 (9.9)		
	TAS	100 (10.9)	99 (11.2)		
	VIC	150 (16.4)	148 (16.8)		
	WA	100 (10.9)	89 (10.1)		
Education	No secondary/tertiary completion	402 (44.0)	350 (39.7)	3.41	0.065
	Secondary/tertiary completion	512 (56.0)	532 (60.3)		
Employment	Unemployed	707 (77.4)	740 (83.8)	11.92	0.001
	Employed, student, home duties, or other$	207 (22.6)	143 (16.2)		
Cultural background	Not CALD or Indigenous	762 (83.4)	708 (80.2)	3.07	0.080
	CALD or Indigenous Australian	152 (16.6)	175 (19.8)		
Substance use treatment in last 6 months	No	398 (43.5)	404 (45.9)	1.01	0.314
	Yes	516 (56.5)	476 (54.1)		
Frequency of injection in previous month	Weekly or less	180 (19.7)	164 (18.7)	1.52	0.677
	More than weekly but not daily	316 (34.6)	309 (35.2)		
	Once a day	155 (17.0)	166 (18.9)		
	Multiple times per day	261 (28.6)	239 (27.2)		
HBV status	HBV-	677 (91.6)	708 (94.1)	3.64	0.056
	HBV+	62 (8.4)	44 (5.9)		
HCV status	HCV-	326 (39.7)	392 (48.8)	13.66	<0.001
	HCV+	495 (60.3)	411 (51.2)		
HIV status	HIV-	804 (98.0)	774 (98.6)	0.73	0.392
	HIV+	16 (2.0)	11 (1.4)		
HCV anti-viral treatment history	Not treated	833 (93.1)	776 (90.3)	4.32	0.038
	Treated	62 (6.9)	83 (9.7)		
History of imprisonment	No	449 (49.1)	393 (45.3)	2.65	0.104
	Yes	465 (50.9)	475 (54.7)		
		M (SD)			
		2006	2012	t	p
Age		34.5 (9.0)	39.2 (9.3)	10.76	<0.001
Age first injected		19.2 (6.0)	19.8 (6.8)	1.97	0.049
SEIFA score		1006.9 (82.0)	1013.4 (85.9)	1.54	0.125

$ Other included carer, retired, volunteer, incapacitation allowance awaiting surgery, and maternity leave.

Table 16

Self-reported rates of six-month mental health problems for the 2006 vs. 2012

cohort

	n (%)				
Problem type	2006 (*N*=914)	2012 (*N*=883)	X^2	*RR* (95% *CI*)$	*p*
Any mental health problem	350 (38.3)	386 (43.7)	5.46	1.14 (1.02 - 1.28)	0.019
Mood problems	274 (30.0)	296 (33.5)	2.60	1.12 (0.98 - 1.28)	0.107
Anxiety problems	140 (15.3)	226 (25.6)	29.25	1.67 (1.38 - 2.02)	<0.001
Psychotic problems	66 (7.2)	82 (9.3)	2.54	1.29 (0.94 - 1.75)	0.111
Personality problems	13 (1.4)	19 (2.2)	1.37	1.51 (0.75 - 3.04)	0.242
Other mental health problems	29 (3.2)	31 (3.5)	0.16	1.11 (0.67 - 1.82)	0.690

$ Risk ratios with 95% confidence intervals using the 2006 cohort as the reference category

Table 17

Self-reported rates of six-month mental health service use in those with a self-

reported mental health problem for 2006 vs. 2012 cohort

	n (%)				
Service type	2006 (*N*=349)	2012 (*N*=385)	X^2	*RR* (95% *CI*)$	*p*
Any mental health professional	245 (70.2)	225 (58.4)	10.99	0.83 (0.75 - 0.93)	0.001
General practitioner	153 (43.8)	133 (34.5)	6.65	0.79 (0.66 - 0.95)	0.010
Psychiatrist	68 (19.5)	78 (20.3)	0.07	1.04 (0.78 - 1.39)	0.793
Psychologist	48 (13.8)	64 (16.6)	1.12	1.21 (0.86 - 1.71)	0.280
Counsellor	60 (17.2)	22 (5.7)	24.30	0.33 (0.21 - 0.53)	<0.001
Community health nurse	10 (2.9)	4 (1.0)	3.26	0.36 (0.12 - 1.15)	0.071
Mental health nurse	15 (4.3)	14 (3.6)	0.21	0.85 (0.41 - 1.73)	0.646
Hospital emergency department	9 (2.6)	8 (2.1)	0.20	0.81 (0.31 - 2.07)	0.652
Psychiatric ward	16 (4.6)	8 (2.1)	3.64	0.45 (0.20 - 1.05)	0.057
Social worker	15 (4.3)	19 (4.9)	0.17	1.15 (0.59 - 2.22)	0.682
Other	14 (4.0)	8 (2.1)	2.35	0.52 (0.22 - 1.22)	0.125

$ Risk ratios with 95% confidence intervals using the 2006 cohort as the reference category

Rates of service use in those with a mental health problem dropped from 2006 to 2012, with decreases in access to GPs and counsellors being the main factors, as shown in Table 17. However, analysing specific service uptake as a proportion of service users (Table 18) demonstrated that the only significant changes over time were an increase in uptake of psychologists and a decrease in consultations with counsellors.

Table 18

Self-reported rates of six-month mental health service use in those who had sought help for 2006 vs. 2012 sample

Service type	n (%)		X^2	RR (95% CI)$	p
	2006 (*N*=245)	2012 (*N*=225)			
General practitioner	153 (62.4)	133 (59.1)	0.55	0.95 (0.82 - 1.10)	0.459
Psychiatrist	68 (27.8)	78 (34.7)	2.62	1.25 (0.95 - 1.64)	0.106
Psychologist	48 (19.6)	64 (28.4)	5.06	1.45 (1.05 - 2.01)	0.024
Counsellor	60 (24.5)	22 (9.8)	17.63	0.40 (0.25 - 0.63)	<0.001
Community health nurse	10 (4.1)	4 (1.8)	2.15	0.44 (0.14 - 1.37)	0.142
Mental health nurse	15 (6.1)	14 (6.2)	0.00	1.02 (0.50 - 2.06)	0.964
Hospital emergency department	9 (3.7)	8 (3.6)	0.01	0.97 (0.38 - 2.47)	0.945
Psychiatric ward	16 (6.5)	8 (3.6)	2.14	0.54 (0.24 - 1.25)	0.143
Social worker	15 (6.1)	19 (8.4)	0.94	1.38 (0.72 - 2.65)	0.332
Other	14 (5.7)	8 (3.6)	1.23	0.62 (0.27 - 1.46)	0.268

$ Risk ratios with 95% confidence intervals using the 2006 cohort as the reference category

In the multivariate analyses, the variable differentiating between the 2006/2012 samples remained a significant predictor, after controlling for socio-demographic and medical differences, of both self-reported mental health problems and utilisation of mental health services (Table 19).

Table 19

Multivariate analyses of mental health problems and service use

Variable		Mental health problems			Service use		
		B (SE)	OR	95% CI	B (SE)	OR	95% CI
Step 1	Constant	0.19 (0.24)	1.21		0.63 (0.39)	1.87	
	Age	-0.01 (0.01)	0.99	0.98-1.00	-0.01 (0.01)	0.99	0.97-1.01
	Age of first injecting	-0.02 (0.01)	0.99	0.97-1.00	0.01 (0.02)	1.01	0.98-1.04
	Being employed	-0.03 (0.13)	0.97	0.75-1.24	0.18 (0.21)	1.20	0.80-1.80
	HCV+	0.02 (0.11)	1.02	0.83-1.25	0.18 (0.17)	1.20	0.87-1.67
	Treated for HCV	0.38* (0.18)	1.45	1.01-2.09	0.07 (0.28)	1.08	0.63-1.85
Step 2	Constant	0.16 (0.24)	1.17		0.68 (0.39)	1.98	
	Age	-0.01 (0.01)	0.99	0.98-1.00	-0.01 (0.01)	1.00	0.98-1.02
	Age of first injecting	-0.01 (0.01)	0.99	0.97-1.00	0.01 (0.02)	1.01	0.98-1.04
	Being employed	-0.00 (0.13)	1.00	0.77-1.28	0.12 (0.21)	1.13	0.75-1.71
	HCV+	0.06 (0.11)	1.06	0.86-1.31	0.13 (0.17)	1.13	0.81-1.58
	Treated for HCV	0.36 (0.18)	1.43	1.00-2.05	0.07 (0.28)	1.07	
	2012 sample	0.28* (0.11)	1.32	1.07-1.63	-0.48** (0.17)	0.62	0.44-0.87

For Mental health problems, R^2=.02 (Nagelkerke). Model χ^2=17.45, p=0.008. For Service use, R^2=.02 (Nagelkerke). Model χ^2=10.65, p=0.100. * $p<0.05$, **$p<0.01$

In the 2012 cohort, of the participants who did not report a mental health problem, 109 (22.4%) had a K10 score exceeding the cut-off score of 27, compared to 62.5% of those who did report a problem (χ^2=141.69, $p<0.001$). When the 109 individuals who exceeded the K10 cut-off (but did not report experiencing a mental health problem) were added to the category of individuals who reported a problem but did not seek help, the 2012 service utilisation rate dropped from 58.4% to 45.5%.

5.6. Discussion

This study is the first to look at changes in Australian IDU mental health outcomes over time. The main findings include an increase in the rate of mental health problems and a decline in service use rates. These data can be interpreted in a number of ways. Firstly, it is possible that the increased rate of mental health problems over time is due to less mental health-related stigma and an increased willingness to report problems. Research has shown that at least some aspects of stigmatising attitudes regarding mental health have improved between 2003/04 and 2011 in Australia (Reavley & Jorm, 2012a) – most likely due to public awareness campaigns such as Beyond Blue (Jorm, Christensen, & Griffiths, 2005). Although other help-seeking barriers would undoubtedly influence service use, if stigma had decreased, this should result in an increased willingness to both access services and report using services to others. This is not reflected in the decrease in service use observed in this study.

Another possibility is that the increased rates of mental health problems are due to improvements in mental health literacy, which can facilitate awareness and thus self-reporting of mental health problems. All else remaining equal, this would indicate that the service use rates were inflated in 2006, thereby also explaining the relative decrease in service use by 2012. Analysis of national Australian surveys in 1995, 2003/04, and 2011 have demonstrated that

there have been significant improvements in mental health literacy in the general population (Reavley & Jorm, 2012b).

An argument could also be made for a genuine increase in mental health problems over time. Australian national health surveys have found a trend towards increasing self-reported mental health problems of similar magnitude in the general community, from 10.7% in 2004-05 to 13.6% in 2011-12 (Australian Bureau of Statistics, 2006, 2012). One study summated the four anxiety specific items from the K10, used in the 1997 and 2007 National Surveys of Mental Health and Wellbeing (NSMHW), and found that there was an increase in the level of anxiety from 1997 to 2007 in the general population (Reavley, Jorm, Cvetkovski, & MacKinnon, 2011). Furthermore, when comparing the NSMHW for 1997 and 2007, there was an increase over time in the rate of DSM-diagnosed anxiety disorders from 9.7 to 14.4% (Slade, Johnston, Oakley Browne, Andrews, & Whiteford, 2009). However, the authors note that this could be due in part to the more liberal diagnostic criteria for anxiety disorders in the latter survey (Slade et al., 2009). In the present study it was an increase in anxiety problems from 15.3% in 2006 to 25.6% in 2012 which resulted in the overall increase in mental health problems. The balance of evidence suggests that a genuine increase in anxiety in IDUs over time is possible.

Finally, it is also possible that the Better Access reform has resulted in reduced service use by IDUs. This would lead to an increased number of people reporting mental health problems as new incident cases of psychiatric morbidity join the cohort of chronically ill cases who have not been successfully

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treated. This finding is somewhat corroborated by the finding in the formal evaluation of Better Access that uptake of services was around 10% lower in the most socio-economically disadvantaged areas (Pirkis, Harris, et al., 2011), given that IDU is associated with socio-economic disadvantage (Boardman et al., 2001; Friedman et al., 2004; Nandi et al., 2010; Ompad et al., 2012; Rhodes et al., 2003; Topp et al., 2012; Williams & Latkin, 2007). However, the greatest proportional improvements in uptake following the introduction of Better Access were amongst those in the most socio-economically disadvantaged areas (Pirkis, Harris, et al., 2011). Another important factor associated with socio-economic status is the role of private health insurance. According to Jorm (2012), while Medicare aims to increase health equality, the various Australian governments have attempted to encourage uptake of private health insurance by requiring co-payments over and above Medicare rebates which favours those of higher socio-economic status. However, a recent Australian study found that in people with mental health problems, there was no difference in access to psychologist or psychiatrist services between those with and without private health insurance (Leach, Butterworth, & Whiteford, 2012). Unfortunately this study did not have access to data regarding the private health insurance of participants so this was not open to analysis.

Although the decrease in service use is of concern, it should be noted that the rates of uptake still remain higher than the most recent service use rate measurements (34.9% in 2007; Burgess et al., 2009) and estimates (46.1% in 2009-10; Pirkis, Harris, et al., 2011) in the general population. However, given

the high K10 scores found in those not self-reporting a recent mental health problem, it is likely that the rates of self-reported mental health problems are an underestimate. Thus, the rates of help-seeking are likely to be inflated as those who seek help are more likely to receive a diagnosis which they can then self-report. By adding 2012 respondents who had a K10 score exceeding the cut-off to those individuals who self-reported a mental health problem but did not seek help, the overall service use rate fell from 58.4 to 45.5%. Notably, this rate is equivalent to estimates of the 2009-10 rate of service use in the general population (Pirkis, Harris, et al., 2011). This suggests that the general community had more room for improvement than IDUs to begin with. Another encouraging sign is the increased proportional use of specialist mental health in the form of psychologists by 2012, who are specifically trained in the treatment of mental health problems. This is also consistent with the shift which has occurred in the general community (Harrison, Britt, & Charles, 2012; Pirkis, Harris, et al., 2011).

5.6.1. Limitations

This study is limited by its reliance on self-report data. However, the veracity of these data were supported through association with scores on the standardised K10 instrument which has been validated in IDUs (Hides et al., 2007). A second limitation is the non-random recruitment of subjects through convenience sampling methods and it is unknown to what degree the IDRS samples are representative of the overall IDU community - particularly those who do not regularly inject and who live in rural areas. This is mitigated to an

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extent by the large sample size and national recruitment. It is possible that IDUs living in less urbanised areas would be at an even greater disadvantage due to having limited access to services (Pirkis, Harris, et al., 2011).

5.6.2. Conclusions

This data showed that rates of self-reported mental health problems increased in regular IDUs from 2006 to 2012 while rates of service access decreased. It is difficult to identify a single cause of these findings given the wide scale mental health reform of Better Access taking place in the context of ongoing public awareness campaigns for mental health issues. The increases in self-reported mental health problem rates are likely due to improvements in mental health literacy and reductions in stigma, although genuine, albeit modest, increases in anxiety are possible. An expanding number of people willing to report problems but stability in the inclination to access services would explain the comparative drop in service use over time. The best-case-scenario of stability in service use rates over time could be seen as a failure of reforms like Better Access and public awareness initiatives to increase access. However, it is evident that IDUs still demonstrate equivalent, if not greater, access to services in comparison to the general population, and had less room to improve prior to the introduction of Better Access. Moreover, reassurance can be drawn from the increases in access to specialist mental health services such as psychologists, which was an important aim of Better Access.

As Jorm argued (2011, p. 700), it is extremely difficult to conduct a methodologically 'pure' evaluation of such broad interventions and "we have to make the most of what evidence is available, however imperfect." This study serves as an important first step in exploring the influence of major changes in mental health policy and public awareness campaigns in Australia on IDUs who constitute a sentinel sub-population in the context of mental health policy and practice. The importance of improved population monitoring of mental health to evaluate the effect of such reforms has been emphasised previously (Hickie, Rosenberg, & Davenport, 2011; Jorm, 2011). This study highlights the need for similar wide scale monitoring in IDUs, and indeed any other disadvantaged groups.

5.7. Addendum

While this thesis is focussed on the CHC population, the preceding sections of chapter 5 contained material published more generally on IDUs. Although approximately half of this sample of IDUs reported having CHC, separate analyses were performed only in those IDUs who reported having CHC. As the results of these analyses were virtually identical to those of the total IDU sample, they were not included in the publication in order for the manuscript to be accessible and relevant to a wider audience. However, they are included below for the purposes of this thesis.

Trends in self-reported mental health problems and service use rates were analysed for those who reported having CHC in the same manner as for the total IDU sample, as reported in chapter 5.4.6. Similar to the total sample, there was an increase in the rate of overall mental health problems as well as anxiety problems specifically from 2006 to 2012 (Table 20). However, in CHC+ IDUs there was also an increase in the rate of mood problems.

Table 20

CHC+ IDUs: Self-reported rates of six-month mental health problems for the 2006 vs. 2012 cohort

Problem type	n (%)		x^2	RR (95% CI)$	p
	2006 (N=495)	2012 (N=411)			
Any mental health problem	193 (39.0)	188 (45.7)	4.20	1.17 (1.01 - 1.37)	0.040
Mood problems	148 (29.9)	155 (37.7)	6.16	1.26 (1.05 - 1.52)	0.013
Anxiety problems	81 (16.4)	110 (26.8)	14.60	1.64 (1.27 - 2.11)	<0.001
Psychotic problems	40 (8.1)	35 (8.5)	0.06	1.05 (0.68 - 1.63)	0.813
Personality problems	7 (1.4)	8 (1.9)	0.39	1.38 (0.50 - 3.76)	0.532
Other mental health problems	13 (2.6)	12 (2.9)	0.07	1.11 (0.51 - 2.41)	0.788

$ Risk ratios with 95% confidence intervals using the 2006 cohort as the reference category

Table 21

CHC+ IDUs: Self-reported rates of six-month mental health service use in those with a self-reported mental health problem for 2006 vs. 2012 cohort

| Service type | n (%) | | X^2 | RR (95% CI)$ | p |
	2006 (N=192)	2012 (N=188)			
Any mental health professional	140 (72.9)	110 (58.5)	8.76	0.80 (0.69 - 0.93)	0.003
General practitioner	87 (45.3)	68 (36.2)	3.29	0.80 (0.62 - 1.02)	0.070
Psychiatrist	35 (18.2)	36 (19.1)	0.05	1.05 (0.69 - 1.60)	0.818
Psychologist	24 (12.5)	28 (14.9)	0.46	1.19 (0.72 - 1.98)	0.497
Counsellor	31 (16.1)	14 (7.4)	6.89	0.46 (0.25 - 0.84)	0.009
Community health nurse	5 (2.6)	3 (1.6)	%	0.61 (0.15 - 2.53)	0.724
Mental health nurse	8 (4.2)	6 (3.2)	0.26	0.77 (0.27 - 2.17)	0.614
Hospital emergency department	5 (2.6)	7 (3.7)	0.39	1.43 (0.46 - 4.43)	0.533
Psychiatric ward	10 (5.2)	4 (2.1)	2.54	0.41 (0.13 - 1.28)	0.111
Social worker	10 (5.2)	8 (4.3)	0.19	0.82 (0.33 - 2.03)	0.662
Other	9 (4.7)	5 (2.7)	1.10	0.58 (0.19 - 1.66)	0.294

$ Risk ratios with 95% confidence intervals using the 2006 cohort as the reference category.
% as ≥ 1 cells had an expected count less than 5, Fisher's Exact Test was used.

Amongst those with a self-reported mental health problem, there was a decrease in service use rates from 2006 to 2012 and a decrease in counsellor uptake rates, while GP uptake rates were not statistically different, due to the smaller sample size and decreased power (Table 21). Amongst service users, there were no significant changes in the uptake of specific services by 2012, although there were similar trends towards higher psychologist use and lower counsellor use of a similar magnitude which failed to reach significance, again due to power constraints (Table 22).

Table 22

CHC+ IDUs: Self-reported rates of six-month mental health service use in those

who had sought help for 2006 vs. 2012 cohort

Service type	n (%)		χ^2	RR (95% CI)$	p
	2006 (*N*=140)	2012 (*N*=110)			
General practitioner	87 (62.1)	68 (61.8)	0.00	0.99 (0.82 - 1.21)	0.958
Psychiatrist	35 (25.0)	36 (32.7)	1.81	1.31 (0.88 - 1.94)	0.179
Psychologist	24 (17.1)	28 (25.5)	2.58	1.48 (0.91 - 2.41)	0.108
Counsellor	31 (22.1)	14 (12.7)	3.70	0.57 (0.32 - 1.03)	0.054
Community health nurse	5 (3.6)	3 (2.7)	%	0.76 (0.19 - 3.13)	1.000
Mental health nurse	8 (5.7)	6 (5.5)	0.01	0.95 (0.34 - 2.67)	0.929
Hospital emergency department	5 (3.6)	7 (6.4)	1.05	1.78 (0.58 - 5.46)	0.305
Psychiatric ward	10 (7.1)	4 (3.6)	1.43	0.51 (0.16 - 1.58)	0.231
Social worker	10 (7.1)	8 (7.3)	0.00	1.02 (0.42 - 2.49)	0.969
Other	9 (6.4)	5 (4.5)	0.41	0.71 (0.24 - 2.05)	0.520

$ Risk ratios with 95% confidence intervals using the 2006 cohort as the reference category
% as ≥ 1 cells had an expected count less than 5, Fisher's Exact Test was used.

In summary, despite the potential for worse outcomes in those with CHC due to the added stigma and psychosocial burden of this disease on top of any burden associated with IDU, there was little evidence of differential trends in this group. This re-analysis performed only on IDUs with CHC found the same trends of similar or even greater magnitudes, some of which failed to reach statistical significance due to the reduced power when effectively halving the sample size. Thus, the discussion of the results of this study in chapter 7 apply equally to IDUs with and without CHC.

CHAPTER VI: STUDY FOUR – DEVELOPMENT OF C-UP PROTOCOL

NB: The treatment booklet and treatment protocol described in this chapter are presented, respectively, in Appendix 1 and 2.

6.1. Statement of authorship

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Name of Principal Author (Candidate): Benjamin J.R. Stewart

Contribution to the Paper: Developed the protocol, consulted key stakeholders to obtain feedback, and wrote the manuscript.

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Contribution to the Paper: Supervised the development of the work and helped evaluate and edit the manuscript.

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6.2. Abstract

Depression and anxiety are highly prevalent in, and detrimental to, people with chronic hepatitis C (CHC). This paper aimed to detail the rationale for, and development of, a CHC-specific treatment protocol. Researchers have observed that mood and anxiety disorders share many commonalities, that multiple disorders frequently co-occur, and that treatment of single disorders lead to improvements in co-morbid conditions. Thus, transdiagnostic treatment may be more parsimonious and effective than traditional disorder-specific therapy. Notably, co-occurring depression and anxiety is highly prevalent in people with CHC. Clinical trials with transdiagnostic treatment have shown promising results, and have been largely based on cognitive behaviour therapy (CBT), which has proven to be effective in the general psychological literature and in populations similar to those living with CHC. Thus, a transdiagnostic, CBT-based protocol was developed, entitled: "C-UP – A Unified Program for people with hepatitis C to manage depression and anxiety." The components of C-UP include psychoeducation, acceptance of distressing emotions, cognitive restructuring, behavioural activation, graded exposure, and relapse prevention. C-UP can be delivered through individual psychotherapy with a mental health professional and may also be self-administered. Preliminary informal feedback from clinical psychologists, CHC workers, and people living with CHC was overwhelmingly positive and helped refine the final protocol. Future research

should more systematically and rigorously examine C-UP to determine its acceptability and potential efficacy.

6.3. Background

People living with chronic hepatitis C (CHC) suffer from high rates of psychiatric morbidity (el-Serag et al., 2002; Stewart, Mikocka-Walus, Morgan, et al., 2012) which is associated with decreased quality of life (Bonkovsky et al., 2007; Gutteling et al., 2010; Häuser et al., 2004), increased fatigue and functional disability (Dwight et al., 2000), exacerbated perception of physical pain (Morasco et al., 2010), and poorer anti-viral treatment outcomes (Leutscher et al., 2010; Martín-Santos et al., 2008). As the treatment of CHC with interferon (IFN) is known to induce symptoms of depression and anxiety (Sulkowski et al., 2011), much of the relevant research to date in this population has focussed on the treatment or prevention of IFN-induced depression.

Open label treatment of incident IFN-induced depression with anti-depressants has been shown to be effective (Hauser et al., 2002; Kraus et al., 2002), as has the prophylactic use of anti-depressants to prevent the development of depression during anti-viral treatment (Jiang et al., 2013). However, whilst pharmacotherapy is helpful for IFN-induced depression, there is virtually no evidence supporting it being beneficial for IFN-induced anxiety (Maddock et al., 2004). Research for the treatment of psychiatric symptoms not induced by IFN treatment is also sparse, although two open-label trials of anti-

depressants for CHC patients with major depression reported a significant reduction in depressive symptoms and an increase in quality of life (Gleason et al., 2002; Gleason et al., 2005).

There are a number of disadvantages to recommending a reliance on pharmacotherapy for managing mental health issues in people with CHC, including side effects and drug interactions, variable effect and tolerability due to pre-existing liver damage, the period of vulnerability before drugs take effect, and the need to sustain pharmacotherapy after anti-viral treatment has ceased to prevent relapse (Asnis & De La Garza, 2006; Neri et al., 2010; Sockalingam et al., 2013). It is arguable then that psychotherapy may be a useful alternative treatment for psychiatric co-morbidity. Moreover, it may be beneficial to combine both pharmacotherapy and psychotherapy, which has been shown to be effective in treating depression in people with chronic diseases (Rizzo et al., 2011) and in the treatment of panic disorder and, albeit with limited evidence to date, social anxiety (Bandelow et al., 2007).

However, there are even less data evaluating the use of psychotherapy in people with CHC. To date, just one randomised controlled trial (RCT) was conducted with 211 Italian patients undergoing anti-viral treatment (Neri et al., 2010). The first group was given cognitive behavioural therapy and interpersonal psychotherapy once a month over the 48 week treatment period, while the second was monitored but did not receive therapy. The psychotherapy provided was not based on a strict protocol but was based on principles of cognitive behavioural therapy and interpersonal therapy and was designed and

structured for each individual patient based on their respective context and needs. The psychotherapy group had a lower rate of adverse psychiatric events and were also less likely to require pharmacotherapeutic intervention to control psychiatric symptoms. Clearly more research is required to determine whether psychotherapy is efficacious in this population.

This paper details the rationale for, and development of, a psychotherapeutic treatment protocol to be used in people living with CHC, either through individual guided psychotherapy or in a self-directed manner. This protocol, titled "C-UP: A Unified Program for people with hepatitis C to manage depression and anxiety" is based on a transdiagnostic approach to cognitive behavioural therapy adapted to fit with the experiences of those living with CHC. For the purposes of this paper, the term transdiagnostic will be used to refer to a method of conceptualising and, subsequently, diagnosing and treating psychiatric symptoms which may encompass multiple mood and/or anxiety disorders, in contrast to the conventional approach of conceptualising symptoms in terms of distinct disorders. C-UP aims to simultaneously treat symptoms of depression and anxiety, thereby increasing quality of life and overall psychological well-being.

6.4. Cognitive behavioural therapy

The main model which C-UP was based on was cognitive therapy (Beck, 1976), mainly known now as cognitive behavioural therapy (CBT; Beck &

Dozois, 2011). According to cognitive theory on which CBT is based (Beck & Dozois, 2011), psychopathology results from dysfunctional beliefs, attitudes, and memories which operate in concert with the responses of the four systems of: Cognition (perception and interpretation of internal/external stimuli); Emotion (feelings such as anxiety, anger, sadness); Motivation (impulse to respond to cognitions or emotions); and Behaviour (the actual response or lack thereof). These systems normally operate together to fulfil various goals, such as increasing pleasure and decreasing pain, but may become highly activated by 'false alarms' (Beck & Dozois, 2011). For example, in panic disorder the cognitive system is over-activated by catastrophic misinterpretations of bodily sensations such as increased heart rate indicating an imminent heart attack.

CBT is a collaborative, structured, and time-limited treatment designed to help patients adopt more functional and adaptive behavioural and cognitive responses to their mental and environmental experiences (Beck & Dozois, 2011). Cognitive responses (including thoughts, attitudes, and beliefs) are examined objectively and critically in a rigorous manner to see whether they are accurate and adaptive (Beck & Dozois, 2011). The emphasis on this process is to test alternative explanations and shift an individual's cognitions towards ones that are adaptive and evidence-based (Beck & Dozois, 2011). This process is achieved through a number of tasks, including Socratic questioning and thought records (Beck & Dozois, 2011). Activities engaged in, other actions, reactions, or even the lack of these behaviours are similarly examined to see if and how they are maintaining problematic emotions and overall patterns of behaviour

(Beck & Dozois, 2011). In so doing, individuals are encouraged to engage in activities and styles of acting and reacting which promote positive and adaptive emotions and/or patterns of behaviour (Beck & Dozois, 2011). Some of the targets of behavioural strategies are to habituate to feared stimuli (achieved through graded exposure to that stimuli), to promote feelings of pleasure or mastery and increase activity (achieved through activity scheduling), and to increase relaxation (breathing retraining and progressive muscle relaxation; Beck & Dozois, 2011). Critically, cognitive and behavioural change can occur simultaneously, such as the learning and change in beliefs and attitudes that can happen through a behavioural experiment which may facilitate habituation to a feared stimulus as well.

CBT was chosen as the model for C-UP for two key reasons. Firstly, it has an extremely robust evidence base, with a recent review of 16 meta-analyses concluding that CBT is efficacious in the treatment of a wide range of psychiatric disorders and other mental health problems, particularly unipolar depression, generalised anxiety disorder, panic disorder, social phobia, post-traumatic stress disorder, and childhood depression and anxiety (Butler et al., 2006). Additional meta-analytic studies have shown that CBT is effective in treating populations similar to people with CHC, including depression in people with somatic disease (Beltman et al., 2010), depression, anxiety, anger, and stress in patients with the human immunodeficiency virus (Crepaz et al., 2008), and adults with alcohol or illicit drug use disorders (Magill & Ray, 2009). The sole trial to date performed with people with CHC demonstrated that combined

CBT and interpersonal psychotherapy was effective in preventing and diminishing IFN-induced psychiatric symptoms (Neri et al., 2010).

Secondly, CBT is the treatment recommended for use in the Medicare-funded Better Access scheme (The Australian Psychological Society, 2007), is endorsed in a review of the evidence-based psychological treatments of mental disorders by the Australian Psychological Society (2010), and is estimated to have been used in approximately 85% of the patients treated under this scheme (Pirkis, Ftanou, et al., 2011). Thus, if the C-UP resource is based on the treatment model that the majority of practitioners in Australia are using and are familiar with, it is likely to maximise its uptake and usefulness.

6.5. The rationale for a transdiagnostic conceptualisation of psychiatric morbidity

A growing body of literature has highlighted the commonalities shared by mood and anxiety disorders (Barlow et al., 2004; Wilamowska et al., 2010) which are collectively referred to as emotional disorders. Research has shown high rates of co-morbidity of emotional disorders, such that having a single anxiety or mood disorder is the exception to the rule of co-morbidity which is routinely seen in clinical practice (Brown, Campbell, Lehman, Grisham, & Mancill, 2001). This has also been demonstrated in Australian national research (Teesson, Slade, & Mills, 2009) and has also been observed in patients with CHC (Dwight et al., 2000; el-Serag et al., 2002; Golden et al., 2005; Navinés et

al., 2012; Rowan et al., 2005; Stewart, Mikocka-Walus, Morgan, et al., 2012). There are several factors which may be contributing to this co-morbidity. Firstly, there is considerable overlap in diagnostic criteria across emotional disorders (Barlow et al., 2004; Wilamowska et al., 2010). For example, generalised anxiety disorder and major depressive disorder share symptoms of fatigue, psychomotor agitation/restlessness, and impairments in sleep and concentration under their classification in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5; American Psychiatric Association, 2013).

Secondly, any given disorder in isolation may constitute a risk factor for developing a subsequent co-morbid disorder and vice versa (Krueger & Markon, 2006; Middeldorp, Cath, Van Dyck, & Boomsma, 2005). For example, an individual with social anxiety disorder may, through social withdrawal, have less opportunity for pleasure and other positively reinforcing experiences, leading to depression. Alternatively, an individual with depression may reduce their engagement in social activity, leading to deterioration of social skills and/or lower confidence in social situations which may progress to social anxiety over time.

Thirdly, the variety of emotional disorders which commonly co-occur in clinical practice may reflect phenotypic variations of a so-called singular, broader general neurotic syndrome or negative affect syndrome (Barlow et al., 2004; Moses & Barlow, 2006; Wilamowska et al., 2010). Support for an underlying syndrome comes from current conceptual models (Barlow, 2000)

and behavioural genetic research in twin and family studies (Hettema, Prescott, Myers, Neale, & Kendler, 2005; Kendler, Prescott, Myers, & Neale, 2003; Middeldorp et al., 2005; Tambs et al., 2009) which posit three shared areas of vulnerability across all emotional disorders, including a genetic diathesis, unique environmental diathesis (i.e. individual experiences which pre-dispose towards multiple disorders), and a shared environmental diathesis (i.e. non-specific environmental factors shared by the family which may pre-dispose towards multiple disorders).

In addition, factor analytic research has demonstrated that the majority of the co-variance in emotional disorders can be accounted for by three latent factors; particularly neuroticism/negative affect, but also extraversion/positive affect and autonomic arousal (Brown, Chorpita, & Barlow, 1998; Mineka, Watson, & Clark, 1998). This concords with the tripartite model of emotional disorders (Clark & Watson, 1991). In this context, there is an increase in negative affect experienced across all emotional disorders, a suppression of positive affect in depression/social phobia and increase in bipolar/cyclothymic disorder, and a suppression of autonomic arousal in generalised anxiety disorder and increase in autonomic arousal in panic disorder/agoraphobia (Brown et al., 1998; Wilamowska et al., 2010).

Neuroscientific research has also shown that similar neural networks are implicated across anxiety and mood disorders, particularly involving over activation of the amygdala (Drevets, 2003; Etkin & Wager, 2007; Shin & Liberzon, 2010; Siegle, Thompson, Carter, Steinhauer, & Thase, 2007).

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Interestingly, increased amygdala activation is also associated with neuroticism (Haas, Omura, Constable, & Canli, 2007; Keightley et al., 2003) and both the presence of trait neuroticism and increased amygdala activation are associated with a polymorphism in the promoter region in the serotonin transporter gene (Caspi et al., 2003; Hariri et al., 2002; Lesch et al., 1996; Pezawas et al., 2005). In addition, similar pathological processes seem to be involved across emotional disorders (Aldao & Nolen-Hoeksema, 2010; Barlow et al., 2004; Mansell, Harvey, Watkins, & Shafran, 2009; Moses & Barlow, 2006), including but not limited to maladaptive coping mechanisms (i.e. behavioural, cognitive, and emotional avoidance) and cognitive appraisals (i.e. overestimating probability and effect of negative events occurring). Studies have also shown that treatment of single disorders leads to clinical improvement in other co-morbid anxiety and mood disorders which were not the focus of clinical attention (Borkovec, Abel, & Newman, 1995; Brown, Antony, & Barlow, 1995; Craske et al., 2007; Emmrich et al., 2012; Newman, Przeworski, Fisher, & Borkovec, 2010; Teng et al., 2013; Tsao, Lewin, & Craske, 1998; Tsao, Mystkowski, Zucker, & Craske, 2002, 2005). This finding has been replicated in naturalistic samples (Davis, Barlow, & Smith, 2010) and in the group therapy setting (Norton, Hayes, & Hope, 2004).

However, the possibility remains that mood and anxiety disorders are distinct, unique disorders which nonetheless share etiological risk factors as well as pathological processes and demonstrate generalised response to therapy focussing on a singular disorder, potentially due to treatments targeting

these shared underlying processes. Irrespective of whether emotional disorders are manifestations of a general neurotic syndrome or distinct disorders which share the aforementioned commonalities, an argument can be made for a transdiagnostic treatment approach which targets the underlying mechanisms which are shared across these clinical presentations (Barlow et al., 2004; Wilamowska et al., 2010).

Having a single transdiagnostic protocol to treat multiple emotional symptoms and disorders may be a more parsimonious and efficient way of delivering evidence-based treatment and may lead to increased and longer-lasting treatment response for patients (Barlow et al., 2004; Wilamowska et al., 2010). The therapeutic potential for transdiagnostic treatment of emotional disorders specifically for people living with CHC is readily apparent when one considers the high rates of co-morbidity between mood and anxiety disorders (Dwight et al., 2000; el-Serag et al., 2002; Golden et al., 2005; Navinés et al., 2012; Rowan et al., 2005; Stewart, Mikocka-Walus, Morgan, et al., 2012). Moreover, the treatment for CHC, involving IFN, induces symptoms of both depression and anxiety (Loftis et al., 2006; Sulkowski et al., 2011).

6.6. Efficacy of transdiagnostic treatments

In recent years, there have been a number of trials conducted in the area of transdiagnostic CBT. In a recent RCT (Farchione et al., 2012), the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP; Ellard,

Fairholme, Boisseau, Farchione, & Barlow, 2010; Wilamowska et al., 2010) was compared to a wait-list control group in 37 patients with principal diagnoses of generalised anxiety disorder, social anxiety disorder, obsessive compulsive disorder, panic disorder with agoraphobia, anxiety disorder not otherwise specified, post-traumatic stress disorder. On average, patients had at least two disorders and 12 patients had co-occurring depressive disorders (Farchione et al., 2012). Unlike the wait-list control group, the UP participants demonstrated significant improvements on measures of clinical severity, anxiety and depression, positive/negative affect, and overall functioning which were maintained over the six month follow-up period (Farchione et al., 2012).

Another randomised trial compared a 12 week transdiagnostic cognitive behavioural therapy group program with 12 weeks of disorder-specific group CBT for 46 patients with social anxiety disorder, generalised anxiety disorder, and panic disorder (Norton & Barrera, 2012). The results indicated equivalence in treatment credibility and efficacy (Norton & Barrera, 2012). A third randomised trial compared 12 sessions of group transdiagnostic CBT with 12 sessions of a comprehensive group relaxation program in 87 patients with principal diagnoses of panic disorder with/without agoraphobia, social anxiety disorder, generalised anxiety disorder, anxiety disorder not otherwise specified, obsessive compulsive disorder, and specific phobia (Norton, 2012). Sixty per cent of the sample had one or more co-morbid diagnoses, including depressive disorders or the above anxiety disorders, in addition to post-traumatic stress disorder, substance abuse, body dysmorphic disorder, adjustment disorder, and

trichotillomania (Norton, 2012). Results showed equivalence in treatment

credibility and efficacy between the transdiagnostic CBT and relaxation therapy

groups, but a lower dropout rate in the CBT group (Norton, 2012). Moreover,

the transdiagnostic CBT was equally effective irrespective of what principal or

co-morbid diagnoses the patients presented with (Norton, 2012).

Several RCTs of transdiagnostic CBT provided via the internet have also

been conducted. One RCT with 131 people with generalised anxiety disorder,

social phobia, and/or panic disorder were randomised to receive an eight

lesson, 10 week program of online transdiagnostic CBT (provided with the

support of either a coach or clinician) or to a wait-list control group (Johnston,

Titov, Andrews, Spence, & Dear, 2011). They found that those receiving the

treatment exhibited significantly lower disorder-specific symptoms and disability

ratings, with outcomes being generally equivalent between those receiving

support from a coach and those receiving support from a clinician (Johnston et

al., 2011). In another RCT, 86 participants meeting criteria for two or more

disorders (including generalised anxiety disorder, panic disorder, panic disorder,

and/or social phobia) were randomised to a 6 lesson, 8 week online

transdiagnostic CBT with weekly email or phone contact with a clinical

psychologist or a wait-list control group (Titov, Andrews, Johnston, Robinson, &

Spence, 2010). The active therapy group demonstrated significantly reduced

symptoms of anxiety across the disorders investigated at 3 month follow-up

(Titov et al., 2010). Another RCT randomised 77 participants to receive an 8

lesson, 10 week program of online transdiagnostic CBT or a wait-list control

group (Titov et al., 2011). The treatment group, 86% of whom met criteria for major depression in addition to an anxiety disorder, exhibited significantly decreased anxiety and depression symptoms (Titov et al., 2011).

Taken overall then, while the evidence base for transdiagnostic treatment is still growing, the results to date are very promising. No research to date has investigated transdiagnostic CBT in people with CHC. This paper documents our contribution to that effort via the design of a transdiagnostic CBT protocol for use with people with CHC and co-morbid depression and/or anxiety. A detailed description of the design of this protocol, titled "C-UP: A Unified Program for people with hepatitis C to manage depression and anxiety," is provided below.

6.7. Format of C-UP

Prior research has suggested that individual psychotherapy is the most acceptable treatment modality for people with CHC, with bibliotherapy (self-directed books or booklets) also being highly endorsed (Stewart et al., 2013). Acceptability is important as it is associated with higher uptake (Dwight-Johnson et al., 2001; Jorm et al., 2000), lower dropout, and improved outcomes for a given treatment (Swift & Callahan, 2009; Swift et al., 2011). However, considerations of efficacy, cost, waiting times, and access in rural and remote areas are also critical. In order to balance these factors, the C-UP was designed

as a brief five lesson, six week program, manualised in a booklet which could be used under the guidance of a therapist or in a self-directed manner.

6.8. The C-UP components

C-UP contains five components, each involving key concepts and skills to be sequentially learnt and added to the participant's psychological repertoire over the course of the program. These components include: (1) Psychoeducation; (2) Emotional acceptance; (3) Cognitive restructuring; (4) Behavioural activation and graded exposure; and (5) Relapse prevention. A detailed description of these components is provided below.

6.8.1. Part 1: Psychoeducation

Goldman (1988, p. 667) defined psychoeducation as "education or training of a person with a psychiatric disorder in subject areas that serve the goals of treatment and rehabilitation, for example, enhancing the person's acceptance of his illness, promoting active cooperation with treatment and rehabilitation, and strengthening the coping skills that compensate for deficiencies caused by the disorder." A recent meta-analysis of four studies found that psychoeducation had a small but statistically significant effect on reducing symptoms of depression and psychological distress (Donker, Griffiths, Cuijpers, & Christensen, 2009). A systematic review of 15 studies found that psychoeducation was associated with an improved clinical course, treatment adherence, and psychosocial functioning in depressed patients (Tursi, Baes,

Camacho, Tofoli, & Juruena, 2013). In a recent multi-centre German trial (Reimer et al., 2013), it was found that providing psychoeducation to CHC patients with genotype 1 and 4 increased their treatment completion and SVR rates

This section of the protocol aims to provide sufficient knowledge to facilitate patient understanding and application of later concepts and techniques, in addition to normalising mental health problems and developing rapport (when provided with therapist contact). The knowledge provided in this psychoeducation component includes what C-UP will involve, a brief overview of emotional disorders (including their epidemiology and clinical characteristics) as well as a cognitive behavioural conceptualisation of these disorders (i.e. the inter-directional relationships between cognitions, emotions, physical sensations, and behaviours within a distressing situation). Fictional yet realistic case stories are used to illustrate the concepts at play in people living with CHC and normalise what may be common shared experiences for C-UP participants. Activities for participants to complete include exploring their goals for treatment, defining what depression and anxiety mean to them, noting which symptoms they experience, and identifying what they believe causes their depression and anxiety, including aspects of their CHC infection. The main activity is a diary which patients use to self-monitor and record their cognitions, emotions, physical sensations, and behaviours in the context of situations they encounter on a daily basis.

6.8.2. Part 2: Accepting difficult emotions

This section of the protocol aims to teach patients about the disadvantages (e.g. suffering) and, mainly, the advantages of negative emotions such as sadness and anxiety (e.g. signalling need for problem solving efforts and marshalling others to support the individual). This section also focusses on examining how avoidance and judgement of distressing emotions further exacerbates such emotions, impairs functioning, and maintains psychopathology (Plumb, Orsillo, & Luterek, 2004), as opposed to the more adaptive strategy of approach and acceptance (Campbell-Sills, Barlow, Brown, & Hofmann, 2006a, 2006b; Levitt, Brown, Orsillo, & Barlow, 2004). In so doing, this section aims to foster a willingness in patients to develop a different attitude towards their distressing emotions, switching from avoidance and judgement of emotions to approach and acceptance. Finally, patients are taught how to practice acceptance of distressing emotions and are asked to record their experiences with practicing non-judgemental acceptance of distressing emotions. Other activities include writing about a time when a negative emotion had a positive effect in their life and listing emotions they struggle with or try to avoid.

6.8.3. Part 3: Cognitive restructuring

Cognitive restructuring is a core component of CBT interventions for mood and anxiety disorders with an ample evidence base supporting it (Beck & Dozois, 2011; Butler et al., 2006). This section aims to give patients an understanding of how cognitive restructuring can help them engage in adaptive,

evidence-based thinking which can subsequently promote a healthier emotional response. Patients will ideally become more aware of their thoughts and better able to assess the validity of their thoughts, identify thinking errors, and generate alternative thoughts. Patients are first reminded about how negative cognitions can maintain distressing emotions and maladaptive behaviours (e.g. in the 'vicious cycle' where depressed mood and poor motivation lead to thoughts centred on the hopelessness of their situation and behavioural withdrawal which maintains depressed mood and low desire for activity). Participants are then taught to identify a 'hot thought' which is the most distressing identifiable cognition in a given sequence of automatic thoughts. Participants are then taught about common thinking errors which occur in automatic thoughts, including magnifying, minimising, taking the blame, and jumping to conclusions. Examples are given using scenarios relevant to those living with CHC. Patients are then taught to evaluate the accuracy of thoughts by assessing evidence for them and subsequently generating alternative thoughts based on the balance of available evidence and logic. The main activity for this section involves daily monitoring of thoughts when experiencing distress, identification of errors in thinking, and generation of alternative thoughts to be evaluated.

6.8.4. Part 4: Behavioural change

This section aims to give patients an understanding of how modifications to their routines and behavioural responses in everyday life can improve their psychological well-being through the use of behavioural activation and graded

exposure, key components in CBT interventions for mood and anxiety disorders (Beck & Dozois, 2011; Butler et al., 2006). The first part of this section focusses on graded exposure, where the individual is encouraged to face their fears in a gradual but progressive manner, which has been demonstrated to be effective even as a standalone treatment for many anxiety disorders (DeRubeis & Crits-Christoph, 1998; Norton & Price, 2007). An explanation is given of how behavioural avoidance can decrease distressing emotions in the short-term but only serves to maintain them in the long-term. Patients are subsequently encouraged to approach distressing situations in order to habituate to the anxiety experienced, stimulate change in beliefs and attitudes about previously avoided situations, and ultimately diminish the frequency and intensity of distressing emotions. However, it is emphasised that an elimination of anxiety is not the goal of the strategy and patients are reminded that distressing emotions are inevitable and serve important purposes. Patients then identify a range of activities or situations previously avoided which they can gradually expose themselves to in order of increasing difficulty, schedule times to engage in these activities, and record their experiences.

The second half of this section focusses on behavioural activation. Behavioural activation is a technique which aims to re-engage patients with positively reinforcing experiences and emotions, typically pleasure/enjoyment and achievement/mastery, and reduce avoidance and experiences of negative reinforcement (Soucy Chartier & Provencher, 2013). Behavioural activation has also been found in meta-analytic research to be efficacious in treating

depression in its own right (Mazzucchelli, Kane, & Rees, 2009). Behavioural activation is also promising as a low-intensity intervention, in that it requires little therapist input and could be provided in a self-help format (Soucy Chartier & Provencher, 2013). This section begins by educating participants about how depressed mood and anhedonia, poor motivation and inactivity and withdrawal maintain each other in a perpetuating cycle. Participants are encouraged to break this 'vicious cycle' by scheduling activities which promote positive feelings of achievement/mastery and enjoyment/pleasure. This schedule is again created in a hierarchy of increasing difficulty yet opportunity for positive feelings over time. Participants then follow this schedule and record their experiences.

6.8.5. Part 5: Relapse prevention

The final section of C-UP focusses on relapse prevention, a core component of most CBT packages (Beck & Dozois, 2011). The aim of this section is to summarise the content covered in the program, consolidate the participants' knowledge of concepts and techniques learnt, and to develop a plan to maintain and build on any improvements made within the program. Firstly, the key concepts are reviewed. The participant is then instructed to contemplate what the signs are when they are in the following stages of wellness: currently psychologically well; becoming unwell; and psychologically unwell. The participant is then asked to brainstorm various strategies to be used at these stages of wellness. Hints are provided for both identifying signs of different wellness stages and planning strategies for maintaining well-ness and prevention or intervention when becoming unwell.

6.9. Preliminary feedback

Once the treatment booklet was developed, a number of key stakeholders were consulted to provide feedback on the protocol. It should be emphasised that this process was not undertaken as a rigorous scientific examination of the acceptability, and certainly not the efficacy, of the protocol. Rather, it was completed as a way of refining the development of C-UP and maximising the success of any future tests of its acceptability and efficacy. As such, the process was more informal and less structured and systematic. Firstly, workers from Hepatitis SA (a community based organisation which provides information and services to South Australians affected by CHC and other forms of viral hepatitis) and a CHC specific counsellor were consulted. Following this, Hepatitis SA workers provided the booklet to some of their peer support workers and community members who were living with CHC. The main aim of this consultation was to ensure the concepts covered and language used were comprehensible and the case stories and examples provided were relevant and appropriate for people living with CHC. The feedback provided was positive, with only minor changes suggested regarding simplification of some of the language used which were implemented.

In addition, two senior clinical psychologists were consulted to ensure that the booklet adequately covered the key therapeutic concepts chosen for C-UP (i.e. the psycho-education, emotional acceptance, cognitive restructuring, behavioural activation, graded exposure, and relapse prevention sections were

covered with sufficient accuracy and comprehensiveness to exert their intended clinical effects). This consultation also sought to ensure that the booklet in general would be comprehensible to participants given the format, length, and language used in the booklet. Both psychologists provided positive feedback on the booklet and only minor changes were suggested regarding the wording of some concepts and questions in the activities. This feedback was also implemented. Finally, the readability of the booklet was also tested. The C-UP booklet had Flesch-Kincaid Grade Level of 8.3, indicating that people with even basic literacy skills would be able to use this resource. Nonetheless, these literacy requirements may be exacerbated by the unique nature of the material covered in that understanding of the C-UP may rely also on "mental health literacy." As such, certain populations including those who are imprisoned, come from CALD backgrounds including Indigenous Australians, or have had interrupted education may find it difficult to self-administer the C-UP, This needs to be assessed in future research, but could potentially be addressed through the provision of more support by a mental health professional and less self-direction when completing C-UP. The final C-UP version can be found in Appendix 1, with a corresponding treatment guide in Appendix 2.

6.10 Summary and directions for future research

This paper has detailed the rationale for, and development of, a transdiagnostic CBT protocol for people living with CHC entitled C-UP. There

are well developed arguments in the broader psychological literature that the spectrum of mood and anxiety disorders exhibit more commonalities than differences. It follows, then, that the treatment of multiple co-morbid emotional disorders, which is typical in people with mental health disorders and in the CHC population, would be more parsimonious. C-UP opted for five key components central to CBT interventions to be provided in a brief individual psychotherapeutic program or in a self-directed manner using the booklet developed. These components include psychoeducation, acceptance of distressing emotions, cognitive restructuring, behavioural activation, graded exposure, and relapse prevention.

Preliminary feedback from key stakeholders including community members living with CHC, workers in the CHC sector, and clinical psychologists familiar with the therapeutic concepts was overwhelmingly positive. However, it is clear that more systematic and rigorous research is required to pilot this resource and gauge its acceptability and practical uptake amongst people living with CHC and, above all, to assess its efficacy in alleviating symptoms of depression and anxiety in people with CHC. An ideal first step in accomplishing these goals would be to run a pilot feasibility trial of the program, either in an individual psychotherapeutic context on in a self-directed manner using the booklet created. If participants of this trial found the program to be acceptable and showed a significant reduction in symptoms of depression and anxiety, a RCT would be appropriate to confirm the efficacy of C-UP in treating mood and anxiety disorders in people living with CHC.

CHAPTER VII: DISCUSSION

This chapter provides an overview and discussion of the key findings of this research. It also identifies the contribution it makes to new knowledge, considers some of its limitations, and suggests potential avenues for further research. The chapter concludes with recommendations for mental health policy and practice in order to improve the assessment and management of co-morbid depression and anxiety in people living with CHC.

7.1. Discussion of key findings and research limitations

This research program produced a number of important findings in the area of CHC and psychiatric co-morbidity. Study one assessed the acceptability of various psychological treatment options in people living with CHC and determined the factors associated with endorsement of a particular treatment modality. The most acceptable treatment mode was individual psychotherapy (endorsed by 83%), followed by bibliotherapy (61%), pharmacotherapy (56%), e-therapy (45%), and group psychotherapy (37%). The most prominent predictor of endorsement for a treatment type was satisfaction with previous use of that treatment. A major limitation of the first study was the failure to obtain data regarding the acceptability of psychotherapy types (e.g. CBT, interpersonal psychotherapy, and acceptance and commitment therapy) and different forms of pharmacotherapy (e.g. classes such as anti-depressants vs. anti-psychotics

and types of anti-depressants such as paroxetine vs. fluoxetine). These data were not obtained due to the difficulty of explaining these concepts with sufficient brevity to ensure response within a postal/online survey and having to rely on recall for separate episodes of treatment with different psycho- and pharmaco-therapies.

Study two investigated the trajectory of symptoms of depression and anxiety in CHC outpatients. The results indicated that the trajectory was poor for the majority of the patients investigated, with baseline rates of depression (33%) and anxiety (44%) increasing to 62% and 67% respectively over the 21 to 62 month study period. Just under a quarter of the sample exhibited sub-threshold symptoms across the study period, while nearly half demonstrated clinically significant depression or anxiety at both baseline and endpoint, and nearly one third of the sample were sub-threshold at baseline yet exceeded the cut-off by endpoint. A methodological limitation of this study was the need for converting endpoint scores on the DASS to HADS scores which were used at baseline. This was addressed by comparing the differences between the baseline HADS and endpoint DASS scores against British community norms for each measure. The results indicated that the disparity between endpoint scores and community norms on the DASS was markedly greater than that between baseline scores and community norms on the HADS.

Other limitations that could not be addressed in this study included the small and self-selected follow-up sample, potentially introducing sampling bias. While the results conflict with most research in other somatic disease

populations which have demonstrated stability or decline in symptoms over time, no prior research has explored this topic in people with CHC. It should be noted that, other than a slightly lower rate of previous anti-viral treatment in responders, there were no differences between the total sample from which baseline data was drawn and the participants who chose to respond to the survey providing endpoint data. Nevertheless, it is still uncertain whether the results in this sample would generalise to all people living with CHC, particularly those in the community not receiving medical treatment. An additional limitation was the variation in the length of follow-up between patients, the lack of controls, and the lack of data regarding potential intervening variables such as psychiatric treatment, medical treatment/changes, social/occupational changes, and other major life events/stressors.

Consequently, it is difficult to determine the factors contributing to the concerning trajectory of depression and anxiety observed, be it the presence of CHC, historical aggravating factors such as substance abuse and psychological trauma, a lack of social support or formal treatment, or, more likely, some combination of these influences. Interestingly, past research has found that the course of symptoms is worse in those who experience co-morbid depression and anxiety (Fichter et al., 2010; Richards, 2011). In a study of 395 CHC South Australian outpatients, half of those who experienced either depression or anxiety exhibited both conditions (Stewart, Mikocka-Walus, Morgan, et al., 2012). As noted in the discussion of study two, disregarding whether patients meet the criteria for a diagnosis, the level of co-morbidity of depression and

anxious symptomatology in the CHC outpatient population from which this sample was drawn (Stewart, Mikocka-Walus, Morgan, et al., 2012) was significantly higher than that in the general community (Crawford et al., 2001). Thus, it is difficult to conclusively state, based solely on the results of this study, that CHC patients experience a poorer trajectory of depression and anxiety than what has been found in the general population or in other somatically ill populations. Nonetheless, this comparatively worse trajectory is concerning and there are plausible mechanisms by which it can be explained.

Study three examined changes in mental health problems and service utilisation patterns in people with CHC over time, from 2006 to 2012 – a period which included the introduction of the Better Access reform as well as a gradual increase in mental health awareness campaigns designed to decrease stigmatisation and increase mental health literacy. A major finding of this study was that self-reported mental health problem rates rose from 38% in 2006 to 44% in 2012, mainly owing to a rise in anxiety rates from 15 to 26%. Simultaneously, there was a decrease in self-reported service utilisation rates, from 70% in 2006 to 58% in 2012. Despite this decline, there was a proportional increase in self-reported access to psychologists from 20 to 28%. These results persisted after controlling for socio-demographic and medical differences between the samples. Again, methodological limitations introduce complexity in interpreting these results. The results may reflect a real increase in mental health problems over time which has been demonstrated in national health surveys for the general Australian community (Australian Bureau of Statistics,

2006, 2012). In particular, the National Surveys of Mental Health and Wellbeing have shown a modest increase over time in anxiety symptoms (Reavley et al., 2011) and anxiety disorder rates (Slade et al., 2009) - although this latter finding may be influenced by changes in the interview schedule used in the 2007 survey.

It is also possible that the results of study three reflect a real decline in service utilisation over time, perhaps due to the socio-economic disadvantage associated with IDU (Boardman et al., 2001; Friedman et al., 2004; Nandi et al., 2010; Ompad et al., 2012; Rhodes et al., 2003; Topp et al., 2012; Williams & Latkin, 2007). While differences in socio-economic advantage between the 2006 and 2012 samples cannot account for the results, as the multivariate analysis controlled for any differences in the two samples, it is possible that the Better Access reform was less beneficial for people with socio-economic disadvantage such as IDUs. This could hypothetically occur through reduction in staffing for public mental health services (which do not charge patients) with the introduction of the Better Access initiative, as there are often co-payments above the Medicare reimbursement for accessing private psychologists under Better Access. Indeed, the formal evaluation of Better Access indicated that service uptake was 10% lower in the most socio-economically disadvantaged areas (Pirkis, Harris, et al., 2011). However, in contrast to this, the evaluation also reported that the biggest increase in uptake following the introduction of Better Access occurred in the areas of greatest socio-economic disadvantage

(Pirkis, Harris, et al., 2011) which is not unsurprising given this cohort would have a higher ceiling for growth in uptake.

As study three relied on self-report of mental health problems, the changes may also be influenced by other factors which affect self-reporting, such as changes in stigma and mental health literacy – particularly given the increase in public awareness campaigns driven by organisations such as Beyond Blue. However, the veracity of the self-report data was supported by the strong association observed between K10 scores and self-reporting a mental health problem in the 2012 sample. Another limitation of this study was the use of convenience sampling to recruit participants, which may limit the generalisability of the results to other IDUs, particularly those who may not inject regularly or who live outside urbanised areas. This is, however, mitigated to an extent by the large sample size and nation-wide recruitment. Regardless of the uncertain cause of the decline, it is clear that the rate of service utilisation, even after the decline, was equivalent, if not better, than that seen in the general Australian community. When the proportional increase in access to psychologists, who are specifically trained in the treatment of mental health problems, is also considered this is an encouraging sign for any efforts at intervening in the mental health treatment of IDUs, with or without CHC infection.

Study four detailed the development of a psychological treatment protocol specifically designed to transdiagnostically treat symptoms of depression and anxiety in people with CHC. This protocol was titled "C-UP: A Unified Program

for people with hepatitis C to manage depression and anxiety." C-UP was based on CBT due to its demonstrable efficacy in treating depression and anxiety (Butler et al., 2006), including in populations sharing characteristics with people living with CHC, such as those with somatic illnesses (Beltman et al., 2010) and people with human immunodeficiency virus (Crepaz et al., 2008). Transdiagnostic treatment was developed in response to a growing literature which suggests that mood and anxiety disorders are more similar than they are different – an approach which has the promise to treat co-morbid emotional disorders simultaneously by addressing common underlying therapeutic targets (Barlow et al., 2004; Wilamowska et al., 2010). This transdiagnostic approach was utilised in this program as a significant proportion of people with CHC experience symptoms of both depression and anxiety (Dwight et al., 2000; el-Serag et al., 2002; Golden et al., 2005; Navinés et al., 2012; Rowan et al., 2005; Stewart, Mikocka-Walus, Morgan, et al., 2012), and the side-effects of the anti-viral treatment for CHC include both depression and anxiety (Loftis et al., 2006; Sulkowski et al., 2011). The protocol is designed to be provided over a six week course of one-on-one psychotherapy or to be self-administered using the booklet developed. The five sections of C-UP cover psychoeducation, acceptance of distressing emotions, cognitive restructuring, behavioural activation and graded exposure, and relapse prevention.

Informal and preliminary feedback obtained from people living with CHC, service providers in the CHC sector, and clinical psychologists was overwhelmingly positive, with only minor changes suggested to the language

used to explain concepts in the booklet. However, this approach lacks the scientific rigour required to validate C-UP as a treatment which people with CHC find acceptable, and no data has been collected regarding the efficacy of this protocol. Although C-UP and its components were carefully researched and developed to maximise the acceptability and efficacy of the intervention, further research is required to test whether this was in fact achieved.

7.2. Strengths of the research and contributions to knowledge

People living with CHC are known to be a difficult population to access and engage in research. Past research has shown that many patients have experienced stigma from health professionals (Stewart, Mikocka-Walus, Harley, et al., 2012; Zickmund et al., 2003) and that communication difficulties between patients and physicians can exist, with 28% of patients in one study feeling their physician had poor communication skills (Zickmund, Hillis, Barnett, Ippolito, & LaBrecque, 2004). Clearly, researchers must bear some responsibility in seeking to engage people with CHC in an appropriate and sensitive way. Undoubtedly, the pervasiveness of stigma contributes to difficulties recruiting people with CHC (Paterson et al., 2007), as prospective participants may have fears of their infection becoming public knowledge following breaches in confidentiality. Moreover, as many people with CHC are also IDUs who can lead changeable lives and may also be reticent to undergo any surveillance due to their involvement in illicit activity, there is no traditional

sampling frame for this population (Hope et al., 2011; Smirnov, Kemp, Wells, Legosz, & Najman, 2014). In addition, there are systematic differences between IDUs who are accessing substance use or medical treatment and who are readily accessible to engage in research, and those who are disengaged from treatment and difficult to access for research. For instance, those engaged in substance or medical treatment are more likely to have a longer, more chronic history of substance abuse (Evans-Polce, Doherty, & Ensminger, 2014; National Institute on Drug Abuse, 1991). Even among people with CHC who are not IDUs, it is likely there are systematic differences between those accessing medical care and those who are not, such as a further progression of liver disease in those seeking treatment. Thus, it is important to conduct research using multiple avenues of sampling and data collection (Smirnov, Kemp, Wells, Legosz, & Najman, 2014; National Institute on Drug Abuse, 1991). One of the major strengths of the present research is the application of this principle in order to answer a number of significant research questions in a population generally considered difficult to research. Study one utilised a postal survey of hospital outpatients supplemented with an online survey of Australians living with CHC in order to increase generalisability beyond CHC patients engaged in tertiary medical care. The use of postal and online surveying promoted participation as there was no need for personal contact, thereby allaying potential concerns about confidentiality and privacy.

The aforementioned difficulties in engaging the CHC population in research are made even more difficult when attempting to research changes

over time, as attrition is likely to be higher in a portion of IDUs who may be more socio-economically disadvantaged and transient than other groups, particularly with the threat of social stigma and legal sanctions given their illicit drug use (Smirnov, Kemp, Wells, Legosz, & Najman, 2014; National Institute on Drug Abuse, 1991). Despite these difficulties, studies two and three examined two important research questions in a cost-effective manner. Study two investigated the progression of depression and anxiety symptoms over time in a single cohort of CHC outpatients by combining two previously used datasets. The baseline measurement used a dataset previously analysed to assess the prevalence and predictors of depression and anxiety (Stewart, Mikocka-Walus, Morgan, et al., 2012), while the follow-up measurement was taken from a sub-sample of participants who also provided depression and anxiety data in study one of this thesis. Study three investigated changes in the IDU population (around half of whom reported having CHC) over time with respect to mental health problems and service utilisation, using the 2006 and 2012 datasets from the National Drug and Alcohol Research Centre's Illicit Drug Reporting System surveys with regular IDUs across Australia. Finally, following the development of the C-UP intervention in study four, feedback was obtained once again from multiple sources, including those living with CHC in the community, and service providers such as psychologists, CHC workers, and a CHC counsellor.

In grappling with the obstacles of recruitment and data collection, this research has made a significant and, importantly, original contribution to the knowledge in this area. Study one established the acceptability of different

psychological treatments from the perspectives of people with CHC, which can be used to inform policy and practice level decisions concerning the management of psychiatric co-morbidity in this population. Study two assessed the course of depression and anxiety over time in CHC patients in an innovative way by applying Rasch analysis to convert follow-up scores on the DASS to HADS scores, the measure used for the baseline measurement, thereby allowing comparison of the scores. Notwithstanding other limitations (which are discussed below), the results of this novel analysis were confirmed through a more conventional, yet indirect, procedure of comparing both baseline HADS and follow-up DASS scores to community norms and examining the disparity between these comparisons.

Study three investigated changes in rates of mental health problems and service use over time in the IDU and CHC population. This was completed for the period from 2006 to 2012 which encompassed the introduction of the major mental health reforms of the Better Access program in Australia and increasing mental health awareness campaigns. While Australian research has examined the impact of Better Access (Pirkis, Harris, et al., 2011) and public awareness campaigns (Reavley & Jorm, 2012a, 2012b), this research has been broad-based in examining the impact on the general public, while the effect of these widespread changes on disadvantaged groups such as IDUs and those with CHC has been omitted in the literature.

Finally, study four involved the development of a transdiagnostic treatment targeting depression and anxiety in people with CHC. In the CHC literature,

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mental health research has generally been restricted to the prevention and treatment of IFN-induced depression during anti-viral treatment with anti-depressants. Only one study has examined the use of psychotherapy for IFN-induced depression and anxiety (Neri et al., 2010). In addition, transdiagnostic treatment is a new area in the general psychological research literature and there has been no application of this type of treatment in any somatic populations, let alone people with CHC. Thus, this was the second study to explore a psychotherapeutic approach to people living with CHC, the first study to examine treatment of depression and anxiety outside of the anti-viral treatment setting, and the first to utilise a transdiagnostic approach.

In closing, this research addressed a number of important questions in a population traditionally deemed "hard to research" through the use of cost-effective and novel methodological procedures. In so doing, this thesis has made a number of original contributions to the existing body of knowledge:

(1) Establishing individual psychotherapy, bibliotherapy, and pharmacotherapy as acceptable psychological treatment tools for people living with CHC;

(2) Reinforcing the importance of prior positive mental health treatment experiences as predictive of future treatment uptake;

(3) Providing preliminary data on the poor symptom trajectories of depression and anxiety in people with CHC;

(4) Providing preliminary data for the CHC+/- IDU population on the increases over time in mental health problem rates and decreases in

service utilisation (which nonetheless remain comparable to the general population and have coincided with, somewhat paradoxically, increases in access to psychologists); and

(5) The development of a transdiagnostic treatment protocol for co-morbid depression and anxiety in people living with CHC which is ready for testing in the context of individual psychotherapy or in a self-directed manner. A more detailed discussion of the findings of this thesis and their limitations and implications follows.

7.3. Recommendations for future research

While this research program has addressed a number of important gaps in the literature, there is scope for further research to address the remaining gaps in knowledge and address some of the methodological limitations inherent in the current research.

One avenue for further research involves the acceptability of mental health treatments. In study one, acceptability for e-therapy and group psychotherapy was found to be significantly lower than other treatment types, which accords with research in the general population for group psychotherapy (McDermut et al., 2001; Sharp et al., 2004) and e-therapy (Gun et al., 2011) yet contrasts with research in inflammatory bowel disease, another gastroenterological condition, for e-therapy (McCombie, Gearry, & Mulder, 2014). This is problematic as e-therapy and group psychotherapy are likely to be more cost-effective than

individual psychotherapy (Gun et al., 2011; Vos et al., 2005). Moreover, there are funding mechanisms in place to provide reimbursement for 10 sessions of group psychotherapy per annum under the Better Access program. Thus, the reasons for the low acceptability for e-therapy and group psychotherapy should be further explored.

Past qualitative research has reported that stigma and fears regarding breaches of privacy and confidentiality are potential barriers to patients seeking mental health treatment in general (Stewart, Mikocka-Walus, Harley, et al., 2012) and this may be particularly relevant to a group psychotherapy setting where other patients are not bound by the same regulatory and legal frameworks regarding confidentiality requirements as practitioners. Future research could explore whether group psychotherapy is acceptable if participation is restricted to other people living with CHC. Further studies should also expand the assessment of acceptability to specific types of psychotherapy (e.g. CBT vs. interpersonal psychotherapy vs. acceptance and commitment therapy), pharmacotherapy types (e.g. anti-depressants vs. anxiolytics vs. anti-psychotics), and for individual drugs (e.g. fluoxetine vs. paroxetine).

Another potential avenue for future research is to replicate the findings of study two using a more rigorous research methodology. This prospective study could attempt to track a larger number of patients from a similar starting point (i.e. diagnosis), with frequent measurements over up to five years (to allow for measurement of disease progression which is slow in CHC), and analysis of other potentially intervening variables such as psychiatric treatment, social

support, major life events or stressors (such as childbirths, relocations, relationship breakdowns, bereavements, or psychological trauma). This data could potentially be compared with controls from the general community, other liver disease populations, and/or other somatically ill populations.

Study three also had methodological limitations which complicated the interpretation of its findings. It is recommended that future research endeavour to track the mental health outcomes of IDUs with and without CHC using more rigorous assessment tools, such as structured clinical interviews based on formal diagnostic criteria. Ideally this research would be conducted regularly in order to assess the impact of population level changes (such as mental health reforms or public mental health awareness campaigns) and specific sub-population level changes (such as structural changes in policies or services in the CHC or drug and alcohol sectors).

Study four detailed the rationale for, development of, and preliminary acceptability testing of a specific treatment protocol for managing depression and anxiety in people living with CHC. As yet, no formal assessment of the acceptability or efficacy of this intervention has been undertaken. It is recommended that a pilot within-subjects trial with a small (N=12) sample (Julious, 2005) be conducted to determine the acceptability of C-UP and provide preliminary estimates of its efficacy. If the intervention were proven to be acceptable to people living with CHC and demonstrated reasonable pre- to post-trial effect sizes, it would be prudent to conduct an RCT to test the efficacy of the intervention versus, for example, a wait-list control. This research could

feasibly be conducted using the booklet in a self-directed manner or via a brief individual psychotherapeutic program. It is also recommended that this RCT also include an analysis of the cost-effectiveness of the intervention.

7.4. Recommendations for policy and practice

This research program was conceived and implemented with a practical and clinical view to improving the management of depression and anxiety in people with CHC. As such, there are a number of implications for policy and practice. The 3rd National Hepatitis C Strategy was Australia's overarching policy framework for 2010 to 2013, with one of the core aims being to "minimise the personal and social impacts of hepatitis C" (Department of Health and Ageing, 2010, p. 7). Without question, the psychological effect of living with CHC must be included in this personal impact. However, the 3rd National Strategy did not directly address the psychosocial side of CHC, beyond identifying people with CHC and co-morbid mental health disorders as a priority population with special needs, which was not expounded on (Department of Health and Ageing, 2010).

The specific Action Plan for enacting the goals of the 3rd National Strategy in South Australia, however, provided more direction for addressing the psychosocial aspects of CHC infection (South Australian Department of Health, 2009). In this Action Plan, the South Australian Department of Health (2009) acknowledged that CHC and its associated physical symptoms, stigma and

discrimination can adversely affect psychological quality of life. The Action Plan also outlined a strategy to improve patient access to allied health professionals with knowledge of CHC, which involved training private and public psychiatry and psychology staff in both metropolitan and rural areas (South Australian Department of Health, 2009). However, no data have been released evaluating the outcomes of this action plan. Moreover, while this strategy may be of benefit to patients who actually access these services, it does little to address factors which influence whether or not they will reach the service at all, such as the assessment and identification of mental health problems, individual and structural barriers to help-seeking (Stewart, Mikocka-Walus, Harley, et al., 2012), and the acceptability of treatments which patients expect to encounter (as explored in study one).

Unfortunately, the recently released 4th National Hepatitis C Strategy (Department of Health, 2014), which aims to guide the national response to CHC from 2014 to 2017, also failed to significantly expand its coverage of mental health. Although the 4th National Strategy did state that CHC care plans should address, among other things, co-morbidities and psychosocial care and support needs, this is not elaborated on (Department of Health, 2014). The 4th National Strategy explicitly states that all aspects of care and support must be addressed to provide effective management of CHC and that this relies on effective relationships and referral processes for mental health services when required (Department of Health, 2014).

It was also recommended that primary healthcare professionals become more involved in the CHC treatment process which would help facilitate the provision of other services necessary for the management and treatment of CHC (Department of Health, 2014). This implicitly includes mental health services which typically require referral from a GP. It has been argued elsewhere that other health professionals, such as hepatologists and gastroenterologists, should be able to refer patients for reimbursable psychological treatment under the Better Access program which is currently restricted to referrals from GPs (Mikocka-Walus et al., 2009; Stewart, Mikocka-Walus, Harley, et al., 2012). Moreover, there have been calls in the broader CHC literature for greater integration of multi-disciplinary support, including psychological and psychiatric care, in the treatment of CHC patients (Ho et al., 2008; Knott et al., 2006; Sylvestre et al., 2004).

Like its previous iteration, the 4th National Strategy fails to specifically address the mental health considerations of CHC infection or make detailed recommendations for the assessment and management of these co-morbidities. The latest Action Plan for the 4th National Strategy has not yet been released and it is recommended that this Plan provide more detail and specific directions for addressing the significant psychosocial aspect of CHC infection, including: (1) assessment and identification of mental health problems; (2) promoting mental health services in a way which minimises the impact of individual help-seeking barriers such as fears regarding stigma and confidentiality; (3) continuing to provide and evaluate CHC training for mental health professionals;

and (4) developing mental health treatment resources specifically for people with CHC.

The specific recommendations born out of the research in this thesis will now be discussed, following the clinical pathway from assessment through to referral and subsequent treatment. Study two revealed a poor trajectory of depression and anxiety over time in CHC outpatients, emphasising the need for improved assessment and management of mental health problems. While the limitations of study two preclude definitive conclusions, it is clear that symptoms must be monitored on a more frequent basis (even in those without a history of symptomatology) as 29% of this sample fell below the cut-off for depression or anxiety at baseline yet exceeded it at follow-up between two and five years later. There are readily available and brief screening inventories which have been psychometrically validated for use with people with CHC, including the Beck Depression Inventory, Hospital Anxiety and Depression Scale (Golden, Conroy, & O'Dwyer, 2007), and Center for Epidemiologic Studies Depression Scale (Clark, Mahoney, Clark, & Eriksen, 2002) for depression, and the Patient Health Questionnaire for depression, generalised anxiety disorder, and panic disorder (Navinés et al., 2012). Routine clinical use of such inventories will facilitate early and reliable identification of patients in need of further assessment and/or referral to specialist mental health care.

The results of study two also highlighted the need for intervention because, without it, it is likely that the mental health of those living with CHC will deteriorate even further than is currently the case, compared to other patient

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groups. Notwithstanding the methodological limitations of study two, there is a pressing need for targeted mental health assessment and treatment in this population. This need exists irrespective of the interpretation of the results of this study, due to the wealth of evidence which has demonstrated the high prevalence of psychiatric co-morbidity (el-Serag et al., 2002; Stewart, Mikocka-Walus, Morgan, et al., 2012) and the deleterious impact this has on patients with CHC with respect to quality of life (Bonkovsky et al., 2007; Gutteling et al., 2010; Häuser et al., 2004), physical symptomatology (Dwight et al., 2000; Morasco et al., 2010), and anti-viral treatment outcomes (Leutscher et al., 2010; Martín-Santos et al., 2008). The only factor which changes based on the interpretation of the results of study two is the urgency with which targeted mental health intervention is needed in this population.

The results of study three demonstrated that, even if service utilisation rates have declined, IDUs (including those living with CHC) are as willing to access treatment for mental health problems as the general population – if not more so. Study three also found that there has been a proportional increase in access to psychologists over time. This gives psychologists and other mental health professionals who work with people living with CHC the opportunity to provide a positive treatment encounter which is both efficacious and acceptable to the client. Since satisfaction with past use of a treatment is a strong predictor of acceptability for future use of that treatment, as reported in study one, providing this positive treatment encounter is imperative. Research has also shown that acceptability of a treatment is associated with its uptake, adherence,

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and success (Dwight-Johnson et al., 2001; Jorm et al., 2000; Swift & Callahan, 2009; Swift et al., 2011). Thus, planning treatment to better match the needs of this population is critical to meeting their mental health needs.

Study four detailed the development of such a treatment, C-UP, which is designed to accommodate the experiences and expectations of people living with CHC. This protocol remains un-tested in people with CHC with regard to both specific acceptability and efficacy. In lieu of this, general treatment protocols administered to people with CHC should be individually tailored to patients, with consideration of their CHC-related anxieties (e.g. fear of disease transmission) and triggers (e.g. stigmatising/judgemental reactions/actions of others). The booklet developed for C-UP may prove a useful resource for clinicians in the planning and delivery of treatment to patients with CHC and co-morbid depression and/or anxiety.

The format of treatment to be given to people living with CHC may also vary. In study one, individual psychotherapy was significantly more acceptable than any other support type, and a very small number endorsed other formal treatments but did not find individual psychotherapy acceptable. By the metric of acceptability then, individual psychotherapy would be the ideal treatment type for this population. However, efficacy and cost also need to be considered, with research showing that in the Australian treatment setting, bibliotherapy is the most cost-effective treatment, followed by CBT from a public psychologist, tricyclic prescription, CBT from a private psychologist/psychiatrist, and serotonin selective reuptake inhibitor prescription (Vos et al., 2005). Moreover, it has been

shown that providing CBT in group treatment is more cost-effective than individual treatment (Vos et al., 2005). However, group psychotherapy was the least acceptable form of treatment to people with CHC in study 1.

Online therapy also has the potential to be very cost-effective (Gun et al., 2011) as, similar to bibliotherapy, it requires limited overhead expenses and can be provided with minimal therapist contact (Ahl, Mikocka-Walus, Gordon, & Andrews, 2013; Van Ballegooijen et al., 2014). Insofar as individual costs to the patient are concerned, both psychotherapy and pharmacotherapy typically involve consultation fees which may be partially or fully subsidised by public or private health care funding, with pharmacotherapy having the added cost of the medication. For self-help treatments such as bibliotherapy or e-therapy, the individual costs may vary depending on the level of therapeutic guidance given and any funding in place for the intervention. Nonetheless, it is likely that these methods would reduce costs for patients due to the decreased expense of providing these treatments. Access to services must also be considered in the Australian context where many people living in rural or remote areas may have limited access to mental health professionals. Where this is the case, self-directed therapies such as bibliotherapy and e-therapy may be the only treatment options available. As e-therapy was the second least preferred form of treatment to people with CHC in study 1, bibliotherapy may be a more ideal candidate.

With regard to the length of treatment to be offered to people with CHC, the results of study one indicated that the average length of psychological

support desired by respondents was 10 sessions of care, which conveniently matches the current limitations of reimbursable psychological support under the Better Access program in Australia. This is important as study one demonstrated that satisfaction with past treatment predicted future treatment preferences. Thus, ten sessions of care seem a reasonable recommendation for treatment length, but as always clinical judgement and individual patient characteristics should take precedence in treatment decisions. With low-intensity interventions such as guided bibliotherapy, recent research has shown that optimal recovery rates occur with four to six sessions, with dose-response declining with longer treatment (Delgadillo et al., 2014).

In study one, it was found that well over half of those taking anti-depressants were still experiencing severe depression or anxiety, consistent with other U.S. research with people with CHC (Nelligan et al., 2008). It is likely that a proportion of patients receiving psychotherapy may still be experiencing clinically significant symptoms, although this has not been researched. Given that this study showed that many respondents found psychotherapy and pharmacotherapy acceptable, clinical practice could consider combining psycho- and pharmaco-therapy. However, research on this subject has yielded mixed findings, with combination therapy only providing additional benefit over monotherapy in the treatment of mood and anxiety disorders in certain contexts (Otto, Smits, & Reese, 2005). Combined therapy appears to provide modest improvements in the acute treatment of depression and in the treatment of people with depression which is chronic, severe, or previously unresponsive to

monotherapy (Otto et al., 2005). CBT and interpersonal therapy appear to help protect against relapse following successful monotherapy with pharmacological treatment (Otto et al., 2005). In the treatment of bipolar disorder, pharmacotherapy is considered necessary in controlling the disorder while psychotherapy can help maintain compliance, treat residual and breakthrough symptoms, and prevent relapse (Otto et al., 2005).

For anxiety disorders, evidence suggests that in the short- to medium-term, combined treatment appears to provide added benefit in reducing anxiety, although medications can negatively impact on long-term maintenance of treatment gains demonstrated through monotherapy with CBT (Otto et al., 2005). Nonetheless, used sequentially, psychotherapy can extend and maintain treatment gains achieved through initial pharmacotherapy (Otto et al., 2005). The field of combination treatment is growing, with research combining psychotherapy with D-cycloserine, an agonist of the glutamatergic N-methyl-d-aspartate receptor which facilitates learning and memory (Otto et al., 2005), demonstrating increased effect in the treatment of social anxiety disorder (Guastella et al., 2008) and panic disorder (Otto et al., 2010). Again, there is little research in people with CHC, although a meta-analysis of three trials found a small but significant benefit of combination therapy for treating depression in chronically ill patients (Rizzo et al., 2011). There has also been successful use of sequential treatment, involving psychotherapy initially to prevent anti-viral induced depression and anxiety in CHC outpatients, followed by pharmacotherapy for breakthrough symptoms (Neri et al., 2010). However,

considering the dearth of research in this area, it is suggested that combination treatment should only be considered on an individual basis depending on the diagnosis, co-morbidities, chronicity, and severity.

7.5. Final comments

The primary aim of this research was to contribute to the existing body of knowledge and resources available in the areas of CHC and mental health. A series of four novel studies were conducted to provide significant insights into mental health treatment preferences, depression and anxiety symptom trajectories, and changes in mental health problem and service utilisation patterns over time in the CHC+/- IDU population. This culminated in the development of a transdiagnostic protocol for treating co-morbid depression and anxiety. This research has demonstrated the need for a greater emphasis on the psychological aspects of CHC infection, from research through to policy and practice.

Prior research had already established the deleterious effect of psychiatric co-morbidity in people living with CHC with respect to quality of life, physical symptomatology, and anti-viral treatment outcomes. This research added to this grim picture by demonstrating that the course of depression and anxiety may be worse in patients with CHC than in the general community or other somatically ill populations and the rate of mental health problems in CHC+/- IDUs has increased over time, while their rate of service uptake has decreased. However,

the rate of service uptake remains comparable, if not higher, to the general community and there has been an increase in access to psychologists. Moreover, acceptability for effective treatment modalities such as individual psychotherapy, pharmacotherapy, and bibliotherapy are high. Finally, this research has resulted in the development of a treatment protocol which has the promise of simultaneously treating symptoms of depression and anxiety.

Notwithstanding the limitations of this thesis and the remaining gaps in the literature, it is anticipated that the contributions this thesis makes to the body of knowledge will lead to improvements in research, policy, practice, and, ultimately, the assessment and management of co-morbid depression and anxiety in people living with CHC.

APPENDICES

Appendix 1: C-UP treatment booklet

Presented in this appendix are images illustrating the entire C-UP treatment booklet which can be given to patients to self-administer, or used as a treatment aid in individual psychotherapy in conjunction with the treatment protocol found in appendix 2. A high quality PDF of the treatment booklet can

be obtained by e-mailing benjamin.j.stewart@adelaide.edu.au or

deborah.turnbull@adelaide.edu.au.

C - UP

A **U**nified **P**rogram

for people with hepatitis **C** to

manage depression and anxiety

This 5 week program will help you:

- Learn more about depression, anxiety, and hepatitis C.
- Learn how to cope with difficult emotions.
- Understand your thoughts and their effect on how you feel.
- Face your fears.
- Get back into your life.
- Maintain your emotional well-being.

C-UP stands for the **Unified Program** for depression and anxiety in hepatitis C. C-UP is a brief, one-on-one, psychotherapy program. C-UP aims to help people with hepatitis C to cope with symptoms of depression and anxiety, and improve their quality of life.

C-UP draws on techniques taken from Cognitive Behavioural Therapy, also known as CBT. CBT has been proven to be effective in treating depression and anxiety. In CBT, the aim is to help people cope with distressing feelings and learn how to think and behave in a way which promotes better mental health. The program has five parts which will be covered over the next 5 weeks. You can build on these sessions by reading this booklet and completing the homework activities.

Week 1: What is depression and anxiety? The first part of C-UP aims to give you a good foundation of knowledge to succeed with this program. After week 1 you should have a better understanding of depression, anxiety, and how they relate to hepatitis C.

Week 2: Managing emotions. This part will teach you how to cope with distressing and difficult emotions.

Week 3: Thinking well. This part will look at thoughts and how these can influence how you feel.

Week 4: Behavioural choices—What can you do? This part of C-UP will look at behaviour (or the choices you make and the activities you take part in) and how this can influence how you feel.

Week 5: How to stay well? The final part of C-UP will look at how to maintain your emotional well-being once you are in a good place.

Activity: Please write below about what you hope to get out of this program and what your goals are:

ACTIVITY: What does depression mean to you? What do you think the word "depression" means?

....

....

....

What is depression?

Everyone has times when they feel very sad or they don't enjoy things they normally would. For some people, this happens more often than for others, or the feeling may be stronger. If it gets worse, this may begin to get in the way of their work, school, or home life. At this stage, this might become a depressive disorder.

There are specific criteria for diagnosing someone with depression, but many people may have some of the same symptoms of depression without reaching the point of a diagnosis.

The common signs/symptoms of depression are:

- Feelings of sadness.
- Loss of interest or pleasure in activities.
- Sleeping more or less than usual.
- Fatigue or loss of energy.
- Larger or smaller appetite and/or putting on or losing weight
- Feeling worthless, guilty, or hopeless.
- Thoughts of death or suicide.
- A loss of motivation.
- Difficulty concentrating or making decisions.
- Using drugs or alcohol to cope with these feelings.

Activity: Circle the bullet points above for the symptoms (if any) that you have experienced. List any others we haven't mentioned here: ....

John's Story

There are a couple of times in my life where I think I've been 'depressed'. I wasn't crying constantly or anything but I just felt really flat... empty. I didn't enjoy the things that I used to find really fun, like going out with friends or playing sport. Despite the fact I was sleeping much more than usual, I somehow still felt tired all the time. I felt like I was stuck in a hole and there was no hope of ever getting out.

Activity: What does anxiety mean to you? What do you think the word "anxiety" means?

....

....

....

What is anxiety?

Similar to depression, everyone has times when they feel anxious, worried, nervous, or stressed.

However, for some people, these feelings start to come up more often and become stronger than for others. These feelings may begin to interfere with their work, school, or home life. People with these experiences may have an anxiety disorder.

Again, there are strict criteria for diagnosing someone with an anxiety disorder, but many people may have some of the symptoms without having a diagnosis.

There are many different anxiety disorders and the symptoms can depend on what type of anxiety is present. However, some common symptoms include:

- Panic or intense fear in certain situations.
- Physical feelings like a racing heart beat, sweaty palms, or muscle tension.
- Feeling very worried a lot of the time.
- Feeling on edge, irritable, or stressed.
- Avoiding situations which bring on these experiences described above.
- Using drugs or alcohol to help deal with anxiety where situations can't be avoided.

Activity: Circle the bullet points above for the symptoms (if any) that you have struggled with. List any others we haven't mentioned here: ....

Mel's Story

I think I've always been an 'anxious' person but it started to really get out of control recently. I get really nervous and wound up in social situations. I stress about what I should say or do and assume people must think I'm stupid or weird. When I start to get anxious I notice my heart pounding, I feel really hot and red in the face, and I get a knotty feeling in my stomach. It's gotten so bad I don't even bother going out or meeting new people any more.

How common are depression and anxiety?

Activity: How many people do you think suffer from anxiety and depression? 1 in 20? 1 in 10? 1 in 3?

Anxiety: .... Depression: ....

Depression and anxiety are very common. 1 in 5 Australians will experience a depressive disorder at some point in their lifetime, while 1 in 7 Australians will experience an anxiety disorder at some point.

Many more may experience significant symptoms of depression and anxiety without having a diagnosis.

In Australians living with hepatitis C, depression and anxiety may be even more common. Over 1 in 5 Australians with hepatitis C may experience symptoms of depression, while 2 in 5 Australians with hepatitis C may experience symptoms of anxiety.

What causes depression and anxiety?

Activity: What do you think causes depression and anxiety?

For some people, depression and anxiety may be triggered by stressful or traumatic life events.

For others, there may not have been a single event, but rather long-term ongoing difficulties and stress.

Family history, personality, physical health problems, and drug and alcohol use can also play a part in causing depression and anxiety.

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What causes depression and anxiety

For people with hepatitis C, there are a number of things that may contribute to depression and anxiety.

Living with hepatitis C brings many challenges such as:

- Managing symptoms such as fatigue.
- Fears around becoming sick, being unable to work or take care of family, or even dying.
- Fears around passing on hepatitis C to loved ones.
- Worrying about telling others about hepatitis C and experiencing stigma, judgement, or rejection.
- Restrictions on lifestyle choices such as drinking alcohol.

People who receive treatment for hepatitis C can also experience depression and anxiety as side-effects of interferon, which is one of the drugs currently used in treatment.

Activity: Is there anything about hepatitis C which you have found difficult emotionally?

....

....

....

....

John's Story

I've been through a lot so when I found out I had hep C I reckon it was the last straw. I had left drugs behind for years by the time I was diagnosed so it came as a huge shock. There were so many unanswered questions which stressed me out. Was this thing going to kill me? Would I be able to work? Information was hard to come by and confusing and most of the doctors didn't seem to care much. I never told anyone I had it 'cause I was worried about being judged or rejected, so I had no one to lean on for support.

The hot cross bun in depression and anxiety

Depression and anxiety can affect you in four different ways. It can affect:

- How you think — or your thoughts.
- How you feel — or your emotions.
- What happens in your body — or your physical feelings.
- What you do — or your behaviours.

Importantly, these four areas can also all affect each other, leading to the hot cross bun model of depression and anxiety shown below.

Situation
(e.g. Attending a birthday party and feeling anxious)

Thought
(e.g. "This will only get worse")

Emotion
(e.g. anxious)

Behaviour
(e.g. leave party)
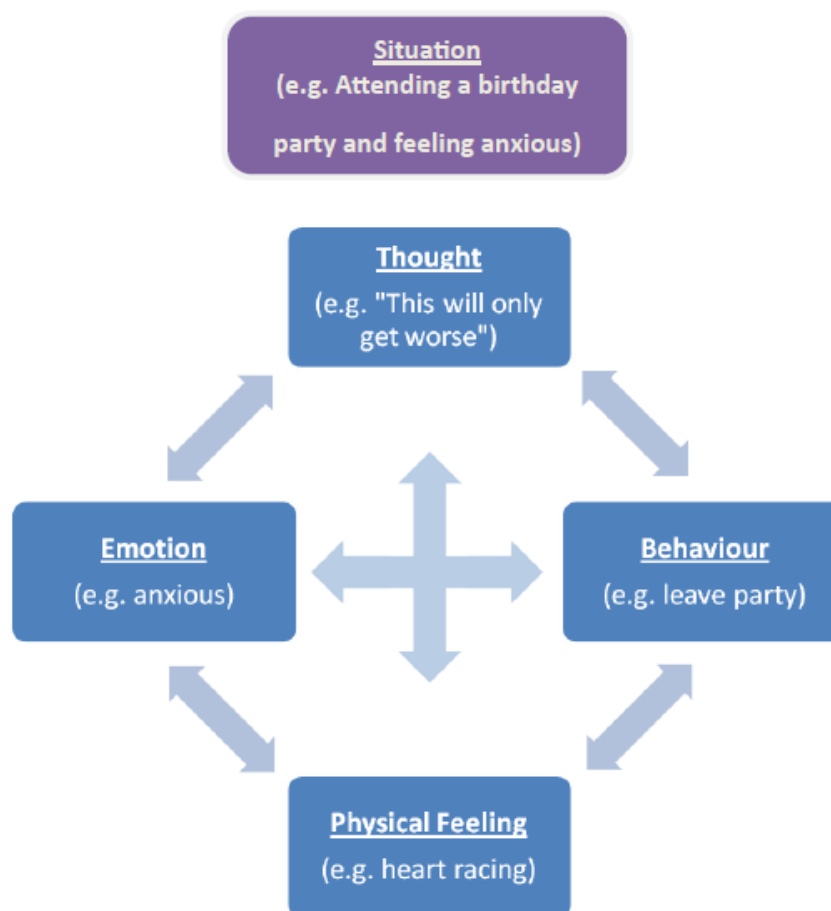
Physical Feeling
(e.g. heart racing)

Because the four areas of thoughts, emotions, behaviours, and physical feelings can all affect each other, if one becomes worse, so can the others — as you can see in Mel's story below.

Mel's Story

I remember feeling really anxious before my brother's 21st birthday party 'cause there would be so many people I didn't know. But it was important to him so I went anyway. Once I was there I started to feel nervous, surrounded by all these people and not knowing what to say or do. I remember thinking "I'm going to do or say something stupid." This only made me feel more anxious. My heart felt like it was pounding out of my chest and I felt red in the face. Then I had thoughts like "This is only going to get worse. I'm going to lose it and make an idiot out of myself." I felt like I had to get out before it became too much so I went home. This took the anxiety away, but pretty soon I began to feel guilty and disappointed in myself for not being there for my brother. I thought about how much of a failure I was. I felt depressed and spent the rest of the weekend in my house.

However, the four areas of thoughts, emotions, behaviours, and physical feelings being connected also means that if one area improves, the others can improve too.

The next sections of C-UP will give you some strategies for managing emotions, thoughts, and behaviours which come along with depression and anxiety.

Activity: Think of a recent situation which was distressing and write down the emotions, physical feelings, thoughts, and behaviours which you noticed.

Situation: ....

Emotions: ....

Physical Feelings: ....

Thoughts: ....

Behaviours: ....

Week 1 — What is depression and anxiety?

Activity: As you did on the previous page, write about any difficult situations or events which occur over the next week in the table below. You don't have to write about it straight away and can come back and complete it later. Spare copies of this table can be found on page 29-30.

Day/Time (When?)	Situation (What happened?)	Emotion (How did you feel? E.g. Sad, angry, worried)	Physical Feeling (What did you feel in your body? E.g. nausea)	Thoughts (What went through your head? E.g. 'I'm such a failure')	Behaviour (What did you do? How did you respond? E.g. Drank a bottle of wine)

Positive effect of emotions

All emotions, whether you like them or not, can have advantages. A likeable emotion like happiness has an obvious advantage to the person experiencing it — they feel great! Other positive effects of a 'good' emotion like happiness could be that the person feels more motivated and becomes more productive at work. Perhaps since they are in a good mood they treat those around them better.

However, when people are suffering from depression and anxiety, there can be many difficult or unpleasant emotions they can experience – sadness, hopelessness, worthlessness, shame, guilt, anger, irritability, nervousness, and worry to name just a few!

Unsurprisingly, these emotions can be distressing and hard to cope with at times. However, it is important to realise that all emotions – even these unpleasant ones – serve an important purpose and are necessary in some way. Negative emotions help us by signalling that something important is going on inside us or around us, and motivate us to act accordingly.

For example, if you had an important deadline coming up for work or study and you had a lot to do to finish on time, you may very well feel stressed — an unpleasant emotion. However, this stress has a positive effect, in that it motivates you to work at the task at hand. If you didn't care then you may be more inclined to watch TV instead!

Activity: Briefly write about a time when an unpleasant emotion has had a positive effect in your life.

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Negative effect of emotions

You just read that negative emotions, while uncomfortable or distressing, can be useful if they serve a purpose. Such as if the emotion leads you to action which solves a problem.

However, sometimes there are problems that can't be solved. Sometimes people don't know how to solve the problem or are afraid of what would happen if they tried. At other times there is no problem they can identify which will help their situation.

Experiencing these distressing and difficult emotions can lead some people to try and avoid these feelings in a number of ways.

One way people use to avoid emotions is distracting themselves by engaging in other activities. The most common method of avoidance is using drugs or alcohol.

While attempts to avoid experiencing a distressing emotion can help you feel better in the short-term, they have unwanted consequences. Research has shown that avoidance of emotions can actually make you more distressed in the long run.

On the other hand, being able to experience distressing emotions, accept them, and work with or manage them can lead to better mental health.

Activity: Write down 3 emotions that you struggle with or try to avoid at times:

1. ....   2. ....   3. ....

Avoiding emotions can be harmful in other ways as well. For example, excessive drinking of alcohol to avoid or dampen emotions can lead to problems at work (i.e. absence or poor performance due to hangovers or related illnesses) or in relationships (i.e. conflicts with a spouse over behaviour during alcohol use). It can also lead to physical harm through accidents or injuries. In people with hepatitis C, alcohol use can be even worse because alcohol can accelerate the damage which hepatitis C does to the liver.

The take home point here then is that trying to avoid emotions doesn't work – in fact, it can often make things worse. While these feelings can be uncomfortable, it is more beneficial to try and accept them. This doesn't mean that you have to enjoy distressing emotions. It doesn't mean you are giving up and resigning yourself to a life of distress. What it means is accepting emotions for what they truly are – something that will come and go, rise and fall, and serve an important purpose.

Accepting difficult emotions

When accepting emotions, the first step is to be open to them—allow them to be there without resisting them or fighting them. The aim is to be a non-judgemental observer of your emotions. This means watching as feelings come and go without judgement or criticism (E.g. "I'm feeling depressed again. Why am I always like this? I'm such a weak person.")

When taking this stance of the observer, we can see that emotions do not necessarily reflect on who we are. For example, if you were feeling angry and wanted to lash out at someone, this is just a feeling — an uncomfortable one, but just a feeling. Having this feeling doesn't make you a mean person.

Emotions also do not have to be reacted to or acted on. Obviously, just because you feel like lashing out at people, doesn't mean you have to. Finally, emotions aren't always a valid reflection of what is going on, but it can be hard to see this at the time. Perhaps you were angry because someone accidentally bumped into you.

If you just took this into account, this seems like an overreaction. Emotions don't always make sense immediately and the true trigger isn't always apparent. But maybe if you looked at it in more detail and notice you had a really rough week and this person had been rude to you in the past, it doesn't seem so unreasonable.

How to accept difficult emotions:

Take the difficult emotion that you are struggling with — it could be anger, sadness, or worry. Take that emotion and imagine it is like a series of huge waves in the ocean, coming towards you as you stand waist deep in the water. Trying to struggle with or avoid this emotion is like running into the path of the oncoming waves — it will take a lot of energy and you might end up in over your head, even drowning. Accepting the emotion and letting it run its course is like riding the wave back into the shore. It takes much less energy and you will end up back on land.

This may seem frightening when the wave first hits and the emotion is in full swing. However, the wave will settle and calm as it reaches the shore – just like emotions will eventually pass.

How to accept difficult emotions:

As accepting emotions is probably a new idea to you, there is an easy way to help you practice this. When you're experiencing a difficult emotion such as anger, say to yourself *"I am feeling angry right now and that is okay. This means my brain thinks there is some kind of injustice here. When I calm down I can try to identify my trigger but for now I can just focus on my breath, sensations, or environment. This feeling is normal and I accept it. Like all emotions, this one will pass eventually."*

With acceptance, you don't need to fixate all your attention on the emotion. It can run its course in the background while you do something else. The aim is to simply be able to experience it without resistance, without trying to avoid it, and without trying to struggle against it. As the 'water' calms, eventually another wave will come, just like distressing emotions will come up again and again throughout your life. This is okay and just provides another opportunity for you to observe and accept the emotion as it passes through without judgement or resistance.

Activity: Practice accepting difficult or distressing emotions over the next week. Use the table below (continues on the next page) to record your experiences. Write down what situation occurred, what you felt, how strong the feeling was, how able you were to accept that emotion without judgment, resistance, or avoidance, and any other comments you wish. Spare copies of this table can be found on page 31-32.

Day Time Situation	Emotion (What did you feel?) Intensity (Was the emotion mild, moderate, or strong?)	Level of acceptance of emotion, out of 10. (How able were you to accept the emotion, without judging, resisting, or trying to avoid the feeling?) Comments (Feel free to write about anything else you noticed in this experience)

Week 2 — Managing emotions

| Day Time Situation	Emotion (What did you feel?) Intensity (Was the emotion mild, moderate, or strong?)	Level of acceptance of emotion, out of 10. (How able were you to accept the emotion, without judging, resisting, or trying to avoid the feeling?) Comments (Feel free to write about anything else you noticed in this experience)

Earlier in the C-UP booklet you learnt about how our emotions, thoughts, and behaviours influence each other. This week we will begin to explore how coming up with new perspectives can change the way you feel and behave.

For example, if you were feeling depressed, you may have thoughts like "My life sucks," "I have nothing going for me," "There is nothing I can do to fix this mess," and "There is no hope." These negative thoughts can directly feed back into the feeling of being depressed. These negative thoughts can also make you less likely to take action and take part in activities. This decrease in activity can also make your mood even worse. The increase in depression can then feed into more negative thoughts and behaviour, like a vicious cycle shown below.
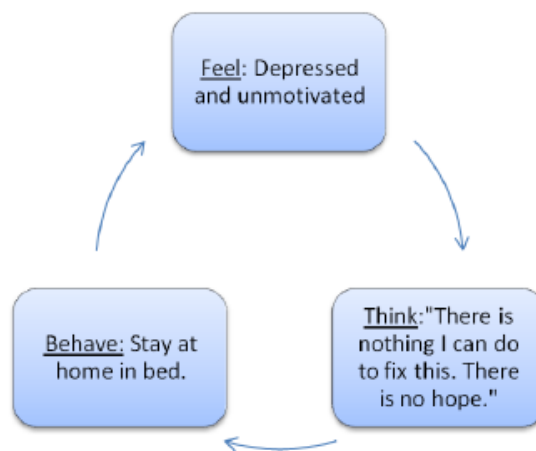
Activity: Usually there is one thought in particular which really distress you – this is called a 'hot thought.' In the example above, "There is no hope" could be that person's hot thought. Describe a recent situation which was distressing for you. Recall one major 'hot thought' which went through your head, then rate how much you believe that thought on a scale from **0 (Don't believe at all)** to **10 (Fully believe this).**

Situation: ....

....

Hot thought: ....

Rate how much you believe in that thought on a scale from 0 to 10: ..../10

Thinking traps

These thoughts can sometimes be unhelpful and, in fact, untrue. This happens when we fall in to thinking traps which make us think more negatively about a situation. This can happen automatically without us even realising. There are four main thinking traps:

Magnifying	Example
One common thinking trap is called 'magnifying'. Magnifying can occur when you overestimate the **chance** of something bad happening. Magnifying can also happen when you overestimate the **effect or severity** of something bad happening.	"I am convinced that I will definitely die from hepatitis C before I get to see my kids grow up. 100%" "If I told anyone I had hepatitis C everyone would find out and no one would want to be close to me. I would have no friends or family left and would be all alone."
Minimising	**Example**
Another thinking trap is called 'minimising.' Minimising can happen when you underestimate the **chance** of something good happening. Minimising can also happen when you underestimate the **effect or benefits** of something good happening.	"I believe there is no chance that my hepatitis C can be successfully treated." "I could tell my friends or family about having hepatitis C, but even if they were supportive this wouldn't make me feel better anyway."
Taking the blame	**Example**
The third thinking trap is called 'Taking the blame.' This happens when you take all the blame and responsibility for something bad which has happened, when in reality you are only partly responsible or even not responsible at all.	"It's my fault that my mum got sick. I should have been there for her more and taken better care of her."

Jumping to conclusions	Example
The last thinking trap is 'Jumping to conclusions.' This can happen when you arrive at a judgement or conclusion about yourself or a situation with little or no evidence to support it.	"I will never get over my depression."
Sometimes evidence which goes against that conclusion is ignored or downplayed.	"Sure they seem friendly and nice to my face but it's just for appearances. They actually hate my guts."
Often times when there are conflicting sides, a black and white perspective will be taken, and there is no balanced or 'grey' view.	"I yelled at my child. Yes, it's the first time it's happened and I apologised, but it makes no difference. I am a terrible mother."
Sometimes when people are jumping to conclusions, they are engaging in 'mind-reading' where they make assumptions about what other people are thinking about them.	"My boss thinks I'm an idiot. I can tell he is laughing at me on the inside."
Other times people might be engaging in 'predicting the future' where they make assumptions about what will happen later on.	"I just told my girlfriend I have hepatitis C. It's just a matter of time before she leaves me."
Finally, some people jump to conclusions through emotional assumptions, where they make judgements or draw conclusions based on what they are feeling.	"I felt so anxious and panicky in the crowd. This proves that it's unsafe for me."

Activity: Can you think of a recent 'hot thought' you had in a distressing situation? (If not, you can use the same thought from page 14). Can you identify any thinking traps you may be caught in?

Thought: ....

Thinking trap: ....

Freedom from thinking traps — Assessing the evidence

Because our thinking is often automatic, it is easy to fall in to these thinking traps without knowing. So it can be helpful to look closely at our thoughts when we are feeling distressed to see if we are getting caught in any thinking traps.

One key way to assess our thoughts is to look at evidence which supports the thought, and evidence which goes against that thought.

This may involve doing some research, depending on what the thought is. If it were something about hepatitis C, talking to your doctor could be helpful. If it was an assumption about a friend or loved one, talking to them to get their opinion could help you gather evidence. Sometimes all you need to do is recall past experiences or think logically about the situation to get the evidence you need. Some examples are provided below.

Original thought	Evidence for thought	Evidence against thought	Balanced thought
"Hepatitis C is going to kill me. I won't get to go to my son's wedding"	Hepatitis C, without treatment and after decades of infection, can lead to serious liver disease. Serious liver disease only develops in a minority of cases.	An effective treatment is available and there are also easy lifestyle changes which can improve my health.	"I will likely live a long and healthy life if I undergo treatment and/or make the right lifestyle choices."
"If I tell my girlfriend I have hepatitis C, she will leave me."	There are people who have experienced stigma about hepatitis C from partners.	I am not a mind-reader and I can't predict the future. My girlfriend is a kind and supportive person and is likely to accept me.	"If she rejects me, she wasn't good for me anyway. But she will probably accept me. With her support I can cope better with hep C."
"I'm a terrible person."	I have made mistakes and there have been times where I didn't treat people I loved the way they deserve.	Everyone makes mistakes. I try to do the right thing. I usually treat my loved ones well. Friends and family have said they appreciate what I do for them.	"No one is perfect, including me. I have made mistakes just like everyone but the important thing is that I continue trying to do the right thing by people."

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Activity: Using what you've learnt about thinking well, write about difficult events which come up over the next week in the table below. Try to identify the 'hot thoughts', rate your belief in these thoughts out of 10, look for evidence for and against the thoughts, name any thinking traps you might be getting caught in, re-rate your belief in the thoughts, and then try to identify a more helpful or balanced thought. An example is provided in the first row. Additional copies of this table can be found on page 33-34.

Day/Time Situation Emotion	Thoughts Identify the 'hot thought' - the one that bothered you the most. Rate belief in hot thought out of 10	What evidence supports the hot thought?	What evidence goes against the thought?	Name any thinking traps you might be getting stuck in. Re-rate belief in thought /10	What is a more helpful or balanced alternative thought?
Monday night. My husband yelled at me. I felt angry, afraid, and worried.	"Jeff is always losing his temper with me lately." "I can't make my husband happy" "My husband doesn't love me anymore." – 8/10 "I am a screw up."	He isn't treating me well lately — this could mean that his feelings have changed.	Jeff has been a jerk to other people as well lately. Just because he's been in a bad mood doesn't make it my fault. Jeff has done nice things too. He said he loved me last week.	"Jumping to conclusions" (If Jeff isn't treating me well, he must not love me anymore) and "Taking the blame" (If Jeff is unhappy, it must be my fault) New belief in hot thought — 2/10.	"Jeff seems to be losing his temper with a lot of people. This isn't necessarily my fault but I could talk to him and see what is going on. I might be able to help him work through whatever is going on.

At the beginning of the C-UP program (page 6), we talked about how emotions, thoughts, and behaviours are all related. In the final part of C-UP, we will look at behaviour and how this can influence how we feel. When we talk about behaviour, this is simply any action you take – anything you do (or don't do). Your behavioural choices can affect how you think and feel.

For example, say a close friend insulted you. You could react (or behave) in a few different ways. One option is to punch them in the nose - this may make you feel satisfied at first. But perhaps later on you might feel guilty because you hurt your friend, and worried that you might not be able to repair the friendship.

Instead of punching them in the nose, perhaps you just ignore the insult and carry on as if nothing happened.

This might make you feel disappointed or ashamed because you didn't stand up for yourself. A different option is that you verbally confront them and tell them that it's not acceptable for them to talk to you like that. This might make you feel confident and proud of yourself for taking a stand in an appropriate way.

As we can see, the behavioural choices we make in everyday situations can have a big impact on how we feel. Behavioural choices can be a reaction to a specific situation. However, behaviour can also be active choices you make without necessarily being a response or reaction to something.

For example, you can choose to invite a friend over for dinner to catch up. Or you could choose to walk the dog through a local park. These behavioural choices can also affect how you feel.

Behavioural avoidance

We will now talk about how you can make better behavioural choices to improve your well-being. In week 2 (page 10) we discussed how attempting to avoid emotions is not effective and can in fact make things worse. Often, people will avoid emotions behaviourally. This means they will do certain behaviours (or avoid doing certain behaviours) in order to avoid the emotions that would otherwise be brought on.

For example, if someone feels anxious in social situations they may avoid going to parties. Someone may avoid going to the doctor because they become depressed when they are reminded that they were diagnosed with hepatitis C there. Some people who feel distressed might consume drugs or alcohol to numb the feelings and distract themselves. These are all types of behavioural avoidance.

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Behavioural avoidance

When talking about avoiding emotions, we learnt that while attempting to avoid emotions might help us feel better immediately, we can actually become more distressed in the long run. This is similar with behavioural avoidance because of how our brains make connections and learn. Let's take the example of someone becoming really anxious when they are in crowded places - like a busy shopping mall. Because this anxiety is very uncomfortable, they leave the shopping mall and immediately feel better. This then reinforces the link between the shopping mall and the anxiety — it teaches their brain that the shopping mall is a dangerous place to be feared.

It also teaches their brain that when they feel anxious, if they leave the situation, that painful feeling will go away. It doesn't give them a chance to test the assumption that the shopping mall is not safe. In the future, they will be more likely to become anxious in this situation, and the anxiety they experience may actually increase.

With more avoidance of the mall, the anxiety may generalise or spread to other areas. Perhaps now they start to feel anxious in smaller local shopping centres and start to avoid these. Then the local deli or 7-11 — with increasing avoidance, this anxiety can spiral out of control.

> **Activity:** List three situations or places that you avoid. Then write the emotion which that situation/place brings on for you.
>
> 1. Situation/Place: .... Emotion: ....
>
> 2. Situation/Place: .... Emotion: ....
>
> 3. Situation/Place: .... Emotion: ....

Graded exposure — Facing your fears

Now imagine the opposite — A person who feels anxious in the busy shopping mall but, like we talked about in week 2, is able to accept the emotion. Imagine they do not behaviourally avoid that emotion by leaving the mall straight away.

Imagine they carry out their shopping as the anxiety rises and eventually falls. They are giving themselves the chance to test the assumption that the mall is dangerous. They are giving themselves the chance to teach their brain that they are able to cope with the anxiety.

Graded exposure — Facing your fears

This means that the anxiety will not be reinforced – the anxiety will not become worse in the future and will not spread to other areas. It might mean that, with repeated practice in these situations, the anxiety will actually lessen over time.

This process is called graded exposure, and it basically involves facing your fears – at a pace that is comfortable for you. You set a goal for what fear you would like to face, and then you set a number of milestones along the way that increase with difficulty up to the final goal. Each milestone is repeated until you are comfortable before moving on to the next milestone.

For the person who is anxious in crowded places. Their ultimate goal might be to be able to go on a shopping spree with their best friend at a large and busy shopping mall when they go on holiday overseas soon. In graded exposure, this would be the final goal, and they would need to set a number of easier milestones to achieve along the way. The first task might be to go to the local delicatessen down the road from the house. This raises minor anxiety for them but is achievable.

After repeated trips to the deli where they now feel confident, the second task may be to go to the nearby supermarket several times which is more difficult for them. The final task may be to repeatedly go to the local mall in their city which normally raises a lot of anxiety for this person but is manageable now that they feel confident in their ability to cope with anxiety.

In this way of facing fears, the person gradually learns they can cope with these distressing feelings. They can also learn that the situation itself is not as dangerous as they thought and the distressing feelings can lessen over time.

Reduction in anxiety with repeated exposures
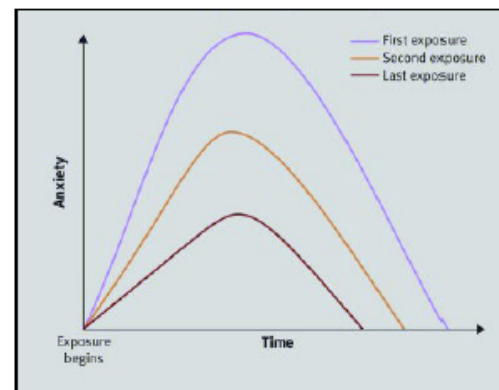
Activity: Using the table on the next page, write tasks for the different levels of predicted anxiety — ranging from very low (about 1 out of 10) to the worst possible anxiety (10 out of 10). Write dates which you could complete these tasks on. It's up to you how many times you want to do that task. Then as you complete the tasks, check the 'Done' box for that date. After you have completed that task enough (i.e. you now feel comfortable doing it) and want to move on to the next one, write the actual anxiety experienced on the final time you did it. Additional copies of this table can be found on page 35-36.

Week 4 — Behavioural choices — What can you do?

Task	Predicted anxiety	Date to complete task	Done	Actual anxiety experienced
	Very low (1/10)	- - - - -	□ □ □ □ □	/10
		- - - - -	□ □ □ □ □	/10
	Low (3/10)	- - - - -	□ □ □ □ □	/10
		- - - - -	□ □ □ □ □	/10
	Medium (5/10)	- - - - -	□ □ □ □ □	/10
		- - - - -	□ □ □ □ □	/10
	High (7/10)	- - - - -	□ □ □ □ □	/10
		- - - - -	□ □ □ □ □	/10
	Very high (9/10)	- - - - -	□ □ □ □ □	/10
	The worst possible anxiety (10/10)	- - - - -	□ □ □ □ □	/10

Behavioural activation — Getting back into your life

As we learnt earlier, graded exposure is about facing your fears and not avoiding situations which lead to negative feelings. Behavioural activation means getting involved in activities and putting yourself in situations which give the opportunity to stimulate positive feelings. Behavioural activation is about getting back into your life.

It is a very common experience for people with depression and anxiety to stop doing things which they used to enjoy or gain pleasure or enjoyment from — like going out with friends or following a favourite hobby like painting.

Often this is because they don't experience the same fun or joy that they used to when doing these things. Some people may also stop doing things which used to give them a sense of mastery or accomplishment, like work or study. Some people may no longer take part in activities which provide both pleasure and mastery such as sport or physical exercise.

This lack of activity can lead to worsened mood and less motivation, which in turn makes it even harder to be active — leading to a vicious cycle as shown below.
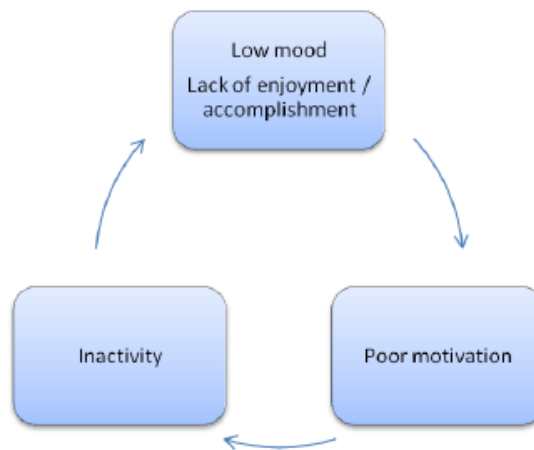
Behavioural activation aims to interrupt this vicious cycle by planning activities which will stimulate experience of pleasure/enjoyment as well as mastery/accomplishment.

These experiences of pleasure and mastery, although small at first, act as a reward, making you more likely to engage in further activity in the future.

Behavioural activation — Getting back into your life

This leads to increased confidence and motivation, making it easier to take part in more activity. In turn, you will have more chances to experience further joy and mastery. Over time, this leads to improvements in mood.

The starting activities are designed to be simple and achievable. They may not give you much pleasure or mastery at the beginning. Over time, the activities should increase in perceived difficulty as well as the potential for experience of enjoyment/mastery. For example, initial tasks for enjoyment might involve listening to a favourite CD, while initial tasks for mastery might involve tidying the house.

The next tasks for enjoyment might involve going out for coffee with a friend, while those for mastery might involve doing some gardening. Advanced tasks for enjoyment might be going out to dinner and a movie with a group of friends, while those for mastery might be attending a group dance or cooking class, for example.

The benefits of behavioural activation are two-fold. Firstly, increased activity in itself is good because you're doing things that are beneficial for you in your life such as health and fitness and maintaining relationships. Secondly, it can lead to improved mood and motivation.
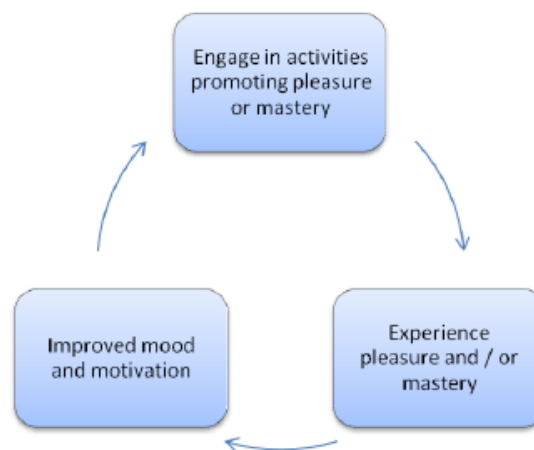
Activity: On the next two pages, you will find two tables. On the first table, list activities which you would like to do. Firstly, try to think of activities which promote pleasure/enjoyment (from minimal enjoyment of 1/10 to maximum enjoyment of 10/10). Secondly, try to think of activities which promote mastery/accomplishment (from low difficulty of 1/10 to maximum difficulty of 10/10). Try to think of any barriers which could prevent you from doing the activity and any solutions to overcome these barriers. On the second table, schedule times to actually do the activities. When you complete the activities, tick the box and record how much pleasure and mastery you experienced out of 10. Spare copies of these tables can be found on page 37-40.

Week 4 — Behavioural choices — What can you do?

Difficulty / enjoyment level	Activity goal (What you would like to be doing)	Barriers (What could get in the way of you achieving this goal?)	Solutions (What you can do to overcome these barriers to achieve the goal)
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

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Week 4 — Behavioural choices — What can you do?

Day & time	Activity	Done	Pleasure experienced (out of 10)	Mastery experienced (out of 10)
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		

Congratulations on completing C-UP! It takes a lot to seek help and advice and it takes even more to stick at it — especially as this booklet has covered issues which can be private, confronting, and distressing at times. So pat yourself on the back! As we reach the end of C-UP, please take a moment to reflect on what you've learnt over the past 5 weeks.

In week 1, you learnt more about depression and anxiety and began to explore how thoughts, emotions, and behaviours can affect each other. You started becoming an observer of your own internal experiences — looking closely at your thoughts, feelings, and how you react to things.

In week 2, you looked at emotions — the good, the bad, and the ugly! You learnt that emotions have positive and negative sides and we learnt that avoiding emotions doesn't work — in fact it makes things worse. And you began to practice accepting distressing emotions, rather than judging them, fighting them, or trying to block them out.

In week 3, you looked more closely at thoughts and how these can influence how you feel and behave. You learnt about thinking traps and how to get out of them by assessing the evidence.

Finally, in week 4, you looked at behaviour — or how you act, react, or don't act at all. We reinforced the message that avoidance is bad — and this includes engaging in behaviours that allow us to avoid distressing emotions. You came up with a plan for beginning to face your fears.

You also learnt about behavioural activation – or getting back into your life. You learnt about how engaging in activities that stimulate feelings of enjoyment and accomplishment can break the vicious cycle of inactivity, low motivation, and poor mood. You also came up with a plan for activities you can do to get back into your life.

What you have learnt from C-UP and the changes you make in your life should improve your well-being. It would be unrealistic to think that your depression and anxiety will completely disappear forever. However, you should feel more equipped to cope with and manage depression and anxiety if and when they arise. To finish C-UP, we will briefly talk about how to stay well.

How to stay well?

The best way to stay well is to have a well-thought out plan for what to do when you are well, what to do when you are becoming unwell, and what to do when you have definitely become unwell. The activity on the following page will help you come up with this plan.

Week 5 — How to stay well?

Activity: Firstly, try to think about what life is like at each of these stages— being well, becoming unwell, and being unwell. What are the signs? How do you feel? How are you thinking? What are you physically doing with regard to your friends, family, work/study, and hobbies?

When I am well...

....

When I am becoming unwell...

....

When I am unwell ....

....

Now try to think of some things you can do at each of these stages.

When things are going well, how do you keep them that way?...

....

....

If you are becoming un-well, what can you do to get back on track?..

....

....

If you have become unwell, what steps can you take to get better?...

....

....

Hint: If you are well, socialising with friends/family and staying active with work/study/hobbies will help promote positive feelings. If you find yourself starting to become un-well, re-reading through the C-UP booklet and applying the strategies may help. Finally, if you think you have definitely become un-well, seeking professional help is recommended. Useful services are listed on page 42 of this booklet.

Day/Time (When?)	Situation (What happened?)	Emotion (How did you feel?)	Physical Feeling (What did you feel in your body)	Thoughts (What went through your head?)	Behaviour (What did you do? How did you respond?)

Spare form (Week 1) — Recording feelings, thoughts, & responses

Day/Time (When?)	Situation (What happened?)	Emotion (How did you feel?)	Physical Feeling (What did you feel in your body)	Thoughts (What went through your head?)	Behaviour (What did you do? How did you respond?)

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Spare form (Week 2) — Accepting emotions

Day Time Situation	Emotion (What did you feel?) Intensity (Was the emotion mild, moderate, or strong?)	Level of acceptance of emotion, out of 10. (How able were you to accept the emotion, without judging, resisting, or trying to avoid the feeling?) Comments (Feel free to write about anything else you noticed in this experience)

Spare form (Week 2) — Accepting emotions

Day Time Situation	Emotion (What did you feel?) Intensity (Was the emotion mild, moderate, or strong?)	Level of acceptance of emotion, out of 10. (How able were you to accept the emotion, without judging, resisting, or trying to avoid the feeling?) Comments (Feel free to write about anything else you noticed in this experience)

Day/Time Situation Emotion	Thoughts Identify the 'hot thought' - the one that bothered you the most. Rate belief in hot thought out of 10	What evidence supports the hot thought?	What evidence goes against the thought?	Name any thinking traps you might be getting stuck in. Re-rate belief in thought /10	What is a more helpful or balanced alternative thought?

Day/Time Situation Emotion	Thoughts Identify the 'hot thought' - the one that bothered you the most. Rate belief in hot thought out of 10	What evidence supports the hot thought?	What evidence goes against the thought?	Name any thinking traps you might be getting stuck in. Re-rate belief in thought /10	What is a more helpful or balanced alternative thought?

Spare form (Week 4) — Graded exposure

Task	Predicted anxiety	Date to complete task	Done	Actual anxiety experienced
	Very low (1/10)	- - - - -	☐ ☐ ☐ ☐ ☐	/10
		- - - - -	☐ ☐ ☐ ☐ ☐	/10
	Low (3/10)	- - - - -	☐ ☐ ☐ ☐ ☐	/10
		- - - - -	☐ ☐ ☐ ☐ ☐	/10
	Medium (5/10)	- - - - -	☐ ☐ ☐ ☐ ☐	/10
		- - - - -	☐ ☐ ☐ ☐ ☐	/10
	High (7/10)	- - - - -	☐ ☐ ☐ ☐ ☐	/10
		- - - - -	☐ ☐ ☐ ☐ ☐	/10
	Very high (9/10)	- - - - -	☐ ☐ ☐ ☐ ☐	/10
	The worst possible anxiety (10/10)	- - - - -	☐ ☐ ☐ ☐ ☐	/10

Spare form (Week 4) — Graded exposure

Task	Predicted anxiety	Date to complete task	Done	Actual anxiety experienced
	Very low (1/10)	- - - - -	□ □ □ □ □	/10
		- - - - -	□ □ □ □ □	/10
	Low (3/10)	- - - - -	□ □ □ □ □	/10
		- - - - -	□ □ □ □ □	/10
	Medium (5/10)	- - - - -	□ □ □ □ □	/10
		- - - - -	□ □ □ □ □	/10
	High (7/10)	- - - - -	□ □ □ □ □	/10
		- - - - -	□ □ □ □ □	/10
	Very high (9/10)	- - - - -	□ □ □ □ □	/10
	The worst possible anxiety (10/10)	- - - - -	□ □ □ □ □	/10

Spare form (Week 4) — Behavioural activation goals

Difficulty / enjoyment level	Activity goal (What you would like to be doing)	Barriers (What could get in the way of you achieving this goal?)	Solutions (What you can do to overcome these barriers to achieve the goal)
1			
2			
3			
4			
5			
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8			
9			
10			

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Spare form (Week 4) — Behavioural activation plan & evaluation

Day & time	Activity	Done	Pleasure experienced (out of 10)	Mastery experienced (out of 10)
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		
		☐		

Spare form (Week 4) — Behavioural activation goals

Difficulty / enjoyment level	Activity goal (What you would like to be doing)	Barriers (What could get in the way of you achieving this goal?)	Solutions (What you can do to overcome these barriers to achieve the goal)
1			
2			
3			
4			
5			
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10			

Spare form (Week 4) — Behavioural activation plan & evaluation

Day & time	Activity	Done	Pleasure experienced (out of 10)	Mastery experienced (out of 10)
		☐		
		☐		
		☐		
		☐		
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		☐		

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Glossary — Explaining key terms

Acceptance: Being able to accept a difficult or upsetting feeling, situation, or thought. Accepting this means being okay with it happening and not trying to stop it or escape from it. Accepting also means not judging the thought/feeling or blaming yourself for having it.

Avoidance: Trying not to experience something unpleasant — such as an upsetting feeling or thought. This might mean distracting yourself, drinking alcohol or taking drugs, or not putting yourself in situations which make you feel or think that way.

Behaviour: Any action you choose to take or not take. Behaviours can also be a reaction, or how you respond to something that happens. Finally, a behaviour can also mean not taking an action or not responding to something that happens.

Behavioural Activation: Becoming more active and getting involved in activities or events. This lets you experience *mastery* and *pleasure* (described below).

Emotion: Any feeling you may have, e.g. sadness, happiness, worry, fear, anger, guilt, shame etc. Sometimes emotions may feel physical (i.e. a knot in your stomach, faster heart beat, dry mouth, nausea etc.).

Graded Exposure: A structured, planned way of facing your fears. This means putting yourself in situations you would normally avoid because they make you feel upset in some way — such as anxious, afraid, or sad.

Hot thought: In a situation where you are very distressed, you will have a few thoughts which are linked with that feeling. The hot thought is the one which is the most intense, or most upsetting to you.

Mastery: The feeling of achievement, accomplishment, or pride you experience when you do something difficult or challenging — how you feel when you succeed in a goal you have set.

Pleasure: The feeling of enjoyment you experience when you do something fun.

Thinking trap: Making a mistake in your thinking, based on assumptions or a lack of information. This can lead to more negative thoughts and make you more distressed. It can also happen automatically without you realizing.

Thought: The 'inner voice' or self-talk that goes on in your head. A lot of the time, thoughts are automatic — they pop into your head, often without you realizing and outside of your control.

If you would like more support with managing depression or anxiety, please contact your general practitioner (GP). The below services may also be helpful:

LifeLine — Crisis support and suicide prevention

13 11 14

Beyond Blue — Information and resources for depression and anxiety

http://www.beyondblue.org.au

Assessment and Crisis Intervention Service (ACIS) — Emergency Mental Health Service

13 14 65

Hepatitis SA — Hepatitis C information and support

8362 8443

MOSAIC — Hepatitis C counselling and support

8245 8100

In emergencies, contact:

000 EMERGENCY

This booklet was designed by Ben Stewart in consultation with psychologists, doctors, and researchers in the area at the University of Adelaide, University of South Australia, and the Royal Adelaide Hospital. The concepts and activities contained within this booklet are drawn from a variety of academic sources. This booklet and the material contained within is provided solely for your personal use and should not be distributed or presented in public forums.

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Appendix 2: C-UP treatment protocol

The following appendix contains the treatment protocol for C-UP, to be used by clinicians, in conjunction with the treatment booklet found in Appendix 2, to guide their transdiagnostic treatment of depression and anxiety in people living with CHC. This appendix is divided into five sections detailing the five separate weeks designed to be used sequentially with the client. The clinician may take more or less time to complete each section or week with the client, depending on their individual circumstances.

A.2.1. Week 1: What is depression and anxiety?

Objectives:

1. Explain the purpose, structure, and content of C-UP to the participant.

2. Work with the participant to set clear and achievable goals for C-UP.

3. Give the participant a basic understanding of depression and anxiety in the context of chronic hepatitis C (CHC).

4. Give the participant a basic understanding of the relationship between cognitions, emotions, physical sensations, and behaviours in the CBT model which C-UP is built on.

5. Set homework tasks.

Details:

1. Explain the purpose, structure, and content of C-UP to the participant.

While it is anticipated that there should be a reduction in symptoms of depression and anxiety through the administration of C-UP, this is not the sole purpose of the program. The primary aim of the program is to foster the capacity to cope with and better manage depression and anxiety. It should be emphasised to participants that C-UP is not intended to be a cure or that depression or anxiety will disappear forever. The structure of C-UP should be covered, including: the number and length of sessions; the expectations of homework activity – which is set collaboratively; and the expectation that the content and strategies learnt will be built upon following the completion of C-UP.

2. Work with the participant to set clear and achievable goals for C-UP.

The provider should work collaboratively with the participant to set goals to achieve while in C-UP. These goals need to be specific and clearly defined, realistic and achievable within the time frame of C-UP, and measurable or capable of being evaluated.

3. Give the participant a basic understanding of depression and anxiety in the context of CHC.

Information should be delivered to the participant regarding depression and anxiety. This includes: what distinguishes the moods of depression and anxiety from clinical disorders (an interaction of severity, distress, and impact on functioning); signs and symptoms; prevalence; and aetiology. This discussion and the accompanying in-session exercises can facilitate a conversation and better understanding of the context in which their symptoms have manifested to the provider. If not, the provider should make particular effort to examine the context in which these symptoms manifest (or triggers) - i.e. is the anxiety centred mostly on social performance/judgement or is depression mostly manifested in poor mood or anhedonia?

4. Give the participant a basic understanding of the relationship between cognitions, emotions, physical sensations, and behaviours in the CBT model which C-UP is built on.

Information should be given to participants about the CBT model and the bi-directional interactive relationships between cognitions, emotions, physical

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sensations, and behaviours in the context of emotional distress. This can lead to a discussion of how these factors can maintain and compound on each other, increasing distress, and, conversely, how manipulation of these factors can be used to de-escalate and alleviate distress.

In-session exercises:

1. Formulate goals for C-UP in collaboration with treatment provider and write in booklet. Goals should be clear, achievable, and measurable.
2. Discuss and write what they think causes depression/anxiety.
3. Discuss and write how prevalent depression and anxiety are.
4. Discuss and write what symptoms they have experienced.
5. Discuss and write details regarding a recent distressing situation and associated emotions, physical sensations, cognitions, behaviours.

Homework exercises:

1. Read Week 1 section in booklet.
2. Complete Activity: "What does depression/anxiety mean to you?"
3. Complete Activity: "Is there anything about hepatitis C you have found difficult emotionally?"
4. Think of and write down details regarding recent distressing situation and associated emotions, physical sensations, cognitions, behaviour (preferable for at least 3, if not 7 -one each day)

A.2.2. Week 2: Managing emotions

Objectives:

1. Review previous week – including lessons learnt, homework exercises, and any significant events.
2. Educate participant about the positive and negative effects of emotions.
3. Educate participant about the effect of avoiding emotions.
4. Educate participant about the effect of accepting emotions.
5. Set homework tasks.

Details:

1. Educate participant about the positive and negative effects of emotions.

Discuss with participants the positive and negative effects of 'good' and 'bad' emotions. Participants are likely to be able to identify the positive effects of good emotions and negative effects of bad emotions but may need help identifying reasons and examples for the alternatives. For example, a negative effect of a good emotion could be the complacency that might be induced if we were constantly happy, sapping motivation for progress or advancement. A positive effect of a bad emotion could be how when in grief, the sadness motivates us and others around us to martial for support and process the loss in order to move on and recover. Other examples can be used from the booklet. This discussion should lead into an example of when a bad emotion has had a positive effect on the participants' life.

2. Educate participant about the effect of avoiding emotions.

Discussion of the positive effect of bad emotions can lead into a conversation about how avoidance of emotions is counterproductive. Provide examples to the participant about how people commonly avoid emotions. Mention can be made of avoiding cognitions and behavioural avoidance but the focus should be specifically on emotional avoidance for this week. Discussion of emotions which the participant struggles with and the ways in which they avoid will be useful for putting this learning into context and planning practice of emotional acceptance and later graded exposure activities.

3. Educate participant about the effect of accepting emotions.

Discuss the alternative action of accepting emotions. Participants should be encouraged to act as a third-person observer of their emotions, noticing what feelings arise without attempts at judgement, criticism, avoidance, distraction, suppression. Participants should be aware that emotions are not necessarily fact or truth, do not need to be reacted to or acted upon, and do not reflect on who they are as a person. If the participant doesn't grasp the ocean waves example used, the quicksand metaphor for emotional acceptance may be used.

In-session exercises:

1. Discuss and write 3 emotions the participant struggles with or tries to avoid at times.

2. Practice accepting an emotion by recalling a recent distressing incident, noticing what emotions or thoughts arise, commentating on these events and their acceptance of it using the script provided.

Homework exercises:

1. Read Week 2 section in booklet.

2. Practice accepting difficult emotions over the next week and fill out table evaluating experience with this strategy (preferable for at least 3, if not 7 - one each day).

A.2.3. Week 3: Thinking well

Objectives:

1. Review previous week – including lessons learnt, homework exercises, and any significant events.
2. Educate participant about how negative thoughts can escalate distressing emotions and maladaptive behaviours.
3. Educate participant about thinking traps.
4. Educate participant about assessing thought validity.
5. Set homework tasks.

Details:

1. Educate about how negative thoughts can escalate distressing emotions and maladaptive behaviours.

Drawing back to Week 1's lessons on how thoughts, emotions, physical sensations, and behaviours influence and are influenced by each other, discuss with participants how negative thoughts can feed into worse mood and maladaptive behaviours, which in turn lead to further negative thoughts, and so on. The example used in the booklet talks about depressed mood, poor motivation, thoughts centred on helplessness and hopelessness, and behavioural dis-engagement. Anxiety examples can be used also to consolidate these points, by explaining the panic cycle of cognitive misinterpretation of increasing physical sensations and anxiety leading to avoidance.

2. Educate participant about thinking traps.

Discuss with the participant how these negative thoughts are sometimes accurate and sometimes inaccurate. Inaccurate negative thoughts often involve a common set of thinking errors or traps. Emphasise how the automatic nature of these thoughts and the emotional distress during which they occur make it harder to pick up on thinking errors/traps.

3. Educate participant about assessing thought validity.

Discussion of thinking errors/traps can lead into a conversation about how this can be rectified - through taking the third-person observer stance as with acceptance of emotions, and assessing the evidence for thoughts. Depending on the type of thought, different types of research can be conducted in order to assess the evidence for and against thoughts. Once this is identified, a more adaptive, balanced alternative thought can be generated. Repetition of this process can foster automaticity in the future.

In-session exercises:

1. Discuss and write about a recent distressing situation, identify a hot thought and belief in that thought.
2. Identify a thinking trap from the thoughts associated with a recent distressing situation.

Homework exercises:

1. Read Week 3 section in booklet.

2. Practice cognitive restructuring over the next week and fill out table evaluating experience with this strategy (preferable for at least 3, if not 7 - one each day).

A.2.4. Week 4: Behavioural choices – What can you do?

Objectives:

1. Review previous week – including lessons learnt, homework exercises, and any significant events.

2. Educate participant about behavioural avoidance.

3. Educate participant about, and formulate plan for, graded exposure.

4. Educate participant about, and formulate plan for, behavioural activation.

5. Set homework tasks.

Details:

1. Educate participant about behavioural avoidance.

Firstly, the participant must have an idea of what behaviour means – basically about the choices made about what to physically do. These choices can be in reaction to something or (seemingly) spontaneous, and they can be active (doing something) or inactive (avoiding doing something). In discussing behavioural avoidance, the link with past discussions of experiential avoidance of emotions/cognitions can be used to help explain the concept. Examples of learning behaviour in animals (rewards vs. punishments) can be used to explain how the brain makes associations in the context of anxiety and avoidance. The generalisation of anxiety to other areas is important to emphasise. This can be explained by assessing the usefulness (in terms of survivability) of being anxious of red-back spiders versus all spiders.

2. Educate participant about, and formulate plan for, graded exposure.

Discussion around avoidance and how it maintains or increases anxiety can be used to begin a discussion of the remedy of graded exposure or facing your fears. Work collaboratively with the participant to formulate a plan for graded exposure. While the participant might be anxious about a multitude of things, this plan should focus on one area as they can then apply this knowledge and skill afterwards to other areas of anxiety. The participant may choose the area to focus on, preferably an area which does induce a significant amount of anxiety and which impedes on their ability to function in some way, such as social anxiety. The plan needs to have clear, achievable goals, evenly spaced with regard to the anxiety they are expected to induce. Participants should be encouraged to complete each task numerous times until they are comfortable with it, before moving on to the next task of higher predicted anxiety.

3. Educate participant about, and formulate plan for, behavioural activation.

The concepts of pleasure and mastery should be explained first to the participant, and how these are normally affected by activities and how this changes in the context of depression. Discussion can return to the previous week's example of the depressive cycle of low mood and motivation, inactivity, and negative thoughts. In explaining how scheduling of activities to induce pleasure and mastery works in interrupting this cycle, emphasis should be placed on how beginning activities may not stimulate a huge amount of

pleasure/mastery but that over time, repeated practice will facilitate success (in other words, fake it until you make it). As with graded exposure, the formulation of the behavioural activation plan needs to be collaborative and involve multiple steps which are evenly spaced and account for the entire range of difficulty and potential for experience of pleasure and/or mastery. Scheduling of activities which can induce both pleasure and mastery simultaneously should be prioritised.

In-session exercises:

1. Discuss and write about three situations or locations which are avoided, and the emotion which is circumvented through this avoidance.
2. Formulate plans for graded exposure and behavioural activation in consultation with provider.

Homework exercises:

1. Read Week 4 section in booklet.
2. Complete tasks set for graded exposure and behavioural activation and record experiences.
3. Return in two weeks.

A.2.5. Week 5: How to stay well?

Objectives:

1. Review previous fortnight – including lessons learnt, homework exercises, and any significant events.
2. Review C-UP as a whole.
3. Educate participant about relapse prevention and formulate a relapse prevention plan.
4. Set homework tasks.

Details:

1. Educate participant about relapse prevention and formulate relapse prevention plan.

As has been discussed throughout C-UP, it should be emphasised that removing depression and anxiety forever is not the goal of this program, and indeed, impossible as these emotions are a natural part of human experience. However, steps can be taken towards preventing the escalation of these experiences into what is considered disordered. This can be achieved by preparing the ability to identify when action needs to be taken and determining what action needs to be taken. Discuss with participants how they can identify when they are well, becoming unwell, and when they are unwell. Focussing on thoughts, emotions, and behaviours as the participants have been trained throughout C-UP to observe these. Functional indicators are also important. In terms of action taken, increasing self-reliance and reducing dependency on

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services is important, as is reducing the risk brought about by avoidance of professional services in the pursuit of self-reliance. The participant should be encouraged to rely on the skills they have learnt, and utilise external supports when those steps fail or when those steps are inappropriate (i.e. in the event of a crisis or when feeling suicidal). Participants can also be encouraged to use their social support network at earlier stages of relapse.

In-session exercises:

1. Formulate relapse prevention plan using the form on p. 28 of the booklet.

Homework exercises:

1. Read Week 5 section in booklet (preferably re-read entire booklet).
2. Continue with graded exposure and behavioural activation plans as required.
3. Work on particular skills using spare forms as required.
4. Follow relapse prevention plan as required.

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