# PROSPECTIVE MEMORY AND SOCIAL COGNITION IN PEOPLE WITH CHRONIC HEART FAILURE

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# List of Abbreviations

ACE-R: Addenbrooke's Cognitive Examination – Revised

**CHF:** Chronic heart failure

HADS: Hospital Anxiety Depression Scale

IADL: Instrumental Activities of Daily Living

**MMSE:** Mini Mental State Examination

NYHA: New York Heart Association

**PM:** Prospective memory

RAVLT: Rey Auditory Verbal Learning Test

**SCHFI:** Self-care Heart Failure Index

**SMD:** Standard mean difference

TMT: Trail Making Test

ToM: Theory of mind

#### Abstract

People affected by chronic heart failure (CHF) suffer from diffuse brain pathology and are consequently at a higher risk of developing cognitive impairment. The aim of this thesis was to examine two areas of cognition in people with CHF, namely prospective memory (PM) and social cognition. This aim was addressed in a series of three experiments. PM and social cognition have not previously been assessed in the CHF population; however, because both of these cognitive processes rely on brain regions that are commonly damaged in people with CHF, it was expected that these areas of cognition would be impaired.

Study 1 assessed PM function, or the ability to remember to perform tasks in the future, in a CHF sample (n = 30) and demographically matched controls (n = 30). A comprehensive cognitive test battery including measures of general cognition was administered. Additionally, a behavioural measure of PM was used. The CHF sample had deficits in some, but not all, general cognitive domains. The key findings of this study showed that the CHF sample had pervasive but modest PM deficits, compared to healthy controls.

Study 2 tested the possibility raised by Study 1 that PM deficits may impair patients' ability to adequately manage their CHF. Study 2 used the same sample as Study 1 (n = 30). The relationship between CHF self-care and other more general cognitive processes was also assessed. Self-care was assessed using the Self-care Heart Failure Index, and medication adherence and functional independence were also assessed. Overall, the findings did not show a statistically significant relationship between cognitive ability and self-care. Finally, Study 3 examined social cognition in people with CHF (n = 31) and demographically matched controls (n = 38). Two core aspects of social cognition were examined: emotion recognition – the ability to correctly distinguish emotions displayed by others; and Theory of Mind (ToM) – the ability to make inferences about the mental states of others. A comprehensive cognitive test battery including measures of more general cognition was also administered. The CHF sample showed deficits on some, but not all cognitive domains, but general memory was preserved. There were no differences in either of the social cognitive constructs between the CHF and control groups. However, in the CHF group, there was a significant positive correlation between global cognition and both emotion recognition and ToM.

A major feature to emerge in the sequence of studies was that, compared to existing CHF studies, the CHF group in this thesis had relatively high cognitive performance and good health status. Prior to this thesis, the pattern of cognitive performance and the significance of cognitive deficits in similar, high functioning CHF groups, were not understood. Despite some cognitive decline, the CHF sample had good abilities to manage day-to-day tasks. The findings of this thesis emphasise that disease management programs should reflect the abilities and needs of the individual.

#### Declaration

This thesis contains no material published elsewhere or extracted in whole or in part from a thesis by which I have qualified for or been awarded another degree or diploma. No parts of this thesis have been submitted towards the award of any other degree or diploma in any other tertiary institution. No other person's work has been used without due acknowledgement in the main text of the thesis.

The ethical principles and procedures specified by the Australian Catholic University's policy document on Human Research and Experimentation have been adhered to in the preparation of this report

Signed

Halen 5/2/2016

Date

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#### **CHAPTER 1: Introduction and Thesis Outline**

#### **1.1 Background and Rationale**

People affected by chronic heart failure (CHF) suffer from diffuse brain damage (Vogels, van der Flier, et al., 2007; Woo, Macey, Fonarow, Hamilton, & Harper, 2003) and have a higher risk of developing cognitive impairment in a number of different domains (Pressler, 2008; Vogels, Oosterman, van Harten, Scheltens, et al., 2007; Vogels, Scheltens, Schroeder-Tanka, & Weinstein, 2007). Findings from pathology studies indicate that damage most frequently occurs to frontal, and to a lesser degree, temporal neural structures (Almeida et al., 2012; Artero et al., 2004; de Leeuw et al., 2001; Kalaria et al., 2004; Vogels, Oosterman, van Harten, Gouw, et al., 2007; Woo, Kumar, Macey, Fonarow, & Harper, 2009; Woo et al., 2003). Importantly, the cognitive impairment that results from this brain pathology has been associated with poorer adherence to CHF self-care (Currie, Rideout, Lindsay, & Harkness, in press), a key non-pharmacological intervention for CHF (Krum et al., 2006).

Although there is substantial research into general cognitive processes in people with CHF, no prior research has examined two specific areas of cognition, namely prospective memory (PM) and social cognition. It seems likely that the cognitive deficits experienced by people with CHF would extend to deficits in PM and social cognition. This is because CHF patients have cerebral abnormalities in frontal and temporal brain regions – areas that are implicated in these processes. This thesis examined a series of questions relating to these specific cognitive processes in people with CHF who are *not* affected by dementia. Each of these is introduced below. First, PM is the ability to remember to perform tasks at some point in the future, such as remembering to take medication or turning off safety appliances at designated time points (Maylor, 1990). PM is not only critical for daily functioning (McDaniel & Einstein, 2007), but this cognitive ability might also be especially relevant for patients with CHF who are required to complete daily *self-care* tasks to manage their chronic illness (Riegel et al., 2004).

Despite how important it is for people with CHF to adhere to self-care recommendations, adequate self-care continues to be difficult for most patients to achieve (Lee, Moser, Lennie, & Riegel, 2011; Moser & Watkins, 2008). Cognitive impairment is one of the multiple factors that impairs self-care (Currie et al., in press). It is not yet known whether there is a relationship between PM function and self-care behaviours. Thus, more research is needed to expand our knowledge of associations between specific cognitive processes that impede optimal self-care.

The final focus of this thesis is emotion recognition and theory of mind (ToM) in people with CHF. These processes are the two core aspects of social cognition. They represent the ability to perceive and correctly distinguish emotions displayed by others (Adolphs & Janowski, 2011), and the ability to make inferences about the mental states of others (Frith & Frith, 2005). Social supports play an important role in CHF health outcomes (Luttik, Jaarsma, Moser, Sanderman, & van Veldhuisen, 2005); therefore the study of social cognition is important in people with CHF because interpersonal relationships critically depend on social cognition (Grossmann, 2010).

#### **1.2 Context of Thesis Project**

The studies included in this thesis were embedded within a larger study (Evaluation of a Heart Failure Screening Tool: Heart-FaST). Therefore, all 2

participants in this thesis were recruited from a pool of participants taking part in the parent study.

This thesis contains four separate papers in the form of published or submitted manuscripts: one Protocol Paper and three original studies. The first three manuscripts (the Protocol Paper and first two studies) focus on aspects of PM function in CHF. The fourth manuscript focuses on social cognition in this group. The first manuscript presents the protocol for the first and second original studies. Study 1 and Study 2 used the same sample, but analysed and presented different variables. Cognitive data from Study 1 were used in Study 2, but additional health-related data for Study 2 were collected at a separate time. A subset of the sample in Study 1 and Study 3 is the same. Figure 1.1 represents the structure of the thesis and the relationship between studies.



Figure 1.1. Structure of thesis and the relationship between studies.

#### **1.3 Structure of Thesis and Study Aims**

The literature reviewed for this thesis is covered in three separate chapters. These review chapters are presented first, followed by each of the four individual manuscripts. Throughout the review chapters, each of the major gaps in the literature will be highlighted. The first literature review (Chapter 2) provides an overview of what is currently known about the association between CHF and cognitive performance, and the relationship between cognitive impairment and self-care. Chapter 2 describes the gaps in existing literature that are addressed within the individual manuscripts.

The second literature review (Chapter 3) provides a detailed overview of PM, developments in the literature over time, and the relationship between PM function and general cognitive abilities. The literature review in this chapter provides the necessary background for the first two studies that focus on the investigation of PM function in people with CHF, and the relationship between PM and self-care.

The third and final review (Chapter 4) presents the existing literature relating to social cognition specifically, and the relationship between emotion recognition and ToM and other more general cognitive processes. This review chapter provides the rationale for the third and final study of this thesis, which examines emotion recognition and ToM abilities in people with CHF.

Paper 1 (Chapter 5) is a protocol that describes the rationale and methodology for the investigation of PM in people with CHF, and the association between PM and self-care.

Study 1 (also Chapter 5) examined PM performance in a group of CHF patients, compared to a group of matched controls. The aims of the study were to:

- Provide the first empirical comparison of PM performance of people with CHF and demographically matched controls;
- Assess whether deficits in PM ability vary according to different types of PM tasks, or whether the deficits are pervasive across all PM tasks; and
- Explore whether PM ability in patients with CHF is related to more general cognitive functioning.

The results of Study 1 showed that patients with CHF had deficits in PM, which were consistent across different types of PM tasks. Therefore, Study 2 (Chapter 6) extended on these findings by investigating whether the PM deficits observed in patients with CHF were related to their self-care behaviours. The aims of the study were to:

- Investigate whether overall PM performance is related to self-care maintenance and management behaviours; and
- Examine whether more general cognitive abilities, such as verbal memory, executive functions, and global cognition is related to self-care maintenance and management behaviours.

Study 3 (Chapter 7) investigated social cognition, the second focus area of this thesis. The aims of this study were to:

- Compare the two key social cognitive abilities, emotion recognition, and ToM of a group of CHF patients, to a group of healthy controls; and
- Investigate whether emotion recognition and theory of mind are associated with general cognitive abilities in people with CHF.

Although each individual study discusses limitations, implications, and future directions, these areas are discussed from a broader perspective in the general discussion chapter (Chapter 8). The final review chapter demonstrates that the CHF sample in this thesis had higher cognitive performance, better health status, and better abilities to manage day-to-day tasks, compared to existing CHF studies. At present, the approach to disease management consists of generalised rather than tailored intervention. Chapter 8 discusses how the results of the original research in this thesis show that interventions should be tailored to the needs of the individual. More specifically, in order to optimise the management of this complex condition, interventions should target individuals with high needs, such as people with poor cognitive performance, poor health status, and those who have difficulties with management of day-to-day tasks.

A research portfolio, the ethics approval letters from the Australian Catholic University and Eastern Health Ethics Committees, and the measures used in the thesis are included in Appendices A to D.

# CHAPTER 2: Selective Review of Literature Examining the Association Between Chronic Heart Failure, Brain Pathology and Cognitive Impairment

### 2.1 Scope and Focus of Review

People with CHF suffer from widespread brain damage and have a higher risk of developing cognitive impairment in a number of domains (Bennett & Sauvé, 2003; Cameron, Worrall-Carter, Riegel, Lo, & Stewart, 2009; Vogels, Oosterman, van Harten, Gouw, et al., 2007; Vogels, van der Flier, et al., 2007; Vogels, Scheltens, et al., 2007). Findings from pathology studies indicate that cognitive impairment is most frequently caused or exacerbated by small vessel brain pathology, causing brain damage to frontal and temporal neural structures (Almeida et al., 2012; Artero et al., 2004; de Leeuw et al., 2001; Kalaria et al., 2004; Vogels, Oosterman, van Harten, Gouw, et al., 2007; Vogels, van der Flier, et al., 2007; Woo et al., 2009, 2003; Zuccalà et al., 1997). With the prevalence of both CHF and cognitive impairment rising with age, the simultaneous burden of both conditions will increase in the same individual (Heckman, Patterson, & McKelvie, 2007). Therefore, it is important to further understand the cognitive profile and impact of impairment in CHF.

The main focus of this chapter is to provide a review of existing research relating to general cognitive functioning of people with CHF. The first part of the chapter provides a broad view of cardiovascular diseases (CVD) and progression to CHF and self-care. The second part of the chapter provides a review of key epidemiological research on the association between CHF and cognitive impairment, and the relationship between cognitive impairment and self-care.

#### 2.2 Cardiovascular Disease and Risk Factors

Cardiovascular diseases (CVD) are pathological processes that affect the heart and blood vessels (Australian Institute of Health and Welfare, 2011). Plaque formation is one of the major pathological mechanisms involved in cardiovascular diseases. Plaque is characterised by an abnormal build-up of fat or cholesterol in the inner lining of the arteries (Australian Institute of Health and Welfare, 2011). The clinical manifestation of CVD varies depending on the type of pathology, and on which blood vessels are affected. The main form includes ischaemic heart disease (coronary artery disease). This may manifest in a number of the following ways: chronic angina; myocardial infarction and/or acute cardiac arrest; atrial fibrillation, which is a form of arrhythmia; cerebrovascular disease, including cerebrovascular accidents (strokes); and peripheral arterial disease, which affects the vessels in the legs and arms (Australian Institute of Health and Welfare, 2011; Lalor et al., 2012).

There are a number of cardiovascular risk factors (CRFs), both clinical and lifestyle, which have been linked to the development of CVD. The major clinical risk factors include hypertension, obesity, hypercholesterolemia, diabetes, and depression. On the other hand, lifestyle factors such as physical inactivity, poor nutrition, tobacco smoking, excessive alcohol intake, as well as advancing age have also been found to increase the development of CVD (Australian Institute of Health and Welfare, 2011; Lalor et al., 2012).

#### **2.3 Chronic Heart Failure Defined**

CHF is considered the severe and end-stage syndrome of CVD. CHF is a clinical syndrome resulting from multiple, long-standing cardiovascular abnormalities, most commonly: coronary artery disease and hypertension (Braunwald,

2013). It is a complex condition that is characterised by structural dysfunction and weakening of the heart. In its most common form, CHF impairs the ability of the left ventricle to either eject or fill adequately with blood to meet the metabolic needs of the body (particularly during physical activity) (Krum et al., 2006).

#### 2.3.1 Manifestation and classification of CHF

People with CHF experience a number of debilitating symptoms that impact on daily functioning and quality of life (Volz et al., 2011; Zambroski, Moser, Bhat, & Ziegler, 2005). Clinical signs and symptoms of CHF occur due to the physiological retention of sodium and fluid resulting in shortness of breath, cough (especially at night), weight gain, and peripheral oedema (swollen ankles, legs, and abdomen). As well, patients suffer from symptoms related to poor circulation, or low cardiac output. These symptoms include lethargy and fatigue, dizziness, arrhythmias, and reduced exercise tolerance (Krum et al., 2006; Krum, Jelinek, Stewart, Sindone, & Atherton, 2011).

The functional grading of CHF is typically based on the presentation and severity of symptoms. The New York Heart Association (NYHA) functional classification (Table 2.1) is used in Australian clinical practice (The Criteria Committee of the New York Heart Association, 1994). The NYHA provides a simple classification by placing patients in one of four categories based on symptoms of breathlessness with varying degrees of activity.

#### **Table 2.1:**

Class	Patient symptoms
Ι	No limitation on physical activity. Normal physical activity does not cause
	fatigue, dyspnoea or palpitations. Asymptomatic dysfunction.
II	Slight limitation of physical activity. Ordinary physical activity results in
	fatigue, palpitation, dyspnoea or angina pectoris. Mild CHF.
III	Marked limitation of physical activity. Less than ordinary physical activity
	leads to symptoms. Moderate CHF.
IV	Unable to undertake any physical activity without discomfort. Symptoms of
	CHF present at rest. Severe CHF.

New York Heart Association Functional Classification

The management of CHF is aimed at reducing symptoms and improving quality of life and survival. There are three primary components of CHF management: 1) pharmacological management, 2) surgical procedures and supporting devices, and 3) non-pharmacological interventions (Krum et al., 2006). The first two aspects are beyond the scope of this thesis. A review of the key non-pharmacological intervention, CHF self-care, is presented in Section 2.4.

## 2.3.2 Individual and economic burden.

Despite a recent decline, Australia still has one of the highest rates of CVD in the world (Australian Institute of Health and Welfare, 2011). CHF affects an estimated 1.5% to 2% of Australians, with approximately 30,000 new cases diagnosed each year (Australian Institute of Health and Welfare, 2011). The burden of CHF increases markedly with age; 1% of people aged 50 to 59 years have this condition; 10% of people aged 65 years and older; and over 50% of people aged 85 years and older (Australian Institute of Health and Welfare, 2011). As the diagnosis is commonly missed in mild to moderate cases, the actual number of people affected could be as high as twice the estimates (Yancy et al., 2013). The ageing population, combined with improved survival after an acute cardiovascular event will lead to a CHF epidemic in Australia within the next two decades (Campbell, 2003; Horowitz & Stewart, 2001; Krum, Tonkin, Currie, Djundjek, & Johnston, 2001).

CHF is characterised by poor health outcomes. Research has found that approximately 59% of men and 45% of women die within five years of the first onset of symptoms of the illness (Najafi, Dobson, & Jamrozik, 2006; Stewart, 2008). A large recent study reported that within one year of hospital discharge, readmissions occurred for 67.4% and death for 35.8% (Dharmarajan et al., 2015). Another study assessed the effect of incident CHF hospitalisation on subsequent mortality in a posthoc propensity-matched design (Ahmed et al., 2008). This involved 1057 pairs of patients: those with CHF hospitalisations during a two-year follow-up, and patients with no CHF hospitalisations; compared to 153 deaths in the latter group, 334 deaths occurred in the CHF hospitalisation group. Thus, patients hospitalised for worsening CHF had a 2.49 times greater risk of subsequent post-two-year mortality.

The relatively high prevalence of this condition and associated morbidity and mortality imposes a high cost of illness and economic burden on the health care system (Clark, McLennan, Dawson, Wilkinson, & Stewart, 2004; Lee, Chavez, Baker, & Luce, 2004; Smith et al., 2012). CHF ranks among the most costly diseases in developed countries, with 1% to 2% of all healthcare expenditure spent on CHF management (Liao, Allen, & Whellan, 2008). Most of the enormous cost associated with the care of people with CHF is the result of re-hospitalisation for exacerbation of symptoms (Liao et al., 2006, 2007). A study of the burden of CHF in Australia reported that, in 2000, there were an estimated 22,000 incidents of admissions for CHF, and approximately 100,000 admissions overall (Clark et al., 2004). It was also reported that healthcare expenditure was around 1.4 million days of hospitalisations at a cost of more than \$1 billion (Clark et al., 2004). As the prevalence of CHF increases, however, expenditure related to the care of people who are affected by CHF is expected to increase substantially (Smith et al., 2012). Given the burden of CHF on the individual and the economic system, a key focus of CHF treatment is on interventions that can improve outcomes post-discharge. Self-care behaviours are of particular focus in this thesis because of its reliance on complex cognitive processes (discussed in Section 2.5.4).

#### 2.4 Self-care

CHF *self-care* (Riegel, Moser, et al., 2009; Riegel, Jaarsma, & Strömberg, 2012; Riegel, Lee, & Dickson, 2011) is a key non-pharmacological therapy that significantly improves outcomes. The *middle-range theory* (Riegel et al., 2012) of chronic illness describes CHF self-care as a naturalistic decision-making process with three unique, but synchronous, elements. These include, *self-care maintenance, self-care management*, and *self-care confidence* (Riegel et al., 2012).

More specifically, *self-care maintenance* behaviours involve symptom monitoring and treatment that improves well-being, preserves health, or maintains physiological and emotional stability (Riegel et al., 2012); for example, adhering to complex medication regiments, restricting fluid intake, and actively monitoring signs and symptoms that may indicate an exacerbation of CHF (Krum et al., 2006, 2011; Riegel, Moser, et al., 2009). Another essential component of this process is weighing each morning after toileting and before dressing and breakfast (Krum et al., 2011; Riegel, Lee, et al., 2011) in order to monitor the body's fluid retention and prevent the occurrence of oedema.

Self-care maintenance is considered the foundation of *self-care management*. This is described as a decision-making process that begins with recognising a change in symptoms and then responding appropriately to worsening symptoms by engaging in active and constructive behaviours, or seeking medical advice (Riegel et al., 2004, 2012). For example, patients recognise a change such as increasing oedema, which is evident by an increase in weight of two kilos or more, evaluate the relevance of the symptom change, decide to take action, and implement a treatment strategy (e.g., taking an extra diuretic dose). The final step involves the evaluation of the response to the action implemented (Riegel et al., 2012). It has been suggested that patients who are most successful at self-care management are able to comprehend the meaning of changes, mentally stimulate options, and decide on an appropriate course of action (Riegel et al., 2012).

The last factor, *self-care confidence*, is not a part of the self-care process *per se*. However, the amount of confidence that a patient has in their ability to successfully carry out self-care behaviours influences the success of self-care maintenance and management (Riegel & Dickson, 2008). Indeed, one recent study found that cognitively impaired patients had less confidence with self-care management (Levin et al., 2014).

#### 2.4.1 Self-care adherence.

Adherence to self-care slows the disease progress and prolongs survival (Lee

et al., 2011; Moser & Watkins, 2008). Research has found that patients who engaged in above average self-care management had a 56% reduction in the risk of all-cause mortality, hospitalisations, or emergency room admission, compared to people who engaged in below-average self-care (Lee et al., 2011). Furthermore, symptomatic CHF patients who were more engaged in self-care management had an event risk (i.e., mortality, hospitalisations, and emergency admission) that was almost equivalent to those who were symptom-free; however, a systematic review found that nonadherence continues to be a major problem (Wal, Jaarsma, & Veldhuisen, 2005). One large study involving 2082 patients from developed and developing countries found that self-care performance was inadequate on all scales and groups (Riegel, Moser, et al., 2009).

*Medication behaviours.* Medication adherence continues to be a problem amongst people with CHF. A systematic literature review of 50 studies (Wu, Moser, Lennie, & Burkhart, 2008) reported varying rates (2% to 90%) of medication adherence, but most commonly adherence was reported to be between 40% and 50%. Medication non-adherence is a significant barrier to enhancing the effectiveness of treatment and one of the most relevant predictors of poor health outcomes in CHF (Molloy, O'Carroll, Witham, & McMurdo, 2012). Specifically, non-adherence to medication has been shown to be responsible for the majority of readmissions for CHF in the United States (Heidenreich, 2004; Ho, Bryson, & Rumsfeld, 2009; Murray et al., 2009; Murray et al., 2004). It has also been reported that medication nonadherence was related to higher risk of cardiac events or mortality (Wu et al., 2009; Wu, Moser, Chung, & Lennie, 2008). A recent trial linked medication non-adherence (defined as < 80%) to all-cause mortality and cardiovascular hospitalisation

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(Fitzgerald et al., 2011). Furthermore, one large study found that medication adherence independently predicted cardiac event-free survival over a three-and-a-half year period (Wu, Lennie, Dekker, Biddle, & Moser, 2013). More specifically, the risk of a cardiac event for patients with medication non-adherence (and depressive symptoms) was five times greater than those who were medication adherent (and without depressive symptoms).

*Weighing, fluid restriction, and symptom monitoring.* Literature involving other self-care behaviours is relatively limited compared to medication adherence, but a number of individual studies have examined other key behaviours. For instance, studies have found that adherence to daily weighing ranges from 12% to 75% (de Lusignan, Wells, Johnson, Meredith, & Leatham, 2001; Jaarsma, Abu-Saad, Dracup, & Halfens, 2000; Michalsen, König, & Thimme, 1998; Moser, Doering, & Chung, 2005); adherence to recommendations for the control of a sodium-restricted diet vary from 50% (Jaarsma et al., 2000) to 88% (Carlson, Riegel, & Moser, 2001); and the lowest reported adherence rate for fluid intake was 23% (Jaarsma et al., 2000). Additionally, symptom-monitoring behaviours are performed infrequently. Several studies have identified that patients delay seeking help for symptom changes (Evangelista, Dracup, & Doering, 2002; Friedman, 1997; Parshall et al., 2001), between five to seven days, but dyspnoea duration ranged from 30 minutes to 90 days before action was taken (Jurgens, Hoke, Byrnes, & Riegel, 2009).

Multidimensional factors have been shown to affect the implementation of self-care behaviours. For instance, depression is common in CHF (Rutledge, Reis, Linke, Greenberg, & Mills, 2006) and can affect an individual's ability to acquire and maintain adequate self-care. Furthermore, factors such as access to relevant and appropriate information and lack of social support are also important influences of self-care (Cameron, Worrall-Carter, Riegel, et al., 2009; Driscoll, Davidson, Clark, Huang, & Aho, 2009; Moser & Watkins, 2008; Sayers, Riegel, Pawlowski, Coyne, & Samaha, 2008). It also seems likely that patients' difficulties partially reflect cognitive deficits. Therefore, more research is needed to understand factors that contribute to difficulties in achieving optimal self-care. Given that the focus of this thesis is on cognition, Section 2.5 provides a review of literature of vascular cognitive impairment.

#### 2.4.2 Assessment of self-care.

The most common way of assessing self-care behaviours in research studies is using the Self-care Heart Failure Index (SCHFI) (v6) (Riegel, Lee, Dickson, & Carlson, 2009) . This measure was used to assess self-care in Study 2 of this thesis. The SCHFI is a comprehensive self-report instrument of self-care practices, and is the only published measure of behaviours that are pertinent to the management of CHF. The SCHFI evolved from the middle-range theory of chronic illness (Riegel et al., 2012), and is made up of three subscales: *maintenance*, *management*, and *confidence*. The SCHFI has been extensively validated among CHF populations around the world, and is often used as a way to measure the effectiveness of education interventions (Cameron, Worrall-Carter, Driscoll, & Stewart, 2009).

Overall, the reliability of the SCHFI is adequate (alpha .76). Furthermore, factor analysis supported the construct validity of the scales, which was consistent with the underlying theory (Riegel et al., 2004). Reliability of the management (alpha .70) and confidence (alpha .82) scales are adequate, but the reliability of the maintenance scale was lower than desired (alpha .56). It might however be expected that the maintenance scale would have low reliability because these items reflect behaviours that are known to vary across different people (Riegel et al., 2004). One of the limitations of the SCHFI is that at present, there is no existing data on its ecological validity. Therefore, self-care outcomes as assessed by the SCHFI may not reflect self-care behaviours in real life.

So far, this literature review has focused on providing an introduction to CHF, and the management of this complex condition through self-care. The last section of this chapter focuses on a review of literature on vascular cognitive impairment, and the relationship between cognitive function and self-care performance; these are the key focus areas of this thesis.

## **2.5 Vascular Cognitive Impairment**

It is now widely recognised that people with CHF are at risk of cognitive impairment. The prevalence of cognitive deficits has been observed in as many as 50% of clinically stable outpatients and up to 80% of hospitalised patients (Bennett & Sauvé, 2003; Cameron, Worrall-Carter, Page, Riegel, et al., 2010; Dodson, Truong, Towle, Kerins, & Chaudhry, 2013; Miller et al., 2012; Pressler, 2008). This form of impairment, which is caused by, or associated with vascular factors, has been termed 'vascular cognitive impairment'. The term refers to the full continuum, ranging from mild deficits to severe cognitive dysfunction (Chertkow, Feldman, Jacova, & Massoud, 2013; Gorelick & Nyenhuis, 2013; Hachinski et al., 2006; Korczyn & Vakhapova, 2010; O'Brien et al., 2003; Rockwood, 2002). Earlier definitions of vascular-related cognition described a range from subclinical, mild cognitive impairment to severe impairment such as vascular dementia (Chertkow et al., 2013; Gorelick & Nyenhuis, 2013). The pathological processes for the full spectrum of syndromes are identical, and the difference between the two merely relates to the severity of the impairment (Mariani, Monastero, & Mecocci, 2007).

The more recent classification of cognitive impairment has been termed *neurocognitive disorders*. This classification is based on the diagnosis in the Diagnostic and Statistical Manual of Mental Disorders – fifth edition (DSM-5) (American Psychiatric Association, 2013), presented in Table 2.2. Similar to the original description, neurocognitive disorders range from delirium, followed by mild neurocognitive disorder to major neurocognitive disorder, and their specific aetiological subtypes (American Psychiatric Association, 2013). The cognitive impairment seen in CHF is often subtle in nature, and would not meet the clinical diagnosis of dementia; for example, one study found that mild cognitive impairment was detected in 73% of a sample who were believed to be a group without any impairment (Cameron et al., 2010). Therefore, given the prevalence of mild forms of cognitive disorder is described below.

## 2.5.1 Diagnostic criteria for mild neurocognitive disorder.

The criteria for neurocognitive disorders have been based on defined cognitive domains. These include areas such as: complex attention; executive function; learning and memory; language; perceptual-motor; and social cognition (American Psychiatric Association, 2013). Notably, each of these broad domains has already been investigated in the CHF population, except for social cognition (Study 3). Table 2.2 details the diagnostic criteria for mild neurocognitive disorder:

#### **Table 2.2:**

## DSM-5 Diagnostic Criteria

Diagnosis for mild neurocognitive disorder

- A. Evidence of modest cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition) based on:
  - 1. Concern of the individual, a knowledgeable informant, or the clinician that there has been a mild decline in cognitive function; and
  - A modest impairment in cognitive performance, preferably documented by standardised neuropsychological testing, or in its absence, another quantified clinical assessment.
- B. The cognitive deficits do not interfere with independence in everyday activities (i.e., at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications) but greater effort, compensatory strategies, or accommodation may be required.
- C. The cognitive deficits do not occur exclusively in the context of a delirium.
- D. The cognitive deficits are not better explained by another mental disorder (i.e., major depressive disorder, schizophrenia).

#### 2.5.2 Vascular processes and related neuropathology.

Vascular cognitive impairment develops through a range of processes. Most commonly, it includes factors such as the severity of cardiac dysfunction (Pressler, Subramanian, Kareken, Perkins, Gradus-Pizlo, Sauve, Ding, Kim, Sloan, Jaynes, et al., 2010; Vogels, Oosterman, van Harten, Scheltens, et al., 2007), duration of CHF (Ekman, Fagerberg, & Skoog, 2001; Vogels, van der Flier, et al., 2007), reduced cardiac output leading to inadequate cerebral perfusion and oxygenation, and accumulation of silent subcortical strokes (Artero et al., 2004; Bennett & Sauvé, 2003; Román, 2004; Saxena & Schoemaker, 1993; Siachos, Vanbakel, Feldman, Uber, & Simpson, 2005; Vogels, van der Flier, et al., 2007; Woo et al., 2003). Vascular-related cognitive impairment can also be caused by cardiovascular risk factors such as age (Insel & Badger, 2002), hypertension (Sierra, Doménech, Camafort, & Coca, 2012), and depression (Hawkins et al., in press; Insel & Badger, 2002; Li, Meyer, & Thornby, 2001), or through moderating effects like individual medication or drug interactions (Riegel, Moser, et al., 2009). In most cases however, the aetiology of cognitive impairment involves both cardiovascular risk factors and circulatory insufficiency. The degree of impairment usually develops gradually over years, and is not typically marked by discrete changes in cognition (Schmidtke & Hüll, 2005). An adaptation of the model of cognitive impairment (Figure 2.1) proposed by Bennett, Sauvé, and Shaw (2005) summarises the processes involved in vascular cognitive impairment discussed in this section.

One major substrate that causes cognitive impairment is large vessel disease, or cortical stroke, which is caused by atherosclerotic disease in a major cerebral artery (O'Brien et al., 2003). The other major form is small vessel disease, which results from pathology in the cerebral arterioles and manifests as small subcortical infarcts and/or white matter ischaemic lesions (Alosco, Brickman, et al., 2013; O'Brien et al., 2003; Román, Erkinjuntti, Wallin, Pantoni, & Chui, 2002; Vogels, van der Flier, et al., 2007). The most frequently observed cerebral abnormalities resulting from small vessel disease include diffuse regions of the subcortical white matter, particularly in the frontal lobes, and subcortical grey matter (Almeida et al., 2012; Artero et al., 2004; de Leeuw et al., 2001; Kalaria et al., 2004; Vogels, van der Flier, et al., 2007; Woo et al., 2009, 2003). Medial temporal and temporal-parietal regions have also been identified as areas of high vulnerability in the presence of grey matter loss (Almeida et al., 2012, 2013; Vogels, van der Flier, et al., 2007; Woo et al., 2009, 2003).



*Figure 2.1.* Summary of mechanisms involved in the development of cognitive dysfunction (Bennett et al., 2005).

## 2.5.3 Cognitive functioning.

Over the past decade, a growing body of research has examined cognitive functioning in people who are affected by CHF. Four literature reviews (Bennett & Sauvé, 2003; Cannon, McMurray, & Quinn, 2015; Hajduk, Kiefe, Person, Gore, & Saczynski, 2013; Pressler, 2008) and one meta-analysis involving 22 studies (Vogels, Scheltens, et al., 2007) have examined different aspects of cognitive functioning in CHF. Although direct comparisons between existing literature cannot be made due to considerable differences in measures used and patterns of results, the evidence strongly shows that deficits in a range of cognitive domains are observed in CHF. It also appears that in the broad CHF population, the type and severity of cognitive impairment may vary from patient to patient. This variability can probably be explained by differences in patient health characteristics (Cannon et al., 2015; Vogels, Scheltens, et al., 2007) and differences in the breadth of measures used (Cannon et al., 2015; Jak et al., 2009).

It would appear that the most commonly observed deficits include decreased attention and concentration, immediate and delayed memory loss, diminished psychomotor speed, and poor executive control (Alosco, Spitznagel, et al., 2013; Bauer et al., 2012; Bratzke-Bauer, Pozehl, Paul, & Johnson, 2013; Hjelm et al., 2012; Vogels, Oosterman, van Harten, Scheltens, et al., 2007; Vogels, Scheltens, et al., 2007). Other areas of cognitive function are also affected, including language, learning, verbal fluency, working memory, and visuospatial function (Bauer et al., 2012; Bratzke-Bauer et al., 2013; Kindermann et al., 2012; Pressler, Kim, Riley, Ronis, & Gradus-Pizlo, 2010).

#### 2.5.4 Relationship between cognitive impairment and self-care.

Many critical aspects of CHF self-care involve responding to cues such as changes in symptoms, and making decisions that are dependent on complex cognitive processes (Cameron, Worrall-Carter, Page, Riegel, et al., 2010). Therefore, poor selfcare does not simply reflect poor compliance. Rather, problems with general memory and attention may impair the perception and interpretation of insidious symptom changes (Dickson, Tkacs, & Riegel, 2007). Memory failures are also likely to impair patients' abilities to remember to perform self-care behaviours. Furthermore, problems with executive function may impair decisions in complex situations, such as interpreting CHF symptom changes and analysing the risks or benefits of implementing self-care actions (Alosco, Spitznagel, et al., 2013; Dickson et al., 2007). It has been argued that deficits in executive functions also contribute to difficulties mastering the complex task involved in complying with prescribed medications, dietary restrictions, and monitoring of fluid and weight (Heckman et al., 2007).

Research into the relationship between cognition and aspects of self-care is a developing area. A recent review described 10 studies that assessed this relationship (Currie et al., in press). Only one study did not support the association between cognitive function and self-care, but this surprising finding was explained by a small sample size of relatively young participants, and mixed methodology (Dickson, Lee, & Riegel, 2011). Additionally, firm conclusions could not be drawn from another because it included a small sample size and no statistical data were available; instead, only mean scores were reported (Riegel, Dickson, Goldberg, & Deatrick, 2007).

Significant associations between cognitive impairment and poorer medication adherence have been reported. Two studies assessed medication adherence using a medication adherence scale or estimator and conducted a comprehensive assessment of cognition (Hawkins et al., 2012; Riegel, Moelter, et al., 2011). Hawkins et al. (2012) found that compared to no cognitive impairment, medication adherence significantly worsened from 78% to 70% for patients with cognitive decline. Riegel and Moelter et al. (2011) also found that compared to participants without cognitive decline and excessive daytime sleepiness, those with mild cognitive impairment (i.e., attention) and excessive daytime sleepiness (which could impair self-care through its effects on cognition) were 2.5 times more likely to be non-adherent to medications. In this study, measures of general memory, working memory, processing speed, and premorbid intelligence were not, however, associated with medication adherence (Riegel, Moelter, et al., 2011). Furthermore, two studies found that reduced cognitive
impairment (i.e., executive functions) was independently associated with medication management (Alosco et al., 2012; Alosco, Spitznagel, et al., 2013), assessed with the Instrumental Activities of Daily Living scale.

Although no prior studies have investigated the relationship between PM function and medication behaviours in CHF, this relationship has been examined in other chronic diseases. A recent review (Zogg, Woods, Sauceda, Wiebe, & Simoni, 2012) found that overall, PM explained unique variance in medication management, when medication adherence was assessed using both self-report measures and electronic medication monitors. Although a review of this literature is beyond the scope of this thesis, these findings are important because they support the ecological validity of PM in the context of medication behaviours (Zogg et al., 2012).

Studies have also assessed the relationship between cognitive function and more global self-care behaviours, rather than medication behaviours specifically. Hajduk and Lemon et al. (2013) found that the average adherence to self-care activities, as assessed with the European Heart Failure Self-care Behaviour Scale, among patients with global cognitive impairment did not differ significantly from those without impairment (1-point difference; 45 point scale). However, impaired memory was associated with lower self-care scores, but not processing speed or executive functions. Five studies that used the SCHFI or European Heart Failure Selfcare Behaviour Scale also demonstrated significant relationships between cognitive impairment and adverse self-care effects, but some discrepant findings were reported. Using a cognitive screening measure, three studies (Cameron, Worrall-Carter, Page, Riegel, et al., 2010; Harkness et al., 2014; Lee et al., 2013) showed that self-care management (i.e., recognising symptoms of worsening CHF) was significantly poorer in patients characterised as cognitively impaired. However, self-care maintenance (i.e., daily weighing) was not consistently compromised.

More specifically, Cameron et al. (2010) found that participants with mild cognitive impairment were 1.27 and 1.33 times more likely to have inadequate selfcare management and confidence, respectively. There were, however, no significant differences in mean self-care maintenance scores between patients with and without cognitive impairment. By comparison, Lee et al. (2013) found that patients with mild cognitive impairment were 14% worse at self-care maintenance, 21% worse at selfcare management, and 51% had worse consulting behaviours. Additionally, Harkness et al. (2014) reported that participants with cognitive impairment also scored significantly lower on self-care management (12.5-point difference; 100 point scale). This study, however, did not report on the impact of cognitive impairment on selfcare maintenance. Despite the methodological differences of these studies, which make it difficult to synthesise results, these data support a strong relationship between cognitive impairment and self-care in people affected by CHF.

#### 2.6 Chapter Summary

This literature review has provided an overview of CHF, illustrating its complexity and burden to the individual and the economy. Self-care was discussed as a key non-pharmacological intervention, which continues to be difficult for many patients to carry out adequately. The second part of this review chapter demonstrated that there is a strong link between CHF pathology and cognitive impairment, and between cognitive decline and self-care. More research however is needed to understand additional factors that contribute to problems in achieving optimal selfcare. No prior research has examined PM function as one specific cognitive difficulty in people with CHF. The next chapter focuses on a review of PM literature.

# CHAPTER 3: Selective Review of Literature Examining Prospective Memory and its Relationship to General Cognitive Processes

#### **3.1 Scope and Focus of Review**

Prospective memory (PM) is one of the most frequent everyday memory challenges, with failures in PM accounting for over half of all memory problems (Maylor, 1990). PM is defined as the ability to remember to perform future intentions, and this type of memory is essential for the successful navigation of everyday life demands (McDaniel & Einstein, 2000). Therefore, the study of PM failures is important because it can have severe consequences on functional independence, for example, forgetting to take medication or forgetting to turn off dangerous appliances (Ellis & Freeman, 2008; Smith, Hunt, McVay, & McConnell, 2007).

Despite its critical role in daily functioning, PM has not routinely been included in clinical and research cognitive assessment batteries, and it is not part of any diagnostic criteria. The study of memory has largely focused on tests of retrospective memory, or the ability to recall information from the past when explicitly prompted (Lezak, Howieson, & Loring, 2004). This is reflected in clinical research and practice where most standard clinical tests of memory are retrospective memory tasks that involve learning and recall of word lists, brief written passages, or figures (Zogg et al., 2012).

In contrast to retrospective memory, the study of PM is a developing area of research that has only attracted research attention in the last two decades. Much of the existing research involving PM has historically focused on normal ageing. Two metaanalyses have shown that PM function declines considerably with age, particularly after the age of 60 (Henry, MacLeod, Phillips, & Crawford, 2004; Uttl, 2008). There is now also an evolving body of research focusing on PM in abnormal ageing (Maylor, Smith, Della Sala, & Logie, 2002; Shum & Fleming, 2009; Thompson, Henry, Rendell, Withall, & Brodaty, 2010; Will et al., 2009), and in various clinical groups (Foster, Rose, McDaniel, & Rendell, 2013; Griffiths et al., 2012; Henry, Rendell, Kliegel, & Altgassen, 2007; Kim, Craik, Luo, & Ween, 2009; Leitz, Morgan, Bisby, Rendell, & Curran, 2009; Mioni, Rendell, Henry, Cantagallo, & Stablum, 2013; Rendell, Gray, Henry, & Tolan, 2007; Terrett et al., 2014). However, no previous research has examined PM function in people who are affected by CHF. This is a surprising omission given that PM is necessary in order to successfully complete many self-care behaviours that people with CHF are expected to undertake; for instance, tasks involving adherence to medication regiments.

To begin this chapter, an adaptation of a common conceptual model of PM is presented (Figure 3.1). This model was chosen because it encompasses the core aspects of PM that will be discussed, and referred to, throughout this chapter. From this model some researchers have focused on the study of PM from a multiphase perspective, suggesting that PM involves four distinct phases (formation, retention, initiation, and execution) (Ellis, 1996; Ellis & Freeman, 2008). However, the study of these phases remains neglected. Furthermore, there is ongoing debate about the involvement of monitoring resources, i.e., whether detection of PM cues involves spontaneous processes and/or strategic ones, such as purposeful clock-checking (McDaniel & Einstein, 2000). The study of monitoring resources has primarily focused on two key task distinctions, namely monitoring of time cues or event cues. Recent studies have also focused on a second task distinction. This involves tasks that occur frequently or regularly versus those that are irregular or relatively infrequent. This literature remains limited, especially within real-life settings. Following a detailed discussion of these components of the PM model, a review of existing literature involving PM is discussed. This chapter concludes with a review of studies that have examined the relationship between PM function and more general cognitive processes.



Figure 3.1. Conceptual model of prospective memory (Zogg et al., 2012).

# 3.2 Prospective Memory Task Characteristics and Phases

PM function involves a series of steps, as illustrated in Figure 3.1. The first process involves forming an intention to carry out a task at some point in the future. This is followed by a time delay during which other, naturally occurring, activities are engaged and where the PM tasks are embedded. Consequently, the ongoing activities need to be interrupted or suspended, and attention shifted to allow completion of the PM task, as planned. These multiple processes have been classified into four distinct

phases (Ellis, 1996; Ellis & Freeman, 2008). To help explain these phases of PM, an example task will be used – remembering to fill a prescription at the chemist while out shopping.

The first phase is referred to as *formation* and involves encoding the original intention and planning the future task. Specifically, this phase involves the retention of intent (that you have decided to do something), retention of content (what you want to do – i.e., fill prescription), and retention of information about when this must occur (when you should retrieve and action the intent – i.e., when shopping) (Ellis, 1996; Ellis & Freeman, 2008).

The second phase is called *intention retention* (Ellis, 1996; Ellis & Freeman, 2008) and is the time period during which the intention must be maintained. This retention period can last from a few minutes, days, or even months. In the meantime, other tasks, referred to as 'ongoing tasks' are being completed. Typically, the cue to the PM task is embedded in the ongoing task. During the interim activity (ongoing task), the individual must switch attention from the ongoing task in order to perform the PM task successfully (Einstein & McDaniel, 1996). In the example task, the retention phase is the period of time from when the doctor writes the prescription, to when the individual successfully performs the PM task while out shopping.

The next phase, *intention initiation* (Ellis, 1996; Ellis & Freeman, 2008), involves an individual monitoring the environment for an appropriate target cue whilst inhibiting other mental activities that are concurrent. The success in this phase depends heavily on how a person monitors the environmental signal to perform the delayed intention (Kliegel, Martin, McDaniel, & Einstein, 2004). In the example task, if the individual is talking on their mobile phone as they pass the chemist, they must

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remember their intention, switch attention from the ongoing activity (e.g., phone call), and walk into the chemist to fill the prescription.

*Execution*, the final phase, involves performing the intended task as previously planned. This phase also involves evaluation of the outcome of the intention to prevent repetition of the task, for instance if it was successfully completed, or to ensure it was carried out accurately if it was postponed or unsuccessful (Ellis, 1996). In the example task, success is determined when the individual fills their prescription. If the person enters the chemist but does not fill the required prescription, this would constitute a PM failure. In existing literature, the final phase has been conceptualised as having two overlapping, but distinct components. These involve the prospective component (remembering *that* a task needs to be initiated at a specific moment in the future) and the retrospective component (remembering the content of the task, i.e., *when* to perform the task and its nature) (Ellis & Kvavilashvili, 2000; Smith & Bayen, 2006). Ellis and Kvavilashvili (2000) reported that this latter component of PM has not received the recognition it deserves; however, research attention in this area is increasing. The distinction between these two components is discussed in detail later in this chapter.

Very few researchers have attempted to disentangle these four phases. In fact, most of the existing studies have focused on the execution phase, which is indexed by the proportion of PM tasks that are correctly executed. The first published study that assessed the formation and execution phases separately involved healthy adults. The findings of that study showed that age, for instance, which reduces PM function (Henry et al., 2004), did not impact all components of PM to an equal degree. Rather, age impacted the planning, initiation, and execution of tasks, but not the retention of tasks (Kliegel, McDaniel, & Einstein, 2000). These findings were replicated in

subsequent studies (Kliegel, Martin, McDaniel, & Einstein, 2002; Martin, Kliegel, & McDaniel, 2003). Despite these preliminary developments regarding the importance of each PM phase, identifying or isolating the specific phase/s that participants have difficulties with, and/or the relative importance of each phase, remains a challenge (Kliegel, Jager, Altgassen, & Shum, 2008).

#### **3.2.1** Processes that facilitate cue monitoring.

An influential model of PM is the multiprocess framework (McDaniel & Einstein, 2000). The theory argues that cue monitoring is facilitated by different processes, depending on the features of the task; for instance, in some situations participants remember PM intentions by monitoring environmental events for the occurrence of the target (Einstein & McDaniel, 2010; McDaniel & Einstein, 2000). This would involve strategic monitoring of environmental cues, including selfreminders or purposeful clock-checking to increase the likelihood of successful task execution (McDaniel & Einstein, 2000). In other situations the presence of a target event or cue can spontaneously initiate retrieval of the PM intention from memory (Einstein & McDaniel, 2010; McDaniel & Einstein, 2000). This occurs through effortless and relatively automatic processes (Einstein & McDaniel, 2005; McDaniel & Einstein, 2000), and describes the person's introspective impression that the task "popped into mind" (Einstein & McDaniel, 1990).

A competing model, the preparatory attentional and memory processes model (PAM), has also been proposed (Smith, 2003; Smith & Bayen, 2004). Similar to the multiprocess framework, the PAM suggests that after forming a PM intention, preparatory attentional processes are initiated (Smith, 2003; Smith & Bayen, 2004). The theory suggests that these processes draw on limited-capacity resources, and can

range from fully conscious strategic-monitoring, to preparatory attentional processes. The key distinction of the PAM theory compared to the multiprocess model is that the PAM theory assumes that retrieval can *only* occur when these attentional processes are engaged (Smith et al., 2007). In other words, this model argues that PM *always* involves effortful monitoring. By contrast, the multiprocess model argues that this is the case sometimes, but that at other times, PM tasks can be carried out relatively effortlessly (McDaniel & Einstein, 2000).

Past research has provided evidence that monitoring is, indeed, involved in PM function (Einstein & McDaniel, 2005; Marsh, Hicks, Cook, Hansen, & Pallos, 2003; Smith, 2003; Smith & Bayen, 2004), as suggested by both theories. However, in a series of five studies, and in support of the multiprocess framework, Einstein et al. (2005) showed that spontaneous retrieval processes *alone* also produced prospective remembering. This was demonstrated in experimental conditions where participants who showed no evidence of monitoring had high PM performance and performed at a level that was equivalent to those who showed evidence of monitoring. This series of experiments showed that monitoring was not *always* necessary for PM retrieval, but instead, that people rely on multiple processes in PM situations (Einstein et al., 2005). The multiprocess model has been used to explain how monitoring resources may differentially apply to a number of different task features. The most prominent in the wider literature, and the most relevant to this thesis, is the distinction between time- versus event-based tasks.

#### 3.3 Time-based Versus Event-based Prospective Memory Tasks

PM tasks have been classified in a number of ways, but the most frequent distinction in the literature is between *time-based* tasks and *event-based* tasks

(Einstein & McDaniel, 1990). Time-based tasks are performed at a specific time, or once a specific time has lapsed (Einstein & McDaniel, 1990, 2005); for example, attending an exercise class (PM task) at 2 pm (time cue). On the other hand, eventbased PM involve remembering to perform an action when some external event occurs (Einstein & McDaniel, 1990, 2005), such as remembering to take medication (PM task) at dinner (event cue). Early research comparing time and event-based tasks has typically argued that the former type of task is more resource consuming than the latter source. Time-based tasks require more strategic monitoring and self-initiated control processes, and are consequently more difficult to perform successfully (McDaniel & Einstein, 2000). By contrast, event-based tasks are considered to be less cognitively demanding because the environmental event serves as a cue to the memory. As such, constant monitoring of the environment is unnecessary for eventbased tasks to be reactivated and performed. However, time-based tasks lack the inherent cue that is present in event-based tasks, and therefore require monitoring of a clock and/or time.

Given that the difficulty of retrieving PM tasks depends on the ease of cue identification, it would be expected that for tasks without associated cues, performance would be worse (Einstein & McDaniel, 1996, 2005). Thus, time-based tasks might be more difficult for people with damage to frontal brain regions. This is because these brain regions are particularly implicated in functions that require executive control (Alvarez & Emory, 2006), such as self-initiated retrieval, or strategic monitoring. Therefore, for people who are affected by CHF, and who frequently have damage to frontal regions, time-based tasks might be more difficult than event-based tasks.

#### 3.3.1 Assessment of time- and event-based tasks.

When considering the assessment of PM in people with CHF, there are a number of approaches to choose from. Each approach has strengths and limitations, and different methods allow testing of different variables. A number of different paradigms have been used to assess time- versus event-based tasks using both laboratory, clinical, and naturalistic measures. A discussion of the criticisms of early PM measures is also presented because it describes the rationale for the development of a relatively new measure (Virtual Week), which was used in this thesis. The following section describes the most common measures.

The very widely used laboratory paradigm often referred to as the McDaniel and Einstein paradigm involves asking participants to remember to press a designated key on the computer keyboard whenever they see a particular PM "target item" (e.g., the word 'rake'). This PM task is embedded in the ongoing task, which involves rating words for pleasantness (Einstein & McDaniel, 1990). In this paradigm, participants must switch from seeing the item as an item that needs to be rated for pleasantness, to thinking about it as a "target item" and a cue for an intended action (Einstein et al., 2005).

Two measurements tools have been development for use in clinical settings. The first is the Cambridge Prospective Memory Test (CAMPROMPT). It is a brief tool, comprising three time- and three event-based tasks that participants are asked to carry out during a 30-minute period, while performing distractor tasks. Although some studies (Fleming et al., 2008) have demonstrated that the CAMPROMPT is a valid measure of PM, strong evidence that this tool predicts everyday PM performance is lacking (Fish, Wilson, & Manly, 2010). The second clinical test is the Memory for Intentions Screening Test (MIST). The MIST was designed to measure PM performance under a number of different conditions, such as type of cue (time, event), type of response (verbal, written), and the length of the delay period (2 minutes, 15 minutes) (Raskin, 2009). This measure has been used in studies of normal ageing as well as with a range of clinical groups (Raskin, 2009). Studies have supported its reliability (Raskin, 2009; Woods et al., 2008) and construct validity (Woods et al., 2009).

The ecological validity of PM measures has often been questioned. Laboratory measures are criticised because they may not reflect the way PM tasks occur in real life (Phillips, Henry, & Martin, 2008). By contrast, naturalistic tasks are criticised largely due to lack of experimental control (Phillips et al., 2008). In naturalistic settings tasks are carried out, over several days, in the everyday life of participants rather than in a short laboratory testing session that is under the control of the experimenter (Phillips et al., 2008). Ecological validity can be considered as a continuum, ranging from relatively strong to weak (Phillips et al., 2008). The strongest type of ecological validity is achieved when the tasks under investigation are part of everyday life (i.e., naturalistic studies). This would include contexts where both the setting of the task and the intention are a part of the participant's routine with no interference by the experimenter (Phillips et al., 2008). Relatively few PM studies achieve this level of ecological validity, especially in laboratory settings. Nonetheless, if the context and familiarity of the PM tasks in the laboratory encourages engagement by the participant, ecological validity is stronger, compared to laboratory paradigms where task materials and task instructions are both abstract and novel (Phillips et al., 2008).

To address each of the concerns about laboratory and naturalistic methods of assessment, a laboratory based PM paradigm, Virtual Week (Rendell & Craik, 2000)

was developed. This measure combines both naturalistic elements and the capacity for experimental control. Virtual Week is a computerised board game that simulates a week in a person's life. In this paradigm participants are required to perform an array of tasks as they move around the board with the roll of a dice. The tasks represent everyday activities such as remembering to buy colouring pencils when shopping or remembering to call the bank at 12 noon. In original versions of Virtual Week, timebased tasks were cued by passing a particular time on the board, which in one sense, could be argued to be an external (i.e., event) cue. In recent versions of Virtual Week, and the one used in this thesis, the distinction between time- and event-based tasks has been more clearly defined with the use of a virtual time clock. That is, in the current version, the only difference between tasks is the cue, which involves an event (where an event cue must be noticed) or a set time (requiring monitoring of the virtual time clock, calibrated to the position of the token on the board). A detailed description of Virtual Week is presented in published manuscripts in Chapter 5.

Virtual Week has been used widely within PM research and has robust psychometric properties (Rendell & Henry, 2009). A study of ageing found a splithalf reliability of .64 and .77 for all regular and irregular tasks, respectively in the young adults groups, and .93 and .92 for regular and irregular tasks respectively in the older adults group (Rose, Rendell, McDaniel, Aberle, & Kliegel, 2010). An earlier study of people with schizophrenia reported a split-half reliability of .90 for the overall measure, and .74 and .66 for the schizophrenia and control groups (Henry, Rendell, et al., 2007). The reliability estimate (Cronbach's alpha) for the overall measure was .89 for Parkinson's disease participants and .81 for the control group (Foster et al., 2013); and .89 for people with traumatic brain injury and .62 for the control group, in another study (Mioni et al., 2013). Virtual Week is also sensitive to differences between clinical and normal populations (Rendell & Henry, 2009), and between healthy older adults and those with dementia (Thompson et al., 2010). One of the key strengths of Virtual Week is that it allows different PM task parameters to be systematically investigated in a controlled manner. In addition to the assessment of time- versus event-based tasks, Virtual Week also allows the study of task regularity.

#### 3.4 Regular and Irregular Prospective Memory Tasks

Only recently, research has started to consider other elements of PM performance, such as task regularity, although there is limited research on this topic using real-life assessment tools. This additional task distinction is between tasks that are regular (repeated frequently), and those that are irregular (less frequent). Foster et al. (2013) argued that a comparison of these repeated tasks versus one-off tasks is important. Foster et al. (2013) used this distinction of tasks in research involving Virtual Week to clarify whether any observed difficulties in PM reflect problems related to poor encoding of the task (retrospective component), or difficulty initiating tasks at the appropriate moment (prospective component).

In everyday life, regular tasks can involve those tasks that are completed according to a fixed schedule; for example, taking medication every morning at 9 am, or locking the door when leaving the house. In contrast, irregular tasks can involve those tasks that do not have a regular schedule of a particular time or event. These types of tasks include infrequent events such as attending a doctor's appointment or going to a friend's birthday dinner. Thus, regular tasks, if repeated enough (e.g., locking door when leaving the house), have the potential to become habitual and automatic. By contrast, irregular tasks, which are only performed occasionally do not become habitual (Terrett et al., 2014). As such, recalling regular tasks compared to irregular tasks is thought to be less effortful (Terrett et al., 2014).

There is now an accumulation of research on this task distinction within the Virtual Week paradigm. In Virtual Week, regular tasks are repeated each virtual day and at the same moments in the game (e.g., medication with breakfast and dinner events that occur at the same board position, each round of the board). The term *regular* implies these tasks are habitual; however, regular tasks in Virtual Week are not repeated enough to become habitual (Foster et al., 2013). For instance, regular tasks in Virtual Week are repeated each virtual day, typically over two to five virtual days. This degree of repetition does not match the much higher number of repetitions of tasks in everyday life, such as locking doors. Within Virtual Week, irregular tasks, however, change from day-to-day. These tasks are "one-off" tasks that are only performed during one virtual day, and change both in terms of the task itself, but also the specific cue that the task was associated with.

Recent studies using Virtual Week have described the several ways that the regular versus irregular task distinction represents low and high retrospective memory demands (i.e., remembering the content of the task) (Foster et al., 2013; Mioni et al., 2013; Terrett et al., 2014). First, in the version of Virtual Week used in this thesis, regular tasks are practiced in the trial day and repeated on each test day, compared to the irregular tasks where participants do not get the chance to practice or repeat tasks. Second, regular tasks are accurately learnt to criterion under the supervision of the experimenter in the trial day at the beginning of the game. Thus, the well-learnt and repetitive nature of regular tasks (Foster et al., 2013).

Third, because regular tasks are repeated across days and each irregular task is unique, there are fewer total cue (e.g., breakfast) and action (e.g., take medication) associations to learn and remember for regular tasks compared with irregular tasks. Whilst Virtual Week studies vary from two to five virtual days, even with only two virtual days, regular tasks have two-actions and four-cues compared to eight-actions and eight-cues for irregular tasks. Finally, the content of the four regular tasks per virtual day is of minimal complexity compared to the four different irregular tasks each virtual day. The regular tasks only involve two relatively simple actions (medication, asthma inhaler) and four cues (breakfast, dinner, 11 am, 9 pm) that are related to one topic (dealing with a health problem). By contrast, the four irregular tasks per virtual day, involve four distinct actions and cues that are unrelated to each other. Furthermore, the content of the action tends to be more complex than for regular tasks; for example, participants are asked to pick up their sister's gym membership card when at the swimming pool. Existing studies that have examined this task distinction are presented later in this chapter.

So far this literature review has focused on describing two competing models of PM, namely the multiprocess model and the PAM theory. Major assessment tools used to measure PM include clinical tools, laboratory and naturalistic based paradigms, and Virtual Week, which combines both laboratory and naturalistic elements. This literature review has also discussed the major aspects of PM, which includes a distinction between time- and event-based tasks, and regular versus irregular tasks.

The remainder of this chapter focuses on literature that has examined PM performance in clinical groups who present with widespread cognitive impairment, and who show robust deficits in PM function. PM in normal ageing has dominated the

existing literature. PM in ageing is not directly related to this thesis, therefore a thorough review of that literature is beyond the scope of this thesis; however, a review of key findings is presented because it provides the context for clinical research – the focus of review in this chapter. Because people with CHF represent an ageing population, PM in normal ageing also provides a context for older adults. Finally, the last section of this chapter provides a review of literature regarding the involvement of more general cognitive processes in PM performance.

# 3.5 Prospective Memory in Normal Ageing

Older adults are known to have executive function deficits and problems with strategic monitoring. It might be expected that the patterns of PM performance seen in healthy older adults, a group with mild cognitive changes, would be similar in groups with more severe cognitive decline, such as people with CHF. Because processing resources are thought to reduce with age (Craik, 1986; Salthouse, 1991), PM should be especially difficult for older adults (Einstein & McDaniel, 2007). Early studies suggested that PM might be spared in ageing (see, Einstein & McDaniel, 2014; McDaniel & Einstein, 2007). However, research over the last two decades has provided evidence of PM decline in older adults. Indeed, two large meta-analyses (Henry et al., 2004; Uttl, 2008) involving PM in ageing have confirmed that older adults have robust deficits in PM overall (Table 3.1).

Research involving PM in ageing has found mixed patterns of performance by older adults. From the perspective that ageing disrupts attentional capacities and selfinitiated retrieval, compared to time-based tasks, event-based tasks would not likely produce large age-effects as they contain external cues or cues that guide retrieval (Einstein & McDaniel, 1990). Seminal literature reviews have reported that studies involving time-based tasks have consistently found age-related deficits (Einstein & McDaniel, 2014; Henry et al., 2004; McDaniel & Einstein, 2007). By contrast, patterns of age-effects seen on event-based tasks are not as clear. While most studies of event-based PM found that older adults were substantially impaired compared to young adults, some evidence of the reverse has been found (Einstein & McDaniel, 2014; Henry et al., 2004; McDaniel & Einstein, 2007). The multiprocess framework was developed in an attempt to explain these mixed findings.

It appears that the direction of PM age-effects is influenced by the extent to which the task depends on automatic processing versus controlled resourcedemanding processing. Meta-analyses by Henry et al. (2004) and Uttl (2008), which are presented in Table 3.1, found that older adults had a consistent PM deficit. That is, there were no significant differences between time- and event-based tasks, as might be expected on the basis that time-based tasks require more strategic monitoring. However, based on the multiprocess view, age-effects might also be expected on event-based tasks in which resource-demanding monitoring or self-initiated retrieval is necessary. Indeed, Henry et al. (2004) found that older adults had significantly smaller deficits in event-based tasks that imposed less demand on strategic processing than event-based tasks that placed high demands on this aspect of cognition. These findings show that the degree of strategic demand *is* an important element of the size of PM deficit in older adults. Thus, in people with CHF, it also might be expected that tasks, which are more resource demanding would produce larger deficits.

# **Table 3.1:**

# Meta-analyses Assessing Prospective Memory in Normal Ageing and Extensively Studied Clinical Groups

Study	Sample	PM type	Assessment	Overall findings
Henry et al. (2004)	56 studies; old and young adults	Event-based (47 studies), time-based (9 studies)	Experimental and naturalistic	In laboratory settings, older participants were outperformed by younger participants on PM overall. Time-based tasks ( $rs = .39$ ) were not statistically more impaired than event-based ( $rs = .34$ ), although time tasks were compromised to a greater extent.
Uttl (2008)	60 studies; old and young adults	Event-based, time-based	Experimental and naturalistic	In laboratory settings, older participants were outperformed by younger participants on PM overall ( $d = 1.13$ ). Time-based tasks ( $d = .95$ ) were not statistically more impaired than event-based tasks ( $d = .77$ ), although decline on time tasks was larger.
Shum, Levin, and Chan (2011)	14 studies; closed head injury and matched controls	Event-based, time-based	Behavioural	Participants with head injury were outperformed by controls on PM overall ( $d = .855$ ). The PM deficit was consistent; time- based tasks ( $d = .818$ ) were not more impaired than event-based ( $d = .822$ ).
Wang et al. (2009)	11 studies; schizophrenia and matched controls	Event-based, time-based	Experimental (1 Virtual Week study)	Participants with schizophrenia were outperformed by controls on PM overall ( $d = 1.353$ ). Time-based tasks ( $d = 1.33$ ) were more impaired than event-based tasks ( $d = .827$ ).
Ramanan and Kumar (2013)	12 studies; Parkinson's disease and matched controls	Event-based, time-based	Experimental (1 Virtual Week study), or naturalistic in conjunction to questionnaires.	Parkinson's disease participants were outperformed by controls on PM overall (SMD = .61). The PM deficit was consistent; time-based (Hedges' $g = .71$ ) tasks were not more impaired than event-based tasks (Hedges' $g = .55$ ), although time-based tasks were compromised to a marginally greater extent.

*Notes. d*, Hedges' *g*, *r*s = pooled effect size; SMD = Standard mean difference.

#### 3.6 Clinical Studies Assessing Time- and Event-based Tasks

In several clinical groups that are affected by neurological changes and widespread cognitive deficits such as people with brain injury, schizophrenia, and Parkinson's disease, profound examples of PM deficits are also observed. As shown in Table 3.1, PM difficulties are a robust feature of each of these groups. In each of these studies, the clinical groups were outperformed by the controls on overall PM, with large effect sizes. Differences in performance of time- versus event-based tasks were also assessed. It was expected that time tasks would be more affected because they require more self-initiated control processes or strategic monitoring and are consequently more difficult. However, in some groups time tasks were not differentially impaired.

For instance, Shum et al. (2011) found that time-based tasks were not differentially impaired in people with brain injury. A lack of difference between timeand event-based tasks was also observed in the meta-analysis by Ramanan and Kumar (2013) with Parkinson's disease participants. These unexpected findings may be due to methodological differences. An examination of the 'ongoing tasks' used in the time- and event-based PM tasks in brain injury suggests that the results reported by Shum et al. (2011) were confounded by differences in the level of difficulty of the ongoing tasks. For example, if the ongoing tasks used with time-based tasks were easier, then the expected difference between the two task types (time- and eventbased) might decrease, or even disappear (Shum, Levin, & Chan, 2011). A review of the individual studies that were included in the meta-analysis by Shum et al. (2011) indicated that this was, indeed, the case in some studies.

Recent adaptations of Virtual Week have carefully controlled for variables that could confound the results. That is, the only methodological difference between timeand event-based tasks in Virtual Week is the cue, as described in Section 3.3.1. Using

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the current version of this measure, Mioni et al. (2013) confirmed that people with traumatic brain injury had less accurate overall PM performance compared to controls. The findings of Mioni et al. (2013), however, also found differences between task types, as might be expected. That is, the deficits observed in people with brain injury were larger for time- than event-based tasks.

Moreover, a large body of research has reported robust deficits in overall PM performance in schizophrenia (Altgassen, Kliegel, Rendell, Henry, & Zöllig, 2008; Chan et al., 2008; Elvevåg, Maylor, & Gilbert, 2003; Henry, Rendell, et al., 2007; Kumar, Nizamie, & Jahan, 2005, 2008; Shum, Ungvari, Tang, & Leung, 2004; Wang, Chan, Hong, et al., 2008; Wang, Chan, Xin Yu, et al., 2008). However, one aspect that remains unclear is whether time- or event-based PM tasks are differentially impaired in this group. Similar to other groups, the mixed findings may be explained by a number of potentially confounding variables, including participant and clinical characteristics (e.g., duration of illness, medication doses, and clinical symptoms). A meta-analysis by Wang et al. (2009) (Table 3.1) was conducted specifically to investigate these mixed findings in the context of schizophrenia. The findings of that meta-analysis concluded that time-based tasks were more impaired than event-based tasks, as expected (Wang et al., 2009).

In summary, the existing literature involving PM in normal ageing and clinical groups has shown that PM deficits are a robust feature of older people and those with a range of clinical diagnoses, despite differences in the approach to the assessment of PM. In addition to the Virtual Week studies that have already been discussed, this measure has also been used with other clinical groups that are affected by widespread cognitive deficits, including people with multiple sclerosis (Rendell, Jensen, & Henry, 2007), substance users (Rendell, Gray, et al., 2007; Rendell, Mazur, & Henry, 2009;

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Terrett et al., 2014), and people with mild cognitive impairment and early dementia (Thompson et al., 2010). In each of the studies, Virtual Week was sensitive enough to detect overall PM deficits in the clinical groups compared to controls. Each study specifically assessed the distinction between time- and event-based tasks. On the basis that time-based tasks require more strategic monitoring, it was expected that performance would be worse on time- than event-based tasks. However, in the context of each of these clinical groups, even a study (Terrett et al., 2014) that used a well-controlled manipulation of time-versus event-based tasks, there were no significant differences between these two task types. That is, these clinical samples showed a significant and relatively broad-based PM impairment.

The distinction between time- and event-based tasks was assessed in this thesis in Study 1. In people with CHF, where frontal brain damage is most commonly observed, it would be expected that time-based tasks would be substantially impaired because it relies on strategic monitoring, which is mediated by frontal brain regions (Alvarez & Emory, 2006). Furthermore, as noted in Section 3.4, one of the benefits of Virtual Week is that it allows for the assessment of regular versus irregular tasks, which has not been investigated in the studies that have been described thus far, but was assessed in Study 1 of this thesis. The remainder of this chapter focuses on a review of studies that have examined to what degree other cognitive processes underlie, or are related to, the deficits in PM that are observed in clinical groups.

#### **3.7 Neuropathology and Sub-processes of Prospective Memory**

There is general consensus that PM is not a single cognitive process. Rather, for optimal performance, PM is thought to require the application of multiple cognitive elements. However, the exact nature and degree of involvement of other cognitive processes remains unclear. The remainder of this chapter focuses on a review of the most extensively studied cognitive domains in this topic, particularly the involvement of executive functions and retrospective memory. First, each of these is briefly introduced, before reviewing the relevant literature.

Neuroimaging research has shown that PM is primarily dependent on prefrontal systems (Simons, Schölvinck, Gilbert, Frith, & Burgess, 2006) and the dorsolateral prefrontal cortex (Braver & Barch, 2002; Costa, Caltagirone, & Carlesimo, 2011; Reynolds, West, & Braver, 2009). Frontal neural structures are also implicated in executive control processes (Alvarez & Emory, 2006). Therefore, two cognitive mechanisms proposed to be involved in PM are executive function and working memory. Executive functions might be involved in a number of PM phases (described in Section 3.2) such as planning the intended action, monitoring the environment for the cue while performing other tasks, inhibiting these other activities, switching to the intended action, and carrying it out as planned (Kliegel, Eschen, & Thöne-Otto, 2004; Shum & Fleming, 2009).

It is also recognised that retrospective memory skills (i.e., the encoding, retention, and retrieval of intentions are involved in PM performance (Kliegel, Eschen, et al., 2004; Shum & Fleming, 2009). The fundamental aspect of PM involves being able to recall what it is that must be done – the content of the task. By contrast to the frontally-mediated executive functions, the medial temporal lobes – specifically the hippocampus – are assumed to play a key role in retrospective memory, and therefore in the retrieval of the content of the PM task (Reynolds et al., 2009).

Viewed this way, PM can be conceptualised as involving sub-processes that strongly rely on the prefrontal cortex and the medial temporal lobes. This conceptual context has inspired studies to assess PM performance in relation to different clinical conditions and their associated cognitive deficits. In people with CHF, damage to both frontal and temporal neural structures has been observed (Vogels, van der Flier, et al., 2007; Woo et al., 2009, 2003). Therefore, in this group, any observed deficits in PM function might relate to deficits in more general cognitive processes, such as retrospective memory or executive functions. The degree to which retrospective memory underlies PM has been assessed by focusing on task regularity, which can be manipulated using Virtual Week. This research is described first, before reviewing the wider PM literature that has examined the involvement of executive functions and retrospective memory.

#### 3.7.1 Involvement of retrospective memory assessed by task regularity.

A number of studies have used Virtual Week to manipulate the degree of retrospective memory demand using regular versus irregular task distinctions. This task comparison can clarify whether any observed difficulties in PM function reflect problems encoding tasks, or of actioning tasks at the appropriate moments. Notably, only a few studies have assessed the involvement of retrospective memory using this approach.

Studies have compared performance on regular and irregular tasks in clinical groups such as traumatic brain injury (Mioni et al., 2013), mild cognitive impairment (Thompson et al., 2010), multiple sclerosis (Rendell, Jensen, et al., 2007), stroke patients (Kim et al., 2009), users of ecstasy (Rendell, Gray, et al., 2007), and long-term opiate users (Terrett et al., 2014). Each has found a consistent deficit across regular and irregular tasks. That is, increasing the retrospective memory demands (i.e., irregular tasks) did not result in a disproportionate impairment in PM performance. The lack of difference on regular and irregular tasks in these groups

suggest that the underlying cause of the poor PM performance that was observed in these clinical groups could not be explained entirely by retrospective memory deficits. Rather, the cause of the PM impairment involved the prospective component – difficulty initiating tasks at the correct moments. If the groups' poor PM performance were solely a result of retrospective memory failure, PM performance should have been weaker on the irregular tasks. This is because regular tasks in Virtual Week impose only minimal demands on the retrospective memory component of the PM task (remembering *what* needs to be done) because the repeated presentation of regular tasks ensures they are well encoded, as discussed in Section 3.4. In some studies, this idea was further supported by the fact that the majority of errors were misses (i.e., failures to respond entirely) (Rendell, Gray, et al., 2007; Rendell, Jensen, et al., 2007), rather than responding at the incorrect moments.

Some studies showed that retrospective memory contributed to the PM difficulties, even when there were no differences in the PM performance of regular versus irregular tasks. For example, in the study involving mild cognitive impairment (Thompson et al., 2010), analyses of covariance showed that retrospective memory contributed most significantly to the PM deficit (Thompson et al., 2010). Additionally, Kim et al. (2009) found that stroke participants were less accurate at recalling the PM task content (retrospective component). This involved recalling what PM task they *should* have completed at the end of each virtual day. Similar findings were reported in long-term opiate users (Terrett et al., 2014). These results suggest that in some clinical groups, retrospective memory ability contributed to overall PM difficulties. However, the lack of difference in PM performance between regular and irregular tasks suggested that the underlying cause of the poor PM seen in these clinical groups cannot be explained entirely by difficulties with the retrospective

component of the PM task (i.e., difficulties remembering the content of tasks). Rather, in each of these studies, there was a specific deficit in the prospective component (i.e., the ability to initiate the task at the correct moment).

#### **3.7.2** Relationship between prospective memory and general cognition.

A larger body of research has investigated the relationship between PM and processes such as executive functions and retrospective memory using established assessment tools, but the findings of this research are mixed.

In the case of people with closed head injury, a meta-analysis of 14 studies found that PM performance was significantly related to three cognitive processes, namely: retrospective memory, executive function, and attention (Shum et al., 2011). These findings are preliminary because only a small number of studies actually assessed other cognitive functions in addition to PM function. Additionally, a limited number of tests were used to evaluate the relationship between different types of PM with different cognitive processes (Shum et al., 2011). Furthermore, an individual study that was not included in the meta-analysis by Shum et al. (2011) also supported the association between PM performance and three different measures of executive function in people with traumatic brain injury (Fleming et al., 2008). Only partial support was reported by a study that used Virtual Week with traumatic brain injury. Mioni et al. (2013) found that one component of verbal fluency (semantic fluency), but no other executive measures, were significantly correlated with one type of PM task (time-based) (Mioni et al., 2013). Thus, more studies are needed to confirm the exact relationship between PM and executive functions.

The involvement of retrospective memory, specifically, has also been assessed in people with traumatic brain injury. One study using Virtual Week found that people

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with brain injury were not differentially impaired in their capacity to recall the PM test instructions (retrospective component) (Henry, Phillips, et al., 2007). This was true even when retrospective memory demands were reduced by using one PM target versus four PM targets. These findings would suggest that in that sample, retrospective memory impairment was not the major factor that underpinned the observed PM deficit (Henry, Phillips, et al., 2007). Consistent with this idea, in a different study involving brain-injured participants, Fleming et al. (2008) found that localised damage to temporal brain regions was not significantly correlated with PM performance. These results suggest that the retrospective component, which is mediated by the temporal lobes, was less important for PM accuracy. In that study, the involvement of executive functions was more substantial.

Other individual studies have also shown that PM performance in schizophrenia is related to various cognitive processes. These included working memory (Twamley et al., 2008; Wang, Chan, Hong, et al., 2008; Wang, Chan, Xin Yu, et al., 2008; West, Bowry, & Krompinger, 2006), IQ, retrospective memory, executive function (Altgassen et al., 2008; Henry, Rendell, et al., 2007; Twamley et al., 2008; Wang, Chan, Hong, et al., 2008; Zhou et al., 2012), as well as attention, processing speed, and learning (Twamley et al., 2008). In three of these five studies (including one that used Virtual Week), retrospective memory and/or working memory contributed the most, and executive function contributed the least (Henry, Rendell, et al., 2007; Twamley et al., 2008; Wang, Chan, Hong, et al., 2008).

The final large component of this literature involves Parkinson's disease participants. A recent meta-analysis of 12 studies showed that PM impairment in this group was more likely related to failures in executive control (i.e., verbal fluency, inhibition, planning, and working memory), rather than retrospective memory (i.e., forgetting the content of the intention) (Ramanan & Kumar, 2013). More specifically, approximately half of the correlations between executive functions and PM were significant in four out of 12 studies. By comparison, less than a quarter of correlations between PM and retrospective memory were significant. A limitation of the retrospective memory findings was that deficits in episodic memory in Parkinson's disease may not be detected if the sole measure used to test retrospective memory is the retrospective component (Ramanan & Kumar, 2013). This involved recall of the PM task instructions, i.e., asking participants what PM task they need to complete. This relatively simple task may not have imposed as much cognitive load as traditional tasks of retrospective memory, and could have elicited ceiling effects. However, even studies that did not find any impairment of the retrospective component reported that participants still showed deficits in traditional measures of episodic memory, which were also associated with PM performance (Ramanan & Kumar, 2013). Therefore, these latter findings still support the involvement of retrospective memory in PM performance in the context of Parkinson's disease.

To sum up the two last major sections, a review of Virtual Week studies that investigated associations of retrospective memory ability to PM, and studies that manipulated the demands on the retrospective memory component have shown mixed findings. In each study, deficits in PM could not be explained by the retrospective memory component of PM, even if retrospective memory contributed to the PM impairment overall. Furthermore, research that has examined the involvement of retrospective memory and/or executive functions using established tests is mixed across studies and clinical groups. It would appear that studies involving Virtual Week have generally demonstrated a stronger involvement of retrospective memory instead of executive functions. In the wider literature, however, these processes seem to be equally involved in PM function. Notably, it is difficult to directly compare results across studies because of differences in the measures used and constructs assessed.

## 3.8 Chapter Summary

The first half of this literature review introduced the four phases of PM and the two major models of PM, namely the multiprocess framework and the PAM theory, which attempt to explain how cue monitoring and PM retrieval occurs. This chapter introduced the longstanding key task distinction in the literature, time- and event-based tasks, and the less prominent distinction between regular and irregular tasks. The second half of this chapter showed that PM deficits are a robust feature of various clinical groups who are vulnerable to widespread neurological changes, although the pattern of PM performance might vary across studies and groups. The chapter concluded with a review of literature regarding the involvement of more general cognitive processes such as retrospective memory and executive functions in PM performance, which remains mixed. This chapter provided a comprehensive review of PM, the first focus area of cognition in this thesis. The following chapter focuses on a review of social cognitive functioning, and the second area of cognition that was examined in this thesis in the context of CHF.

# CHAPTER 4: Selective Review of Literature Examining Emotion Recognition and Theory of Mind, and Relationship to General Cognition

# 4.1 Introduction and Focus of Review

The last two review chapters showed that the most developed areas of cognition involving neuropsychiatric or neurocognitive disorders include executive functions, attention, working memory, and general memory. Only recently has there been a shift in the literature towards the study of social cognition. This is an important cognitive domain that has been included in the DSM-5 diagnostic criteria for mild neurocognitive disorder, as outlined in Chapter 2. Social cognition however remains less developed compared to more general cognitive processes, and this aspect of cognition has not been researched in people with CHF.

Broadly, social cognition is defined as "the ability to construct representations of the relation between oneself and others and to use those representations flexibly to guide social behavior" (Adolphs, 2001, p. 231). Social cognition includes processes that are involved in perceiving, interpreting, and generating responses to the intentions and emotions of other people, and bringing social judgments to decision making (Adolphs, 2003; Adolphs & Janowski, 2011; Fiske & Taylor, 2013). Social cognition is multi-dimensional and involves four key constructs, namely emotion recognition, social perception and knowledge, theory of mind (ToM), and attribution bias (Bellack et al., 2007; Green et al., 2008; Penn, Corrigan, Bentall, Racenstein, & Newman, 1997; Penn, Sanna, & Roberts, 2008).

Two dimensions of social cognition that have received particular attention in the literature are emotion recognition and ToM. Emotion recognition refers to the ability to accurately perceive and use affective information, most commonly from expressions of the face and eyes (Adolphs, Damasio, Tranel, & Damasio, 1996). The related construct, ToM, refers to the capacity to represent one's own mental states, and make inferences and attribute the mental state of others (Premack & Woodruff, 1978). These two constructs were the focus of Study 3 in this thesis.

The first part of this literature review describes each of these constructs and their measurement methods, and a brief overview of the neuropathology of social cognition. The second part of the chapter reviews the existing literature on emotion recognition and ToM in other clinical groups, the relationship between social cognition and more general cognitive processes, and the functional importance of each of these social cognitive constructs. The chapter concludes with a brief overview of the relationship between social support and outcomes in the CHF population.

# 4.2 Emotion Recognition Defined and Measurement Methods

Emotion recognition (also called emotion processing or affect recognition) is one important aspect of human social interactions (Adolphs & Janowski, 2011) that develops very early in life, around the age of one (Grossmann, 2010). Emotion recognition is the ability to decode emotional information (i.e., what a person is feeling) by correctly perceiving and recognising emotions in other people (Adolphs, 2002; Adolphs & Janowski, 2011). Emotion recognition has generally been assessed from observations of facial expressions, vocal inflections, body posture, or some combination of these (Adolphs & Janowski, 2011). The commonly studied emotions are referred to as the "basic" emotions, and include happiness, surprise, fear, disgust, and sadness (Ekman, 1973). The recognition of these basic emotions has been studied in various clinical groups, most commonly in people with schizophrenia (Kohler, Walker, Martin, Healey, & Moberg, 2009; Marwick & Hall, 2008), children with Autism Spectrum Disorders (Harms, Martin, & Wallace, 2010), and brain injury (Babbage et al., 2011; Heberlein, Padon, Gillihan, Farah, & Fellows, 2007; Radice-Neumann, Zupan, Babbage, & Willer, 2007).

Instruments that test emotion recognition typically involve still (i.e., static) facial photographs (Edwards, Jackson, & Pattison, 2002). Participants are asked to specify the emotions depicted by each image. The *Ekman 60 Faces* test (Ekman & Friesen, 1976) is the most widely used measure to assess this construct (Edwards, Jackson & Pattison, 2002), and was used as the primary measure in Study 3 of this thesis. In this task, participants are presented with slides featuring extensively validated photographs of human faces that depict one of the six "basic" emotions. Participants are asked to choose between six options to identify the emotion that best describes the emotion being displayed in the picture (Ekman, 1973).

Other, less common static measures, which involve adaptations of the sets of slides of the Ekman 60 Faces test are also used (Edwards et al., 2002; Tottenham et al., 2009). Furthermore, although emotion recognition is most commonly assessed with static facial expressions, some researchers have used drawings, cartoons, or dynamic stimuli such as films, videos, or vocal stimuli (Edwards et al., 2002). However, a recent methodological review of emotion recognition reported a tendency for the development of materials for a particular study with no attention to psychometric properties (Edwards et al., 2002). For this reason, in Study 3 the Ekman 60 Faces test was chosen because it is the most validated (Edwards et al., 2002).

## 4.3 Theory of Mind Defined and Measurement Methods

The second core aspect of social cognition is ToM. This construct involves the ability to understand that others have mental states that are different from one's own,

and the capacity to infer the mental states of others (i.e., others' beliefs or intentions) (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001; Premack & Woodruff, 1978). ToM is subsumed by a broader construct known as *empathy*. Empathy is one's understanding of others' mental state (Blair, 2005; Eslinger, 1998; Rankin, Kramer, & Miller, 2005). Empathy has an affective component and a cognitive one. The former refers to a person's emotional response to the affective state of another. The latter, cognitive component, refers to ToM (Baron-Cohen & Wheelwright, 2004). Most ToM studies have been carried out in children with Autistic Spectrum Disorders (Baron-Cohen, 2000), and in adults with schizophrenia (Brüne, 2005; Harrington, Siegert, & McClure, 2005) and brain injury (Martín-Rodríguez & León-Carrión, 2010).

There are a number of different measures of ToM. The *Reading the Mind in the Eyes* test (Baron-Cohen et al., 2001) has the practical feature of being simple to administer. This measure was used in Study 3 of this thesis. This task involves 36 static pictures of the eye regions illustrating emotionally charged or neutral mental states. The Mind in the Eyes test involves the matching of the semantic definition of a mental state (e.g., "worried", "annoyed") to a picture of the eye-region displayed in the picture. This measure is the most extensively validated and most commonly used test of ToM in various clinical and non-clinical groups (Vellante et al., 2013).

Another type of ToM task consist of short stories and questions about the stories, such as the false-belief task (Sprong, Schothorst, Vos, Hox, & Van Engeland, 2007). This type of task may take a variety of forms, which assess the ability to understand that someone can hold a belief that is different from the actual situation (Sprong et al., 2007). The typical false-belief task, which was developed for use with children, involves a participant being presented with a character in a room who places an object in a certain location (e.g., a basket) before leaving the room. While the

subject is out of the room, another character enters the room and moves the object to another location (e.g., a drawer). Participants are then asked where the original character will look for the object when she re-enters the room. The correct answer (i.e., that the original character will look in the basket) requires attributing a false belief to the original character. This task has been adapted for use with adult participants.

Additional ToM tasks that involve short stories involve intention-inferencing measures that assess the ability to infer a character's intentions from information in the story (Sprong et al., 2007). Additionally, the ability to understand indirect speech such as irony, hints or metaphors has also been used to assess ToM (Sprong et al., 2007). ToM can also be assessed through vocal phrases (Rutherford, Baron-Cohen, & Wheelwright, 2002; Vellante et al., 2013), dynamic visual stimuli, or a combination of verbal and visual stimuli (Golan, Baron-Cohen, & Hill, 2006). Whilst there are a number of different measures of ToM, there is a lack of research on the psychometric properties of different tasks (Harrington et al., 2005). For that reason, Study 3 used the Mind in the Eyes test because it is the most validated.

### 4.4 Neuropathology Involved in Social Cognition

There have been many studies that have started to describe the brain basis of social cognition. Meta-analyses of neuroimaging studies involving emotion recognition (Phan, Wager, Taylor, & Liberzon, 2002) and ToM (Carrington & Bailey, 2009) have reported that the prefrontal cortex and the limbic system (temporal lobe) play a specific role in both of these social cognitive constructs. White matter pathology appears to be particularly important because it leads to slowed communication between frontal and other brain regions (Filley, 2005). Recent models of brain function have suggested that the connectivity provided by white matter is critical for information transfer between neural networks, and for the efficiency of higher brain function (Filley, 2005). More specifically, white matter pathology results in reduced connection between frontal and subcortical brain regions (Jokinen et al., 2006). These neural structures are known to be involved in the processing of emotional signals (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000; Ruffman, Henry, Livingstone, & Phillips, 2008), and are critical for decoding facial expressions of affect (Adolphs et al., 2000). Indeed, studies have shown that people with acquired brain injury, which often involves diffuse axonal injury (Adolphs et al., 2000), have deficits in emotion recognition. A more detailed review of these studies is discussed in the next section of this chapter. Additionally, deficits in ToM could also be expected in the context of white matter pathology because ToM relies on widespread cortical neural networks that include frontal and temporal systems (Apperly, Samson, Chiavarino, & Humphreys, 2004; Decety & Jackson, 2004).

#### 4.5 Emotion Recognition and Theory of Mind in Clinical Groups

In several clinical groups with neurological changes and widespread cognitive deficits, both emotion recognition and ToM are also affected. A summary of metaanalyses involving two extensively studied groups, namely schizophrenia and people with brain injury is presented in Table 4.1.

Schizophrenia is the most extensively studied group with regards to social cognition (Penn et al., 2008) including emotion recognition (Kohler et al., 2009) and ToM (Sprong et al., 2007). In the case of schizophrenia, profound and consistent deficits in each of these social cognitive constructs have been observed, irrespective of the type of measure that is used, as shown in Table 4.1 Notably, the meta-analysis

by Sprong et al. (2007) included studies that used varied measures of ToM but excluded studies that used the Mind in the Eyes test. However, as shown in Table 4.1, even when the Mind in the Eyes test was used, findings were consistent and support a deficit in ToM in schizophrenia (Harrington et al., 2005).

There is also growing interest in social cognitive deficits following brain injury. Meta-analyses involving emotion recognition and ToM in this group are also presented in Table 4.1. While each study that was included in the meta-analyses was relatively small, the results overall showed robust deficits in both emotion recognition (Babbage et al., 2011) and ToM (Martín-Rodríguez & León-Carrión, 2010). The meta-analysis conducted by Martín-Rodríguez and León-Carrión (2010) excluded studies that used the Mind in the Eyes test because so few used this measure. However, even in individual studies, the findings based on this measure showed a consistent pattern of impairment in ToM (Havet-Thomassin, Allain, Etcharry-Bouyx, & Le Gall, 2006; Henry, Phillips, Crawford, Ietswaart, & Summers, 2006).

Despite the overall consensus in the literature that impairments in emotion recognition exists in schizophrenia and brain injury, findings conflict over the impact of emotion valence on impairment. Some studies find impairments in negative emotions in general, while others find the greatest deficits for particular negative emotions (e.g., sadness, anger, fear, and disgust) compared to positive ones (e.g., happiness, joy and surprise). Yet others have reported no effect of emotional valence. These conflicting findings were examined in systematic reviews in schizophrenia (Marwick & Hall, 2008) and traumatic brain injury (Bornhofen & McDonald, 2008; Radice-Neumann et al., 2007). Each of these reviews confirmed that the ability to recognise emotions through facial expressions was specifically impaired when negative emotions were portrayed but not when positive ones were used.
# **Table 4.1:**

# Methodological Reviews and Meta-analyses Assessing Social Cognition in Clinical Groups

Study	Sample	Construct	Assessment	Overall findings
Edwards et al. (2002) <sup>a</sup>	29 studies; schizophrenia and matched controls	Emotion recognition	Static photographic images, speech, and combination of both	People with schizophrenia showed deficits on visual and auditory measures of emotion recognition compared to controls.
Kohler et al. (2009) <sup>b</sup>	86 studies; schizophrenia and matched controls	Emotion recognition	Static photographic images	People with schizophrenia showed a robust and large deficit ( $d = .91$ ) in emotion recognition compared to controls, irrespective of the type of task.
Harrington et al. (2005) <sup>a</sup>	30 studies; schizophrenia and matched controls	ТоМ	False-belief, Mind in the Eyes	Consistent findings showing people with schizophrenia were significantly impaired compared to controls.
Sprong et al. (2007) <sup>b</sup>	29 studies; schizophrenia and matched controls	ТоМ	False-belief, indirect speech, intention-inferencing, excluded the Mind in the Eyes	People with schizophrenia showed a robust deficit in ToM compared to controls, irrespective of the type of task. The overall effect was large ( $d = 1.13$ ).
Babbage et al. (2011) <sup>b</sup>	13 studies; traumatic brain injury and matched controls	Emotion recognition	Static photographic images	People with traumatic brain injury showed robust and large ( $d = 1.11$ ) deficits in emotion recognition compared to controls.
Martín-Rodríguez and León- Carrión (2010) <sup>b</sup>	26 studies; acquired brain injury and matched controls	ТоМ	False-belief, indirect speech, social faux pas (verbal and non-verbal); excluded the Mind in the Eyes	People with acquired brain injury showed robust deficits in ToM, with moderate to severe impairments ( $d = .52$ to .87), compared to controls.

*Note. d* = pooled effect size. <sup>a</sup> Review paper <sup>b</sup> Meta-analysis

Finally, there is emerging interest in social cognition in people with multiple sclerosis, a disorder that is associated with diffuse demyelination of white matter (Kutzelnigg et al., 2005). Studies involving multiple sclerosis have identified impairments in several aspects of social cognition. For instance, decoding of emotional states (Beatty, Orbelo, Sorocco, & Ross, 2003), difficulties processing emotional information from static and dynamic images (Phillips, Henry, Scott, Summers, & Whyte, 2011), and impairments in identifying facial expressions of negative emotions (Henry et al., 2009). Studies have also identified difficulties in emotion recognition and ToM using verbal (Ouellet et al., 2010; Pöttgen, Dziobek, Reh, Heesen, & Gold, 2013) and non-verbal tests (Banati et al., 2010; Henry et al., 2009).

In summary, deficits in emotion recognition and ToM are seen in several clinical groups that have widespread cognitive impairment and neurological damage involving white matter. These findings are relevant because in CHF, typical patterns of brain damage include subcortical white matter pathology and reduced grey matter volume (Vogels, van der Flier, et al., 2007; Woo et al., 2009, 2003). That is, the damage most frequently occurs in diffuse regions known to be involved in both emotion recognition and ToM.

#### 4.6 Relationship Between Social Versus Non-social Cognition

Social cognition and more general cognition are related, but separate, constructs (Brüne, 2005; Harrington et al., 2005). Conceptually, it has been suggested that social cognition involves *affective* and *cognitive* processing. By contrast, general cognition, or non-social cognition, is relatively affect-neutral (Adolphs, 2003; Fiske & Taylor, 2013). Viewed this way, general cognitive processes provide the foundation that is necessary for social cognitive processing (Penn et al., 1997).

The vast majority of research into the relationship between social cognition and general cognition comes from studies involving schizophrenia. Studies using statistical modelling techniques, factor analyses, or meta-regression (Allen, Strauss, Donohue, & van Kammen, 2007; de Achával et al., 2010; Kohler et al., 2009; Sergi et al., 2007; van Hooren et al., 2008) have provided evidence that social cognition is related to, but distinct from, general cognitive functions (e.g., executive functions, processing speed, verbal fluency, and verbal memory). This distinction is also observed at the neural level because activation circuitry for social cognition and general cognition are independent (Adolphs, 2009; Brunet-Gouet & Decety, 2006; Pinkham, Penn, Perkins, & Lieberman, 2003; Van Overwalle, 2009).

### 4.6.1 Social and non-social cognition, and functional outcome.

There is a growing body of literature investigating the relationship between social cognition and general cognition and different types of functional outcome. This thesis focused on the relationship between general cognition and social cognition, but not how each of these were related to functional outcome; however a review of the interrelations between these three areas is presented because it highlights that social cognition plays an important role in mediating the relationship between general cognition and functional outcome.

A summary of research involving schizophrenia, which has dominated this literature, is presented in Table 4.2. Two meta-analyses (Fett, Viechtbauer, Penn, van Os, & Krabbendam, 2011; Schmidt, Mueller, & Roder, 2011) examined the degree to which poor social cognition was influenced by general cognitive impairment, and the

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impact of both social cognition and general cognition on functional outcome. The findings from this literature have shown that general cognitive processes (i.e., executive functions, memory, and processing speed) affect social cognitive abilities, which consequently impact general functioning such as quality of life. The literature involving emotion recognition is more developed and shows a fairly consistent modest relationship between emotion recognition and community functioning, social skills and social behaviour. By comparison, studies involving ToM have received far less attention in terms of functional significance. Table 4.2 shows that a number of diverse tasks of general cognition and functional outcome were used. Studies have often also reported diversity in clinical and demographic characteristics of different samples with the same diagnosis. For this reason, a clear theoretical account of precisely which aspects of general cognition might be most salient for social cognition remains unclear. Despite this, there is consistent evidence showing that some aspects of general cognition are related to social cognition, and that at least part of the relationship between general cognition and functional outcome is mediated by social cognition.

# **Table 4.2:**

Meta-analyses Assessing the Relationship Between Emotion Recognition and ToM and Non-social Cognition with Functional Outcome

	Sample	Social cognition	General cognition	Functional outcome	Findings
Fett et al. (2011)	52 studies; schizophrenia	ToM, emotion recognition & processing, social perception & knowledge	Reasoning & problem solving, processing speed, attention & vigilance, working memory, verbal and visual learning & memory, verbal comprehension, verbal fluency	Community functioning (independent living skills, social/work functioning), social behaviour in the milieu, social problem solving, social skills (eye contact)	1. Social cognition was more strongly related to community functioning than general cognition (16% variance explained versus 6%); 2. The various general cognitive domains differed in strength of their relationship to different domains on functional outcome, with small to large effect sizes ( $\mu_{\rho}$ = .16 to .39); and 3. The largest effect size between social cognition and functional outcome was evident for the association between ToM and community functioning ( $\mu_{\rho}$ = .48), but the effect was smaller for emotion recognition and social behaviour in the milieu ( $\mu_{\rho}$ = .22).
Schmidt et al. (2011)	15 studies; schizophrenia	Emotion recognition, ToM, social schema, social knowledge	Processing speed, verbal fluency, working memory, and verbal/visual memory	Vocational, social, psychological: Global Assessment of Functioning Scale (DSM-IV)	1. All general cognitive domains ( $\beta = .38$ ) were directly related to functional outcome; 2. The direct relationship from general cognition to functional outcome did not remain significant ( $\beta =$ .15) when social cognition was entered as a mediator; and 3. Social cognition (emotion recognition and social schema) was significantly associated with general cognition ( $\beta = .67$ ) and was predictive of functional outcome ( $\beta = .35$ ), explaining 21% of the variance in functional outcome.

*Notes.*  $\beta$  = standardised regression coefficients;  $\mu_{\rho}$  = average correlation.

# **4.6.2 Importance of social functioning.**

As demonstrated in Section 4.6.1 and Table 4.2, there is now considerable evidence to show that difficulties with emotion recognition and ToM are associated with impairments in social functioning. Importantly, interpersonal relationships depend on intact social cognition. Therefore, it is likely that deficits in either emotion recognition or ToM could affect social support and/or social isolation. People with CHF represent an ageing group with debilitating symptoms that increase depression rates (Johansson et al., 2013; Rutledge et al., 2006) and social isolation, and reduce quality of life (O'Loughlin et al., 2010; Volz et al., 2011). For these reasons, people with CHF have an increased need for social support.

Only a few studies have focused on the relationship between social support and outcomes in CHF, and none have examined social cognition. The available literature has shown that social functioning plays an important role in CHF outcomes. For instance, depression reduced over time for those with greater social supports (Friedmann, Son, Thomas, Chapa, & Lee, 2013; Graven & Grant, 2013). Lack of intimate network support (i.e., from a spouse) (Murberg & Bru, 2001) and social isolation (Friedmann et al., 2006; Murberg & Bru, 2001) were significant predictors of mortality (Murberg & Bru, 2001). Furthermore, patients with high levels of support reported better self-care than patients with low or moderate levels (Gallagher, Luttik, & Jaarsma, 2011). Consistent with these individual studies, a review of 17 studies (Luttik et al., 2005) involving CHF found that increased social support, particularly emotional support, reduced hospital readmissions and mortality.

# 4.7 Chapter Summary

This chapter provided an overview of the second focus area of this thesis, namely social cognition, and two core aspects of social cognition, which include emotion recognition and ToM. The second half of this chapter showed that deficits in each of these social cognitive constructs are a robust feature of clinical groups that have widespread neurological changes. This review chapter also showed that social cognition is related to aspects of more general cognitive processing, such as executive functions and memory, but the exact nature of this relationship remains unclear. The chapter also highlighted that social functioning in people with CHF has benefits on the health outcomes of this group.

# CHAPTER 5: Introduction Into the Investigation of Prospective Memory in People with Chronic Heart Failure

The literature review presented in Chapter 2 showed that research into the cognitive functioning of people affected by CHF is relatively developed. However, no prior study has investigated whether the cognitive deficits observed in CHF extend to deficits in PM function. This chapter is the first of two chapters that focuses on PM function in this population. Two published manuscripts are included in this chapter.

The first part of the chapter is a methodological protocol used in the subsequent two studies. This Protocol Paper also describes the evaluation of the association between 'Heart-FaST', a heart failure screening tool, and PM performance, which was undertaken by the parent study and is not presented in this thesis.

The second part of this chapter is Study 1, the first empirical assessment of PM function in people with CHF compared to health controls. The primary aim of Study 1 was to determine whether any observed deficits in a CHF sample would be specific to a particular type of PM task type, or pervasive regardless of the PM task features. To assess this, a behavioural measure of PM was used (Virtual Week) (Rendell & Craik, 2000) to systematically investigate different PM task parameters focusing on two task features, PM cue (time-based, event-based) and PM task (regular, irregular). A further aim of Study 1 was to investigate the relationships between important cognitive domains and PM performance in this sample. To achieve this, measures of executive functions, verbal memory, working memory, and global cognition were administered.

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This chapter provides a greater understanding of the cognitive profile of people with CHF, beyond the cognitive domains that have typically been assessed in existing studies. The research presented in Study 1 provides an argument for why it is necessary to focus on PM research in this population, in consideration of how PM might be important for CHF self-care.

# Paper 1: Protocol

The following chapter is a manuscript that has been published in *BMC Cardiovascular Disorders*.

Habota, T., Cameron, J., McLennan, S. N., Ski, C., F., Thompson, D. R., & Rendell, P. G. (2013). Prospective memory and chronic heart failure. *BMC Cardiovascular Disorders*, *13*, 63–71. doi:10.1186/1471-2261-13-63.

# **5.1 Protocol Paper**

Title: Prospective memory and chronic heart failure: Study protocol

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# Abbreviations:

ACE-R: Addenbrooke's Cognitive Examination – Revised; CHF: Chronic heart failure; HADS: Hospital Anxiety and Depression Scale; Heart-FaST: Heart-Failure Screening Tool; MS: Multiple sclerosis; NART: National Adult Reading Test; PM: Prospective memory; RAVLT: Rey Auditory Verbal Learning Test; SCHFI: Self-care Heart Failure Index; TMT: Trail Making Test; WAIS-IV: Wechsler Adult Intelligence Scale-IV.

# **Competing interests:**

The authors declare that they have no competing interests.

Keywords: Chronic heart failure, self-care, cognitive function, prospective memory

# Figures:

- Figure 1. Virtual Week
- Figure 2. Virtual Week prospective memory task
- *Figure 3*. Virtual Week event card
- *Figure 4*. Virtual Week prospective memory task execution
- *Figure 5.* Recruitment protocol

## 5.1.1 Abstract

**Background:** Patients with chronic heart failure (CHF) experience a number of debilitating symptoms, which impact on activities of daily living and result in poor quality of life. Prospective memory, which is defined as memory to carry out future intentions, has not been investigated in this group. However, emerging evidence suggests CHF patients have difficulties with cognitive processes related to prospective memory. Self-care, which partly relies on prospective memory, is essential in symptom management and preventing acute clinical deterioration. This study aims to measure prospective memory in CHF patients, and examine the relationship between prospective memory and CHF self-care.

**Methods/Design:** A comprehensive neuropsychological assessment will be conducted to assess a range of cognitive functions and psychopathology. The primary focus will be an assessment of prospective memory using a well-established behavioural measure; Virtual Week. Thirty CHF patients attending a nurse-led management program will be recruited from three hospital sites in Melbourne, Australia and their self-care behaviours will be assessed using the Self-care Chronic Heart Failure Index (SCHFI), a validated self-report tool. An additional 30 healthy controls, matched on age, gender, and IQ will be recruited from the general community.

**Discussion:** This is a group comparison study that will provide an evaluation of the prospective memory abilities of CHF patients. The findings of this research will provide insight into whether prospective memory may be hindering patients' ability to perform adequate self-care.

## 5.1.2 Background

Patients with chronic heart failure (CHF) represent a rapidly increasing and vulnerable group of individuals with a dismal prognosis (Fonarow et al., 2012). Despite significant improvements in the multidisciplinary management of CHF (Lindenfeld et al., 2010) most patients experience debilitating symptoms that impact on activities of daily living, quality of life, and anxiety and depression, which contribute to increased and frequent hospitalisations, and reduced survival (Volz et al., 2011). Due to the poor outcomes associated with CHF, management of this significant chronic condition is a major economic drain on valuable healthcare resources (Smith et al., 2012). Multidisciplinary CHF management programs have evolved over recent years to enable the clinical application of evidence-based treatments that reduce economic and patient burden by improving health outcomes such as hospital readmissions (Jovicic, Holroyd-Leduc, & Straus, 2006; Yu, Thompson, & Lee, 2006).

A key strategy within CHF management programs is to promote and engage patients to perform specific self-care behaviours (Riegel, Moser, et al., 2009). CHF self-care comprises maintenance and management strategies that involve a set of complex cognitive behaviours and decisions (Riegel, Lee, & Dickson, 2011). Selfcare maintenance includes performing behaviours that help maintain clinical stability, for example medication adherence, and fluid and sodium restriction (Riegel et al., 2011). Self-care management includes symptom monitoring, for example daily weighing to monitor and recognise changes in symptoms, and then responding to pertinent changes (Riegel et al., 2011). A case in point is the need to weigh daily and then to respond appropriately to increases in body weight of 2kg or more. Often, patients do not follow through on this, and despite regular weighing, do not initiate the response needed when there is an increase in weight (White, Howie-Esquivel, & Caldwell, 2010). Optimal engagement in self-care has the potential to reduce negative health outcomes such as clinical instability, reduce unplanned hospitalisations, and improve survival (Lee, Moser, Lennie, & Riegel, 2011). Despite the significant research attention towards promoting CHF self-care, many patients have low success in acquiring the necessary skill sets (Riegel, Driscoll, et al., 2009). This is often considered to reflect poor motivation or compliance, due to multiple patient and clinical factors (Cameron, Worrall-Carter, Riegel, Lo, & Stewart, 2009; Oosterom-Calo et al., 2012). However, the patient's cognitive ability to respond to vital cues, and initiate appropriate actions, is also critical in predicting engagement in self-care (Cameron et al., 2010).

Cognitive dysfunction has been observed in as many as 75% of patients in select CHF populations (Cameron et al., 2010; Pressler, 2008) and it has been linked to changes in cerebral pathology resulting from reduced cerebral perfusion and oxygenation (Bennett & Sauvé, 2003). Consequently, multiple cognitive domains appear to be diminished in CHF patients including language, attention, working memory, visuospatial function, psychomotor speed, and executive function (Kindermann et al., 2012; Pressler, Kim, Riley, Ronis, & Gradus-Pizlo, 2010). These cognitive deficits may compromise patients' reasoning and decision-making abilities, thereby limiting their ability to perform self-care (Cameron et al., 2010).

Prospective memory (PM) is defined as memory to carry out future intentions (Rendell & Henry, 2009). It involves different phases of forming an intention, holding onto this intention for some time, and then initiating and carrying out the intention at a set time or situation (Kliegel, Mackinlay, & Jäger, 2008). These phases require the application of multiple cognitive domains including attention, working memory, retrospective memory, and executive functioning (Shum & Fleming, 2009).

Therefore, prospective memory may also be impaired in CHF patients with significant ramifications in performing self-care tasks. A multiprocess framework has often been used to describe prospective memory functioning. Depending on specific demands of different tasks, or task features, remembering may be either elicited by effortless and automatic processes, or by strategic, attention-demanding processes that include monitoring of the environment for relevant cues (McDaniel & Einstein, 2000).

A key distinction between different prospective memory tasks is that some are event-based and others are time-based. Event-based tasks are triggered by an event cue and require monitoring of the environment for that cue (Einstein & McDaniel, 2005). For example, "when I get home in the afternoon [task cue], I have to take my diuretic [PM task]". On the other hand, time-based tasks are performed at a specific time, or once a specific amount of time has lapsed (Einstein & McDaniel, 2005). This latter type of task requires more strategic monitoring and self-initiated control processes, and consequently results in greater deficits (McDaniel & Einstein, 2000). Another important task distinction is whether a task is regular (same task each day), or irregular (different task each day). Regular tasks impose less demand on retrospective memory (remembering what needs to be done), compared to irregular tasks (Foster, Rose, McDaniel, & Rendell, 2013; Rendell, Gray, Henry, & Tolan, 2007).

Failures in prospective memory are often exhibited by individuals with neurological disorders that impact on functional independence (Shum & Fleming, 2009; Thompson, Henry, Rendell, Withall, & Brodaty, 2010). Further, a general decline in prospective memory is found in normal ageing, particularly after the 60s (Henry, MacLeod, Phillips, & Crawford, 2004). Failures in prospective memory have the potential to lead to rapid clinical deterioration in patients with CHF with serious consequences on health outcomes. We propose that prospective memory is crucial for appropriate CHF self-care, for example in tasks involving medication, daily weighing, and initiating an appropriate response to changes in weight.

# 5.1.3 Aims

The aims of this study are to determine if: 1) prospective memory ability of CHF patients is impaired compared with an age-matched group, 2) CHF patients exhibit more prospective memory failures in event-based or time-based tasks than matched controls, 3) prospective memory deficits in CHF patients are globalised, or specific to a particular type of prospective memory task, 4) prospective memory ability correlates with self-care maintenance behaviours, management skills, and confidence, and 5) prospective memory ability correlates to functioning as assessed by the Heart Failure Screening Tool (Heart-FaST). Findings from this study will contribute to our understanding of the factors that predict adequate engagement in CHF self-care and provide avenues for developing appropriate interventions.

### 5.1.4 Methods/Design

This study will use a group comparison design to examine the prospective memory abilities of patients with CHF. Groups will be matched on age, gender, years of education, and premorbid intelligence estimated/indexed by the National Adult Reading Test (NART) (Nelson, 1982).

# **Participants**

Participants will include adults 18 years and over, although due to the prevalence of CHF in the elderly, the majority of the sample will be above 50 years. The CHF group will have a confirmed diagnosis of CHF based on national guidelines (Krum et al., 2011). All participants will be recruited from a nurse-led CHF management program at one of three public hospitals in Metropolitan Melbourne, Australia. Patients will be excluded if they reside in a residential aged high care facility, have a documented history of moderate-to-severe cognitive impairment or dementia (based on the Addenbrooke's Cognitive Examination – Revised; ACE-R; Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000) or have a terminal diagnosis. Participants who do not have sufficient comprehension to read English without the need of a translator will be excluded. The control group will be recruited through flyer advertising in the general community, and snowball recruitment. Participants being considered for the control group will be excluded if they have a history of CHF or neurological disease, and/or have had recent treatment (past three months) for an acute cardiovascular problem.

### CHF participant descriptive data

Information relating to a range of participant variables will be collected in order to characterise the sample. These variables include demographic details, number and quality of social supports, education level, occupation status and history, history and current treatment of depression and/or anxiety, and comorbid illness burden (measured using the Charlson Comorbidity Index). Cardiac related history will also be obtained, including cardiovascular risk factors, length of time living with chronic heart failure, type of chronic heart failure diagnosis, chronic heart failure aetiology, prior treatments for chronic heart failure (beyond medical therapy), observations of clinical features, and self-care behaviours (measured using the Self-care Chronic Heart Failure Index v6; SCHFI) (Riegel, Lee, Dickson, & Carlson, 2009) and ability (measured using Heart-FaST) (Cameron, Ski, et al., 2013).

The SCHFI is a comprehensive self-report instrument of self-care practices pertinent to the management of CHF. The SCHFI comprises 15 items rated on a 4point response scale. It has three subscales: maintenance, management and confidence (Riegel, Lee, et al., 2009). Self-care maintenance items assess treatment adherence and symptom monitoring to prevent clinical deterioration, for example fluid restrictions and daily weighing. Self-care management items assess the ability to recognise changes in CHF symptoms, evaluate the significance of the changes, and make decisions on treatment actions, for example in the event of > 2kg weight gain a treatment action would be to take an extra diuretic. Self-care confidence items measure perceived ability to engage in each self-care phase and help to explain why some patients master self-care and others do not (Riegel, Jaarsma, & Strömberg, 2012). Scores from each of the three self-care scales are transformed to 100-point scales; higher scores reflect better self-care. Self-care management scores are only computed for those patients reporting CHF symptoms of ankle swelling or trouble breathing in the previous three months (Riegel, Lee, et al., 2009). Scaled scores > 70 are considered to indicate adequate self-care (Riegel, Lee, et al., 2009). The SCHFI is a reliable measure of self- reported self-care skills and behaviours and has been extensively validated among CHF populations around the world (Cameron, Worrall-Carter, Driscoll, et al., 2009).

The Heart-FaST was developed to assist clinicians in applying educational and support strategies based on self-care capacity (Cameron, Ski, et al., 2013). Unlike the

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SCHFI, which primarily assesses self-care practices, the Heart-FaST is a unique instrument that assesses identified barriers in patient engagement in self-care behaviours. The construction of the Heart-FaST was based on the results of extensive literature review, development and testing of the InCOGNITO conceptual model (Cameron, Worrall-Carter, Riegel, et al., 2009) and expert opinion in carefully selecting relevant items. The Heart- FaST comprises three salient domains recognised as barriers to CHF self-care: cognitive, emotional and physical functioning. Possible scores on the three Heart-FaST domains are: 0 to 3 on physical functioning, 0 to 20 on cognitive functioning, and 7 to 49 on emotional functioning. Lower scores indicate higher functioning on each domain and better self-care capacity (Cameron, Ski, et al., 2013). Levels of functioning across each Heart-FaST domain are graded as low, medium or high. Nursing recommendations and guidelines directed at applying individual educational and support strategies for each level of functioning have been developed. Initial pilot data indicates that the Heart-FaST is a valid instrument for assessing self-care capacity in patients with CHF and is likely to aid nurses in tailoring support strategies to promote effective CHF self-care (Cameron, Perona, Ski, & Thompson, 2012).

# **Cognitive measures**

#### Global cognition

The Addenbrooke's Cognitive Examination – Revised is a short, sensitive cognitive screening test that measures five cognitive domains; attention/orientation, memory, verbal fluency, language and visuospatial abilities. Lower scores suggest poorer cognitive performance (Mathuranath et al., 2000). The ACE-R is sensitive to

early stages of dementia (Mathuranath et al., 2000) and will be used to identify and exclude potential participants who have moderate-to-severe cognitive impairment.

## Primary measure

Prospective memory will be the primary focus of this research project and will be measured using the well-established behavioural measure, Virtual Week (Rendell & Craik, 2000); a computerised board game that simulates a week of everyday activities (Figure 1). The study will use a shortened two day version of the game. A key advantage of Virtual Week is that it allows tasks with different task features (event, time, regular, irregular) that closely represent activities in real life, to be investigated systematically in a controlled manner. Virtual Week has been used widely within prospective memory research and has demonstrated robust psychometric properties (Rendell & Henry, 2009; Rose, Rendell, McDaniel, Aberle, & Kliegel, 2010). A study using a group of participants with schizophrenia found the split-half reliability estimate to be .90 for the overall measure (Henry, Rendell, Kliegel, & Altgassen, 2007). In another study using a clinical sample, the reliability estimate was reported to be .89 for Parkinson's disease patients and .81 for the control group (Foster et al., 2013). It has been successfully used in previous research within clinical and normal populations (Rendell & Henry, 2009); including several studies with abnormal ageing (Thompson et al., 2010), and it is an interesting and intuitive task for users which are important features for maintaining motivation for task completion.

Participants will move a token around the board game on the roll of a dice, with each circuit of the board representing one virtual day. As participants move around the board, a series of events occur (e.g., 'you go to the library') where the participant is required to make choices about the tasks relevant to the event (e.g., mode of transport to library). At some of these events, participants have to remember to perform a prospective memory task. For example, at the beginning of the game, participants might be asked to remember to 'drop in the dry cleaning' (PM task) when 'shopping' (irregular, event-based task; Figure 2). As they move around the board, they will be instructed at several points during the day, to pick up an 'event card' when they land on, or go past, an 'event' square (represented by an 'E'). If the event card is 'shopping' (Figure 3), participants should action the prospective memory task by clicking on a 'perform task' button and selecting the prospective memory task that needs to be performed (Figure 4). Other tasks will have to be performed at a specified time of day. For example, participants will be asked to attend a meeting with a librarian at 3 pm (irregular, time-based task). They will be required to monitor a virtual clock in the game (calibrated to position of token on board) and perform the task by clicking on the 'perform task' button at the specified time period. The perform task button reveals a list of possible tasks for participants to select. Participants will also be asked to take medication at the 'breakfast' and 'dinner' event cards each day (regular, event-based task), and take their asthma inhaler at two time points during the day (regular, time-based task).

#### Characterisation measures

## Premorbid intelligence

The *National Adult Reading Test* (Nelson, 1982) will be used as an index of premorbid intelligence. This is a word-recognition test of vocabulary knowledge that requires participants to read aloud 50 English words of increasing difficulty that do not follow normal phonetic rules, for example, 'chord'. Scores on the NART correlate

with general IQ, including Verbal IQ and Perceptual IQ (Strauss, Sherman, & Spreen, 2006). On the basis of number of errors in pronunciation, a Full-Scale IQ estimate of the Wechsler Adult Intelligence Scale – Revised can be derived. The NART is a frequently used test that is a valid and reliable measure. It has high construct validly (Crawford, Stewart, Cochrane, Parker, & Besson, 1989), and internal reliability estimates are reported to be above .90 (Crawford, Parker, Stewart, Besson, & De Lasey, 1989).

# Psychopathology

The *Hospital Anxiety and Depression Scale* (HADS) (Zigmond & Snaith, 1983) is a 14 item questionnaire, which will be used to asses psychopathology. Seven of the items relate to anxiety and seven relate to depression. Responses are provided on a Likert scale, and scores on each scale are interpreted in ranges: normal (0-7), mild (8-10), moderate (11-14), and severe (15-21). The two subscales have a mean correlation of .56, and the mean Cronbach's alpha is .83 for anxiety and .82 for depression (Bjelland, Dahl, Haug, & Neckelmann, 2002). The HADS has been used successfully in psychiatric patients and in the general population (Bjelland et al., 2002).

### Executive functioning

Four measures will be used to assess participants' executive functioning. Executive functions are higher order thinking processes.

The *Trail Making Test* (TMT) (Crowe, 1998) assesses planning ability and divided attention. It is a pencil and paper test and consists of two parts. In Part A,

participants are required to draw lines to connect circles that are numbered consecutively; in Part B, participants must connect circles that are numbered and lettered, alternating between the numeric and alphabetic sequences. The total time taken to complete the task is measured. Faster performance on the TMT indicates higher levels of planning ability. The TMT has successfully been used within normal and clinical groups (Strauss et al., 2006), and the reliability for neurologically stable groups is reported to be at least .70 for Part A and Part B (Levine, Miller, Becker, Selnes, & Cohen, 2004).

The *Hayling Sentence Completion* test (Burgess & Shallice, 1997) assesses cognitive initiation and inhibition. First, participants verbally complete 15 sentences with an obvious response. For example, when presented with the sentence "The captain wanted to stay with the sinking ...", they must provide the word 'ship'. In the second part, participants have to suppress the obvious response and complete 15 sentences with an unrelated word. The participant's response times for each section, and their errors, determine their overall score. High split-half reliability coefficients have been reported for a brain impaired sample (Hayling 1 time = .93; Hayling 2 time = .80; Hayling errors = .72), but reliability is more varied (.35 to .83) for healthy adults (Burgess & Shallice, 1997).

The *Digit Span*, a subtest of the Wechsler Adult Intelligence Scale-IV (WAIS-IV) (Wechsler, 2008) is a measure of working memory, which is the ability to mentally hold and manipulate new information within a limited time frame. Participants are verbally presented with a string of numbers (e.g., 7-2-8-6) and they are required to remember and repeat these numbers in a specific order, either forwards (e.g., 7-2-8-6), backwards (e.g., 6-8-2-7), or in sequence (lowest to highest, e.g., 2-6-7-8). Participants are scored out of 16 for each section of the test. Reliability coefficients for the WAIS-IV Digit Span are all reported to be above .90 (Wechsler, 2008).

The final measure of executive functioning is an adaptation of the Controlled Oral Word Association task, which is a measure of *verbal fluency* (Benton, Hamsher, & Sivan, 1994). Two types of verbal fluency will be assessed, phonemic and categorical. In the phonemic verbal fluency task, participants are required to orally generate as many words as they can beginning with the letters P, R and W, excluding proper nouns, numbers, and repetitions of the same word with a different suffix. Participants are then required to name as many animals as they can, beginning with any letter, as a measure of their semantic verbal fluency. Participants are given one minute for each task. Although other letter combinations have been used previously, differences between versions appear to be negligible; correlations of .82, or higher, have been reported for two sets of letters (e.g., PRW, CFL) (Benton et al., 1994; Strauss et al., 2006).

# Verbal memory

The *Rey Auditory Verbal Learning Test* (RAVLT) (Rey, 1958) will be used to measure verbal memory and provides a measure of immediate recall, delayed recall and recognition. This test involves a list of 15 words, which an examiner reads aloud. The participant's task is to repeat all the words they can remember, in any order. This procedure is carried out a total of five times. After a 20-minute delay period filled with other activities, the participant is asked to recall as many words as possible. Finally, a recognition test is administered. Participants are presented with a list of 30 words (15 distracter items, and the 15 list words), and are asked to identify as many of the list words as possible. The RAVLT is a recognised measure of memory that is widely used in research as well as in clinical practice (Strauss et al., 2006). The RAVLT has a high internal reliability of .90 for the total score (van der Burg & Kingma, 1999).

# Procedure

A research assistant, in collaboration with the CHF nurses, will screen and recruit participants for the CHF group. A detailed history will be collated based on patient self-report information and review of medical records. Around three months later, participants will be tested in a single session, lasting between two to three hours. The delay of three months will be built in to ensure that participants are medically stable when they complete the neuropsychological assessment. The ACE-R will be administered first to assess each participant's cognitive functioning. Virtual Week will be administered next, followed by the remaining measures. Participants will be offered at least one break throughout the session and will be encouraged to take additional breaks as needed. The study protocol and the inclusion and exclusion criteria are illustrated in Figure 5.

### 5.1.5 Data analyses and power calculation

A descriptive analysis of all variables will be performed. A mixed factorial ANOVA will be used to examine main effects and interactions of prospective memory tasks, across CHF patients and healthy controls. Statistical significance will be considered at a *p*-value of < .05. As participants will be required to perform different prospective memory tasks (event-based, time-based, regular, irregular),

analyses will also examine whether prospective memory lapses are specific to a particular task, or pervasive across tasks. Comparisons based on normative samples will also be reported for the cognitive screen (ACE-R), measure of premorbid intelligence (NART), three measures of executive function (TMT, Digit Span, Hayling), and verbal memory (RAVLT; Trials 1-5).

Sample size estimations are based on a previous study using Virtual Week with a clinical sample involving multiple sclerosis (MS) patients (Rendell, Jensen, & Henry, 2007). Almost half of patients with MS develop neurocognitive dysfunction in the areas of memory, attention, concentration, and executive function (DeSousa, Albert, & Kalman, 2002). The cognitive deficits in patients with MS are modest compared to CHF patients; therefore the following power calculation is a conservative estimate. Based on the magnitude of difference in prospective memory performance between MS patients and matched controls (Rendell et al., 2007), to get an effect size of .84, a sample of 60 (30 in each group) will produce a power of .89.

Exploratory correlation analyses will be conducted to examine the relationship between different prospective memory types (event, time, regular, irregular) and the three domains of self-care: self-care maintenance behaviours; management skills; and confidence. Further exploratory correlations will investigate the relationship between the three clinical factors (cognitive, emotional and physical functioning) assessed by the Heart-FaST, and self-care ability. Preliminary correlations will also be conducted to examine the association between Heart-FaST and the behavioural measure of prospective memory, Virtual Week. Ethics

This study has been approved by the Eastern Health Research and Ethics Committee (LR39/1112), and the Human Research Ethics Committee of the Australian Catholic University (V2007 08 69; 2012 O4V). Informed consent will be obtained from all the participants in the study.

#### 5.1.6 Discussion

The results of this study will be the first to provide insights into the prospective memory difficulties experienced by patients with CHF. The study will test the hypothesis that prospective memory abilities are impaired, compared to healthy controls. Prospective memory failures experienced by CHF patients could affect selfcare, for example by forgetting to pick up prescription medications from the pharmacist, forgetting to attend doctor appointments, forgetting to take daily medications and performing daily weighing, and failing to respond to > 2kg changes in weight, all of which are considered crucial for the management of their condition (Riegel, Moser, et al., 2009). Therefore, this study will also test the hypothesis that prospective memory is a significant predictor of a patient's ability to engage in selfcare behaviours and respond appropriately when sudden changes occur. If the findings indicate that prospective memory is associated with poor self-care outcomes, it will provide directions for research addressing cognitive impairments experienced by CHF patients. The findings also have the potential to provide avenues for implementing individually tailored patient education and support strategies, dependent upon individual capabilities identified through screening.

A fundamental approach to improving adverse CHF patient outcomes and associated healthcare costs lies in applying individualised education and support 87

strategies (Cameron, Ski, & Thompson, 2012). Improving prospective memory alongside the individualised application of educational and support strategies is likely to enhance critical everyday self-care actions and decisions. Combining these two complimentary approaches into CHF management programs will increase the likelihood of enhancing functional independence for individuals diagnosed with CHF.

A number of practical considerations in undertaking this study have been considered and addressed. Given that CHF patients are typically older adults, a touch screen will be made available for participants who are either unwilling or unable to use a computer and mouse for testing. Using a simulated touch screen with participants pointing on screen and experimenters operating mouse overcame previous reluctance or difficulties of adults using a computer when playing Virtual Week (Rendell et al., 2012). We acknowledge that the length of neuropsychological testing may cause fatigue, particularly in the CHF group. Therefore, participants will be provided breaks as necessary. Alternatively, testing will be divided across two sessions within a one-week period in order to avoid significant cognitive fluctuations between sessions. All CHF participants will be tested at approximately three months following enrolment into a CHF management program; this will ensure that patients are tested during a period when they are more likely to be clinically stable.

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Figure 1. Virtual Week.



Figure 2. Virtual Week – prospective memory task.



Figure 3. Virtual Week – event card.



*Figure 4*. Virtual Week – prospective memory task execution.



Figure 5. Recruitment protocol.

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## Study 1

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#### 5.2 Study 1

Title: Prospective memory impairment in chronic heart failure

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#### **Abbreviations:**

ACE-R: Addenbrooke's Cognitive Examination – Revised; CHF: Chronic heart failure; DS: Digit Span; HADS: Hospital Anxiety Depression Scale; NYHA: New York Heart Association; PM: Prospective memory; RAVLT: Rey Auditory Verbal Learning Test; TMT: Trail Making Test.

**Keywords:** Prospective memory, chronic heart failure, Virtual Week, executive functions, retrospective memory, cognitive functions

## **Tables:**

Table 1. Clinical Characteristics of the CHF Group

Table 2. Participant Characteristics

- Table 3. PM Accuracy: Mean (SD) Proportion of PM Tasks Executed at Different

   Time Points
- Table 4. Recognition of PM Task Content: Mean (SD) Proportion of PM Task andPM Cue Pairs Matched Correctly

## **Figures:**

Figure 1. Screening and recruitment process.

#### 5.2.1 Abstract

**Objectives:** Although cognitive deficits are common in patients with chronic heart failure (CHF), no study to date has investigated whether these deficits extend to the capacity to execute delayed intentions (prospective memory, PM). This is a surprising omission given the critical role PM plays in correctly implementing many important CHF self-care behaviours. The present study aimed to provide the first empirical assessment of PM function in people with CHF. The key dependent measure was a laboratory measure of PM that closely simulates PM tasks in daily life – Virtual Week.

Methods: A group comparison design was used, with 30 CHF patients compared to 30 demographically matched controls. Background measures assessing executive functions, working memory, and verbal memory were also administered. Results: The CHF group exhibited significant PM impairment, with difficulties generalising across different types of PM tasks (event, time, regular, irregular). The CHF group also had moderate deficits on several of the background cognitive measures.

**Conclusion:** Given the level of impairment remained consistent even on tasks that imposed minimal demands on memory for task content, CHF-related difficulties most likely reflects problems with the prospective component. However, exploratory analyses suggest that difficulties with retrospective memory and global cognition (but not executive control), also contribute to the PM difficulties seen in this group. The implications of these data are discussed, and in particular, it is argued that problems with PM may help explain why patient engagement in CHF self-care behaviours is often poor.

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#### **5.2.2 Introduction**

Chronic heart failure (CHF) is a clinical syndrome resulting most frequently from long-standing coronary heart disease (Braunwald, 2013). It is a complex condition characterised by structural dysfunction and weakening of the heart muscle which, in its most common form, impairs the ability of the left ventricle to either eject, or fill adequately, with blood to meet the body's needs (Krum, Jelinek, Stewart, Sindone, & Atherton, 2011). The annual incidence of CHF approaches 10 per 1000 population in those over 65 years of age (Lloyd-Jones et al., 2002), with this age group accounting for more than 80% of CHF morbidity and mortality (Bui, Horwich, & Fonarow, 2010). Despite significant improvements in the multidisciplinary management of CHF (Lindenfeld et al., 2010), most patients experience debilitating symptoms that impact on activities of daily living, quality of life, and mental health, contributing to frequent hospitalisations, and reduced wellbeing (Volz et al., 2011).

A frequent secondary complication of CHF is cognitive impairment. Cognitive deficits have been observed in as many as 50% of clinically stable outpatients, and up to 80% of hospitalised patients (Bennett & Sauvé, 2003; Cameron et al., 2010; Pressler, 2008). The domains of cognition that are impaired most frequently are attention and concentration, memory, psychomotor speed, and executive control (Alosco et al., 2013; Vogels, Oosterman, et al., 2007; Vogels, Scheltens, Schroeder-Tanka, & Weinstein, 2007), but other areas are also affected, including language, working memory, and visuospatial function (Kindermann et al., 2012; Pressler, Kim, Riley, Ronis, & Gradus-Pizlo, 2010).

These cognitive difficulties appear to primarily be caused by damage to diffuse regions of the subcortical white matter, particularly in the frontal lobes, and to subcortical grey matter nuclei, particularly the thalamus, basal ganglia and brainstem (Artero et al., 2004; de Leeuw et al., 2001; Kalaria et al., 2004; Vogels, van der Flier, et al., 2007). Medial temporal and temporal-parietal regions are also vulnerable to grey matter loss (Almeida et al., 2012; Woo, Macey, Fonarow, Hamilton, & Harper, 2003; Zuccalà et al., 1997). Collectively, these findings show that CHF patients display relatively frequent cerebral abnormalities in frontal and, to a lesser degree, temporal neural structures. This is important because these brain regions have been specifically implicated in prospective memory (PM; Braver & Barch, 2002; Costa, Caltagirone, & Carlesimo, 2011; Reynolds, West, & Braver, 2009), which refers to the ability to remember to carry out intended plans at specific points in the future (Rendell & Henry, 2009).

Surprisingly, this critical cognitive ability has not yet been examined in CHF patients. It is important to understand the nature and severity of PM difficulties in this population given that PM is implicated in a wide variety of functional behaviours (Ellis & Freeman, 2008). In the present study, we were particularly interested to determine whether specific aspects of PM are differentially impaired. Given that frontal brain regions are amongst the most severely affected in CHF, and that these neural substrates are implicated in executive control operations, it might be anticipated that those aspects of PM that require control operations such as self-initiated retrieval, or strategic monitoring may be disproportionately affected.

A key distinction within PM task types is between event-based and time-based tasks. Event-based tasks are triggered by event-based cues and require monitoring of the environment to detect the cues (Einstein & McDaniel, 2005). For example, returning home in the afternoon (PM event) acts as a cue for taking a diuretic medication (PM task). Conversely, time-based tasks are performed at a specific time, or once a specific amount of time has elapsed; for example, taking medication (PM task) at 9 am (Einstein & McDaniel, 2005). As time-based PM tasks require more strategic monitoring and self-initiated control processes than event-based PM tasks (McDaniel & Einstein, 2000), they may be particularly impaired in patients with CHF.

Another task distinction, emerging from research involving a computerised assessment paradigm known as Virtual Week, is between PM tasks that are regular and those that are irregular (Foster, Rose, McDaniel, & Rendell, 2013). In this paradigm, regular tasks are frequently repeated and are well learned, while irregular tasks occur only once. Irregular tasks impose substantially greater demands on retrospective memory because they are not as well learned (Foster et al., 2013; Terrett et al., 2014). Foster et al. (2013) argue that a comparison of repeated versus one-off tasks is important, because it can clarify whether observed difficulties in PM reflect poor encoding of the task (the retrospective component) as opposed to difficulty initiating the task at the appropriate moment (the prospective component). Because of the particular involvement of frontal structures in CHF, any PM difficulties are unlikely to be explained entirely by the retrospective component, but are likely to also reflect deficits related to the prospective component.

The overarching goal of the present study was to provide the first empirical comparison of PM ability in people with CHF and demographically matched controls. It was predicted that people with CHF would show impaired PM performance, compared to controls, and that these impairments would be greater for time relative to event-based tasks, and for irregular relative to regular tasks.

#### 5.2.3 Methods

The study was approved by the Human Research Ethics Committees at Eastern Health and the Australian Catholic University. A detailed study protocol has been described in Habota et al. (2013).

## **Participants**

The Chronic Heart Failure (CHF) group was recruited from a pool of participants taking part in the parent study (n = 96) (13 participants were paid AUD \$10 per hour, the rest were volunteers). To be eligible for the parent study participants had to have a documented diagnosis of CHF based on national guidelines; specifically, cardinal symptoms (fatigue) and clinical features of congestion (exertional dyspnoea, lung crepitation), and objective evidence of cardiac impairment determined from echocardiography (Krum et al., 2006). All participants were outpatients actively engaged in a nurse-led CHF management program or CHF clinic, in one of three public hospitals in Metropolitan Melbourne, Australia. Participants were excluded if they resided in a residential aged high care facility, had a terminal diagnosis, a documented history of dementia, or could not read English. The screening and recruitment process for the CHF group is presented in Figure 1.

(Insert Figure 1 about here)

We did not exclude people with psychiatric illness, but participants' global cognition was screened using the Addenbrooke's Cognitive Examination – Revised (ACE-R) (Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000). Anyone who showed signs of potential dementia, as operationalised by a score lower than 82, was

excluded. There were no participants with head injury. The final sample of CHF patients consisted of 30 adults aged between 40 and 86 (M = 70.03, SD = 11.88) who were predominantly male (63%). CHF severity was assessed using the New York Heart Association (NYHA) classification based on symptoms of breathlessness with varying degrees of activities, ranging from no symptoms with moderate activities (Class I), to severe symptoms at rest (Class IV). The first two categories represent no or mild CHF symptoms, and the last two categories represent moderate or severe symptoms. As shown in Table 1, most participants (70%) had relatively mild CHF symptoms (functional classification I or II). Participants with left ventricular dysfunction (i.e., 70% systolic), and ischaemic (50%) heart failure were dominant. On average, participants had a moderate level of comorbid disease burden (Charlson Comorbidity Index mean = 3.17). Notably, four had moderate to severe renal disease, and time since initial diagnosis was almost three years (M = 33.19 months, SD =55.03). Excluded or ineligible participants from the pool of 96 did not differ significantly from the final sample on age, gender, years of education, or NYHA classification.

#### (Insert Table 1 about here)

The control group was recruited from the general community (13 participants were paid AUD \$10 per hour, the rest were volunteers). Potential participants were excluded if they reported a history of CHF or neurological disease, had received treatment during the past three months for an acute cardiovascular problem, or could not read English. Thirty-three participants were initially recruited, but two were excluded due to cognitive difficulties (one based on a score below 82 on the ACE-R,

and one because they did not understand the instructions of the primary measure). A further participant withdrew before completing the primary measure. Therefore, the final control group consisted of thirty adults. The control group did not significantly differ from the CHF group in gender distribution (57% male vs 63% male;  $\chi^2$  (1) = .28, p = .597). As shown in Table 2, there was a trend towards higher proportions of cardiac risk factors in the CHF group, but these group differences were not significant (all ps > .083). Table 2 also shows that the two groups were closely matched in age, education, and estimated IQ as indexed by the National Adult Reading Test (Nelson, 1982).

#### (Insert Table 2 about here)

#### Procedure

At the time of recruitment into the parent study, demographic and health related data (presented in Table 1) were collected using patient self-report and by reviewing medical records. After a delay of approximately three months, to ensure that participants were medically stable, all other measures were administered individually in a three-hour session. The ACE-R was administered first, followed by Virtual Week, and then the remaining cognitive measures. CHF health characteristics were not reassessed at this time.

#### Design

A mixed factorial, matched group comparison design was used. *Group* (CHF, control) was the between-groups independent variable. The two within-group variables were *PM cue* (event-based, time-based), and *PM task* (regular, irregular).

#### Measures

Global cognition

The *Addenbrooke's Cognitive Examination – Revised* (Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, J. R., 2000) was used to identify and exclude participants with possible dementia.

Analyses were based on raw scores for all measures, except for the National Adult Reading Test and the Hayling Sentence Completion Test, which were converted to scaled scores.

#### **Background Measures**

General intelligence

The *National Adult Reading Test* (Nelson, 1982) was used to index premorbid intelligence (IQ). Estimated IQ was calculated using the formula provided in the administration manual (Nelson, 1982).

## Psychopathology

The *Hospital Anxiety and Depression Scale* (Zigmond & Snaith, 1983) was used to screen for symptoms of anxiety and depression. The level of emotional symptomology was calculated separately for anxiety and depression (seven items each).

## Executive function – cognitive flexibility

The *Trail Making Test* (Reitan, 1992) was used to assess cognitive flexibility. It is a pencil and paper test consisting of two parts. Part A, required participants to draw lines to connect circles that were numbered consecutively. Part B required participants to connect circles that were numbered or lettered, alternating between the numeric and alphabetic sequences. The Trails B minus Trails A difference score was used as a measure of cognitive flexibility (Lamberty, Putnam, Chatel, Bieliauskas, & Adams, 1994).

#### Executive function – inhibition

The *Haling Sentence Completion Test* (Burgess & Shallice, 1996) was used to assess cognitive inhibition. The key condition required participants to suppress their prepotent response when completing a sentence. A total score was obtained by tallying errors and time taken (in seconds) to complete the task.

### Executive function - initiation

*Verbal fluency* was extracted from the ACE-R and used as a measure of cognitive initiation. Both phonemic and categorical fluency were assessed. For the former, participants were required to orally generate as many words beginning with the letter P as they could within one minute. For the latter, participants were required to name as many animals as they could within one minute. A composite verbal fluency score was used.

### Working memory

The *Digit Span* subtest from the Wechsler Adult Intelligence Scale-IV (Wechsler, 2008) was used to measure working memory. Participants were verbally presented with a string of numbers (e.g., 7-2-8-6) and were required to remember and repeat these numbers in a specific order, either forwards (e.g., 7-2-8-6) or backwards (e.g., 6-8-2-7). A single composite score was used to index this construct.

#### Verbal memory

The *Rey Auditory Verbal Learning Test* (RAVLT) (Rey, 1958) was used to measure verbal memory and provided a measure of immediate recall, delayed recall, and recognition. The examiner read aloud a list of 15 words. Participants were required to repeat all the words they could remember, in any order. This procedure was carried out five times. After a 20-minute delay, participants were asked to recall as many words as possible. A recognition test was then administered where participants were presented with a list of 30 words and were asked to identify as many of the list words as possible.

#### Prospective memory

A shortened version of *Virtual Week* (Rendell & Craik, 2000) was used to assess PM (for a review see, Rendell & Henry, 2009). Virtual Week is a computerised board game that simulates a week of everyday activities. Virtual Week has been used widely within PM research and has robust psychometric properties (Rendell & Henry, 2009; Rose, Rendell, McDaniel, Aberle, & Kliegel, 2010). It is also sensitive to differences between clinical and normal populations (Rendell & Henry, 2009).

In the present study (for detailed description see, Habota et al., 2013), participants used a computer mouse to move a token around a computerised representation of a board-game board after rolling a die. Each lap of the board represented one virtual day. At the beginning of each 'day', they were given a list of PM tasks that they had to remember to action. As participants moved around the board, a series of ongoing activities were presented in the form of 'events'. At some of these events, participants had to remember to perform a PM task. For example, at the beginning of the game, participants were asked to remember to "drop in the dry cleaning" (PM task) when "shopping". As they moved around the board, they were instructed at several points, to pick up an 'event card'. When they picked up the event card "shopping", which served as the task cue, they had to remember to action the PM task by clicking on a 'perform task' button and selecting the correct task. Other PM tasks had to be performed at a specified time of day (e.g., "attend a meeting with a librarian at 3pm"). They were required to monitor a virtual clock on the screen (calibrated to the position of the token on the board) and perform the relevant task by clicking on the 'perform task' button at the specified time period. The perform task button revealed a list of possible tasks for participants to select from, including distractor items.

Participants completed three virtual days; one day was a trial day to ensure that they understood the objectives of the game, and the following two days were test days. During each test day, participants were given eight tasks to remember to perform. Four tasks were regular, each occurring two times (take medication at the "breakfast" and "dinner" event cards, and take the asthma inhaler at two virtual times of day, 11 am and 9 pm). Four tasks were irregular, each occurring only once (two event-based tasks and two time-based tasks).

Responses were counted separately for each possible response type (*correct, missed, little late, late, little early, and early*) and were expressed as a proportion of the total number of PM tasks (16 tasks, eight per virtual day) in each of the four categories: regular event, regular time, irregular event, and irregular time. *Correct* responses were defined as those performed within the window of time that started

when the token arrived at (or went past) the target position on the board and closed when the dice was rolled again. *Missed* responses were defined as those that the participant did not remember at any time. *Little late* responses were defined as those that participants remembered after the correct criterion but before the next hour (on the virtual clock) for time-based tasks and before the next event card for event-based tasks. *Lot late* responses were defined as those made after the little late criterion and before the end of the virtual day. *Little early* were defined as responses made before the correct time and after the previous event card for the event-based tasks and 1 hour before the expected time for time-based tasks. Finally, *lot early* responses were defined as those made before the little early criterion and after the start of the virtual day.

#### Recognition test of PM task content

After completing each virtual day, participants' memory for the content of the PM tasks they were required to complete during that virtual day was tested. This recognition test provided an index of the retrospective component. Participants were presented with a list of PM tasks on the computer screen (e.g., take medication), which they had to match with the corresponding PM cue (e.g., at breakfast and dinner) from another list. The sample size for this measure was smaller (CHF n = 19, controls n = 24) than the others (n = 30) due to clerical error. Importantly, missing value analyses for all variables showed that data was missing at random.

#### 5.2.4 Results

#### **Participant characteristics**

As shown in Table 2, while the CHF group generally performed worse than controls on all eight cognitive tests, differences were only significant for cognitive inhibition, cognitive initiation, immediate recall, recognition, and global cognition. The two groups also did not differ in negative affect.

#### Analysis of Prospective Memory accuracy

The dependent variable, PM performance, was expressed as the proportion of Virtual Week tasks completed correctly for each of the four categories of tasks: regular event, regular time, irregular event, and irregular time (Table 3). Data were analysed with a 2 x 2 x 2 mixed analysis of variance (ANOVA) with the between-subjects variable of *group* (CHF, control), and the within-subjects variables of *PM task* (regular, irregular) and *PM cue* (event-based, time-based). *Group* did not interact with any of the variables (all  $Fs \le .94$ ,  $ps \ge .337$ ) but the main effect of *group* approached significance (F(1, 58) = 3.76, p = .057,  $\eta_p^2 = .06$ ); there was a trend toward people with CHF (M = .51, SD = .35) performing more poorly than controls (M = .64, SD = .31).

There were also main effects of *PM task* (F(1, 58) = 11.01, p = .002,  $\eta_p^2 = .16$ ), and *PM cue* (F(1, 58) = 5.55, p = .022,  $\eta_p^2 = .09$ ), and a two-way interaction between *PM task* and *PM cue* (F(1, 58) = 15.23, p < .001,  $\eta_p^2 = .21$ ). For irregular tasks, all participants performed worse on time-based (M = .43, SD = .31) than event-based tasks (M = .62, SD = .30), (F(1, 58) = 23.00, p < .001,  $\eta_p^2 = .28$ ), but time and event did not differ for regular tasks (F = .38, p = .543). Further tests of simple effects showed that participants were worse on irregular (M = .43, SD = .31) than regular (M

= .64, SD = .32) for time-based tasks ( $F(1, 58) = 32.81, p < .001, \eta_p^2 = .36$ ), but irregular and regular did not differ for event-based tasks (F = .03, p = .854).

#### Analysis of missed Prospective Memory responses

These analyses were then repeated for the proportion of tasks missed (rather than completed correctly). *Group* did not interact with any variables (all  $Fs \le .20$ ,  $ps \ge$  .660), but there was a main effect of *group* (F(1, 57) = 4.52,  $p = .038 \eta_p^2 = .07$ ); the CHF group (M = .26, SD = .31) missed more responses than the controls (M = .16, SD = .21). There were also main effects of *PM task* (F(1, 57) = 13.43, p = .001,  $\eta_p^2 = .19$ ), and *PM cue* (F(1, 57) = 5.01, p = .029,  $\eta_p^2 = .08$ ), and a two-way interaction between *PM task* and *PM cue* (F(1, 57) = 7.79, p = .007,  $\eta_p^2 = .12$ ). Tests of simple effects showed that for irregular tasks, participants missed more time-based (M = .33, SD = .29) than event-based tasks (M = .20, SD = .22), (F(1, 57) = 10.133, p = .002,  $\eta_p^2 = .15$ ), but time and event did not differ for regular tasks (F = .21, p = .648). Further tests of simple effects showed that participants missed more irregular (M = .33, SD = .29) than regular (M = .15, SD = .27) time-based tasks (F(1, 57) = 23.32, p < .001,  $\eta_p^2 = .29$ ), but regular and irregular did not differ for event-based tasks (F = .111, p = .298).

Table 3 displays the types of errors made by the CHF and control groups. The CHF group made more misses than other types of errors. However, in the control group, missed responses were less prominent among the error types. The number of errors was typically low. The two groups had similar proportions of little late, little early, and lot early, but the CHF group had more errors on the lot late category, at least for regular event-based tasks.

(Insert Table 3 about here)

#### Analysis of memory for task content

An ANOVA was conducted to assess the number of tasks recognised at the end of each day. The dependent variable was the proportion of the six PM tasks that participants correctly matched for each of the four categories of tasks: regular event, irregular event, regular time, and irregular time. Data were again analysed with a 2 x 2 x 2 mixed ANOVA with the between-subjects variable of group (CHF, control), and the within-subject variables of PM task (regular, irregular) and PM cue (event-based, time-based). There was no main effect of group, PM task, or PM cue (all Fs  $\leq 1.77$ , ps  $\geq$  .270). *Group* however interacted with *PM task* (*F*(1, 41) = 7.89, *p* = .008,  $\eta_p^2$  = .16). Tests of simple effects showed that for irregular tasks the CHF group (M = .66, SD =.31) matched fewer tasks correctly than controls (M = .86, SD = .31), (F(1, 41) = 6.58, p = .014,  $\eta_p^2 = .14$ ), but group did not differ for regular tasks (F = .20, p = .657). Further tests of simple effects showed that for the CHF group, matching was worse for irregular (M = .66, SD = .31) than for regular tasks (M = .84, SD = .31), (F(1, 41))= 7.58, p = .009,  $\eta_p^2 = .16$ ) but, for the control group, performance did not differ between regular and irregular tasks (F = 1.28, p = .265). Table 4 displays descriptive statistics for the proportion of correct matching of PM task and PM cue. It can be seen that the control group's performance was consistent across task type, whereas performance for the CHF group varied, with the lowest proportion of tasks matched correctly on irregular time tasks.

(Insert Table 4 about here)

#### Analyses of shared variance

Exploratory analyses were then conducted to examine the potential role of other cognitive processes in the observed group difference on the proportion of missed PM tasks. Six 2 x 2 x 2 mixed ANCOVAs were conducted with the between subjects variable of group (CHF, controls), and the within subjects variable of PM task (regular, irregular) and PM cue (event, time), and one of the following variables entered as a covariate in each ANCOVA: cognitive inhibition, cognitive initiation, verbal memory (immediate recall), verbal memory (recognition), global cognition, and memory for task content. The dependent variable was the proportion of missed responses. Results showed that the small effect size ( $\eta_p^2 = .07$ ) in the original ANOVA was reduced by a small amount following entry of each covariate. Specifically, the effect size  $(\eta_p^2)$  dropped to .05 (cognitive inhibition and initiation), .04 (recognition), .03 (global cognition), .02 (immediate recall), and .02 (memory for task content). Thus, whilst each of these measures individually covaried with the PM deficit observed in the CHF group, global cognition, immediate recall (verbal memory), and memory for task content appeared to covary more than either of the two executive functions. Covarying for each of these variables reduced the statistical significance of the group main effect (all ps > .103). Out of interest, we also covaried cognitive flexibility and working memory (even though they did not significantly differ between groups in univariate analyses) but found that, as with other executive function measures, the degree of covariation was not substantial.

#### Analysis of CHF severity and missed Prospective Memory responses

On the basis of the NYHA scale, participants were classified into low CHF severity (Class I and II; n = 21), and high CHF severity (Class III and IV; n = 9).

Exploratory analysis of prospective memory performance revealed a non-significant trend, t(28) = 1.38, p = .178, d = .51, towards more missed PM responses by the high severity group (M = .35; SD = .30) compared to the low CHF severity group (M = .22; SD = .20).

#### **5.2.5 Discussion**

Although a large body of literature has shown that people with CHF present with deficits in a range of cognitive abilities (Pressler, 2008; Vogels, Scheltens, et al., 2007), this is the first empirical assessment of PM function in people with CHF relative to controls. Results indicated that the CHF group exhibited generalised PM impairment, with significant and similar sized deficits evident across all task parameters assessed (event, time, regular, irregular). These findings are consistent with studies that have used Virtual Week to examine PM in other clinical groups who are affected by both localised and diffuse neurological brain pathology, including people with multiple sclerosis, schizophrenia and other schizoaffective disorders, prior strokes, and long term or acute substance use (Henry, Rendell, Kliegel, & Altgassen, 2007; Kim, Craik, Luo, & Ween, 2009; Rendell, Jensen, & Henry, 2007; Terrett et al., 2014). While there is some variability in results across these different clinical groups, all show consistent deficits in PM, irrespective of specific PM task demands.

The poor PM performance of the CHF group does not appear to be a result of poor timing (i.e., it does not appear that CHF patients scored poorly because they performed PM tasks a little early or a little late). Rather, CHF patients missed more tasks altogether. However, there was also a non-significant trend suggesting that the CHF group completed fewer tasks at the correct moment. It is possible that this subtle trend might have reached statistical significance with a larger sample size.

The lack of variability in the CHF patients' impairment across PM task types suggests that the underlying cause of their poor PM performance cannot be explained entirely by retrospective memory deficits. Regular tasks in Virtual Week impose only minimal demands on retrospective memory (i.e., remembering what needs to be done) because the repeated presentation ensures they are well encoded. If the CHF participants' poor performance were solely a result of retrospective memory failure, PM performance should have been relatively weaker on the irregular tasks than on the regular tasks. Thus, these findings suggest the cause of the observed PM impairment involves the prospective component. Consistent with this idea, we found that when participants were asked what PM tasks they *should* have completed (at the end of each virtual day), they correctly recalled the content of around 80% of the PM tasks. This was the case for both groups. In other words, the CHF group was no worse than the control group at encoding what they had to do (i.e., the retrospective component), but had more difficulty initiating the PM tasks at the correct moments.

Although the CHF group in the current study was relatively high functioning, in line with other literature, they did show deficits in a number of cognitive domains relative to controls, including cognitive inhibition, cognitive initiation, verbal memory (immediate recall and recognition), and global cognitive ability (Pressler, 2008; Vogels, Oosterman, et al., 2007; Vogels, Scheltens, et al., 2007). In contrast, no significant differences were observed on measures of cognitive flexibility, working memory, or delayed recall, although there was a consistent trend towards poorer performance by the CHF group.

Exploratory analyses examining the potential influence of these other cognitive abilities showed that the group difference in episodic memory overlapped substantially with the group difference in PM performance. This pattern was observed when using an established verbal memory tests (RAVLT) and also when participants' memory for the specific Virtual Week tasks content was assessed. Thus, while the primary analyses implicate a deficit in the prospective component for the CHF group, these further analyses highlight that retrospective memory is also important. Interestingly, executive functions and working memory had a more modest impact on the group differences in PM. However, interpretation of ANCOVAs requires caution in a non-randomised study because the loss of statistical significance may reflect loss of power (Miller & Chapman, 2001). For this reason, we focused on effect sizes rather than statistical significance, but even so, these findings require replication before firm conclusions can be drawn.

Although the ANCOVA findings need to be interpreted cautiously, they suggest that the CHF group's poorer retrospective memory may have influenced PM performance to a greater degree than executive functions. However, the lack of difference in PM performance between regular and irregular tasks in the original ANOVA suggests that residual variance is attributable to a separable prospective component. Thus, taken together, the findings indicate that difficulties with retrospective memory contribute to, but do not fully explain, the deficits observed in the prospective component, or the failure to initiate an action even after the intended action had been committed to memory. Interestingly, a similar pattern was observed in a study involving people with dementia and mild cognitive impairment (Thompson, Henry, Rendell, Withall, & Brodaty, 2010).

CHF participants in the present study were relatively high functioning. Specifically, people with indicators of dementia were excluded, and 70% of the sample had no, or only mild, heart failure symptoms. In addition, subjective ratings of depression which, in other studies has been shown to contribute to PM impairment (Kliegel et al., 2005; Li, Weinborn, Loft, & Maybery, 2013), were within the normal range. Thus, in the wider population of patients with CHF, where medical and emotional symptoms are often more severe, PM failures are likely to be more pronounced.

A strength of this study is that participants with CHF were well characterised and were closely matched to the control group on important demographic variables (demographics, estimated IQ, and depression). However, some limitations must be acknowledged. The secondary analyses focusing on memory for task content had a reduced sample size and may have been underpowered to detect group differences. In addition, because of the cross-sectional nature of the study, it was not possible to establish whether the PM deficits existed prior to, or are the results of CHF. We found a promising non-significant trend toward better PM performance by patients with low CHF severity compared to high severity. However, as most participants were high functioning this analysis was underpowered, with too few participants (n = 9) in the high severity CHF group. Another related limitation was that CHF characteristics were assessed on recruitment, but were not reassessed at time of testing (typically three months later). Thus, cardiac severity was not entirely clear, and it may have changed for the better over time with medical management. Future studies are therefore needed to investigate whether measures of CHF severity (NYHA classification, Brain Natriuretic Peptide assays), are directly associated with PM performance.

Although preliminary, these data have clear clinical relevance. A key strategy within CHF management programs is to encourage patients to perform specific selfcare behaviours to maintain clinical stability and recognise and respond early to changes in clinical symptoms (Riegel, Lee, et al., 2009). Key behaviours include medication adherence, fluid and sodium restrictions, daily weighing to monitor and recognise oedema, and then, in the cases of symptom changes, responding by altering fluid intake or diuretic use (Riegel et al., 2011). However, despite the considerable emphasis in clinical practice on promoting CHF self-care, many patients have low success in completing self-care plans (Clark et al., 2014; Jaarsma et al., 2013). The present findings raise the possibility that PM difficulties may be contributing to poor self-care.

In conclusion, in this group of high functioning CHF patients, PM capacity was found to be impaired across all aspects of PM. If these preliminary findings are confirmed in larger studies, then strategies to increase self-care adherence within the CHF population may need to include PM training (Zogg, Woods, Sauceda, Wiebe, & Simoni, 2012).

#### 5.2.6 Acknowledgements

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## Table 1:

# Clinical Characteristics of the CHF Group

Health characteristics	%
NYHA classification	
Class I	6.7
Class II	63.3
Class III	26.7
Class IV	3.3
Heart failure type	
Systolic	70.0
Diastolic	13.3
Mixed	10.0
Unspecified	6.7
Heart failure aetiology	
Ischaemic	50.0
Non ischaemic	30.0
Idiopathic	3.3
Other	16.7

*Notes.* NYHA = New York Heart Association.



Figure 1. Screening and recruitment process of the CHF group<sup>1</sup>.

<sup>&</sup>lt;sup>1</sup> The 12 ineligible participants had not yet reached the 3-month delay period (discussed in procedure section) during which the study was being conducted.

## Table 2:

# Participant Characteristics

	CHF group			Control group					
	n	%		n	%		$\chi^2$	р	
Cardiac risk factors (%)									
Hypercholesterolemia	13	43.3%		11	36.7%		0.41	.523	
Hypertension	20	66.7%		14	46.7%		3.00	.083	
Smoking	11	36.7%		9	30.0%		0.41	.520	
Diabetes	5	16.7%		4	13.3%		0.17	.677	
Obesity	6	10.0%		2	6.7%		0.26	.612	
Demographic (M)		М	SD		М	SD	t	р	d
Age (years)	30	70.03	11.88	30	69.93	5.96	0.04	.967	0.01
Education (years)	30	11.13	3.44	30	12.08	2.89	1.16	.252	0.30
Estimated IQ	29	111.93	6.78	30	114.54	5.31	1.65	.105	0.43
Global cognition and mental h	ealth								
ACE-R	29	90.79	4.64	30	93.07	4.00	2.02	$.048^{*}$	0.53
Anxiety (HADS)	29	6.10	3.52	30	6.53	3.88	0.45	.658	0.12
Depression (HADS)	29	5.00	2.83	30	4.17	3.03	1.10	.280	0.28
Executive functions									
Cognitive flexibility (TMT)	26	71.85	34.15	29	58.42	32.61	1.49	.142	0.40
Inhibition (Hayling)	28	3.11	1.93	26	5.42	1.47	4.93	<.001***	1.35

Initiation (Verbal fluency)	30	29.60	6.28	30	33.10	6.93	2.05	$.045^{*}$	0.98
Working memory (DS)	27	17.70	3.16	30	19.63	4.67	1.84	.071	0.48
Verbal memory (RAVLT)									
Immediate recall	26	41.31	8.48	28	48.89	8.09	3.36	.001**	0.91
Delayed recall	24	8.96	2.39	28	10.04	2.85	1.46	.149	0.41
Recognition	23	13.22	1.35	28	13.89	1.03	2.03	$.048^{*}$	0.56

 $\overline{d}$  = Cohen's d index of effect size. Effect sizes: small = 0.2; medium = 0.5; large = 0.8 (Cohen, 1988). \*p < .05 \*\*p < .01 \*\*\*p < .001

Notes. ACE-R = Addenbrooke's Cognitive Examination – Revised; d =Cohen's d index of effect size; DS = Digit Span; HADS = Hospital Anxiety Depression Scale; RAVLT = Rey Auditory Verbal Learning Test; TMT = Trail Making Test (B minus A).

## Table 3:

Group	PM task type	Proportion correct	Missed	Little late	Lot late	Little early	Lot early
CHF	Regular event	.53 (.41)	.23 (.30)	.07 (.15)	.15 (.22)	.02 (.09)	.00 (.00)
	Regular time	.63 (.32)	.19 (.32)	.12 (.17)	.03 (.10)	.01 (.05)	.04 (.12)
	Irregular event	.57 (.31)	.23 (.27)	.05 (.12)	.03 (.11)	.02 (.06)	.11 (.17)
	Irregular time	.33 (.30)	.39 (.33)	.07 (.11)	.16 (.18)	.02 (.06)	.03 (.09)
Control	Regular event	.69 (.33)	.08 (.18)	.08 (.17)	.08 (.15)	.06 (.13)	.00 (.00)
	Regular time	.66 (.32)	.11 (.20)	.13 (.16)	.02 (.06)	.03 (.09)	.06 (.14)
	Irregular event	.68 (.29)	.18 (.16)	.04 (.12)	.01 (.05)	.04 (.09)	.06 (.13)
	Irregular time	.53 (.31)	.26 (.23)	.08 (.16)	.10 (.16)	.01 (.05)	.03 (.10)

PM Accuracy: Mean (SD) Proportion of PM Tasks Executed at Different Time Points

*Notes.* PM task (regular, irregular) and PM cue (event-based, time-based) were within-group independent variables for the PM measure, Virtual Week; Proportion correct = executed at correct time; Missed = missed altogether; Little late = executed little late; Lot late = executed very late; Little early = executed little early; Lot early = executed very early.

## Table 4:

	CHF = n = n	- I	Control group $n = 24^{a}$		
PM task content	М	SD	М	SD	
Regular event	.84	.33	.80	.38	
Regular time	.83	.31	.79	.38	
Irregular event	.78	.28	.85	.32	
Irregular time	.55	.32	.86	.30	
Overall	.75	.20	.83	.25	

Recognition of PM Task Content: Mean and SD Proportion of PM Task and PM Cue Pairs Matched Correctly

<sup>a</sup> Sample size is smaller than original (n = 30) due to loss of data.

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Zuccalà, G., Cattel, C., Manes-Gravina, E., Di Niro, M. G., Cocchi, A., & Bernabei, R.

# CHAPTER 6: Introduction Into the Investigation of the Relationship Between Prospective Memory and Self-Care

The findings presented in Study 1 showed that people with CHF have pervasive deficits in PM, or the ability to initiate tasks at the correct moments, irrespective of different task demands. These findings raised the possibility that PM impairment might be related to poorer self-care. This is likely as remembering to take medications correctly has been strongly related to PM ability in other groups with chronic disease (Zogg et al., 2012). However, no previous study has investigated whether PM performance is related to self-care behaviours in people with CHF. This chapter presents the second and final study of PM function in this group.

The main objective of Study 2 was to investigate whether a relationship existed between PM function and self-care maintenance and management behaviours. To assess this, the same cohort reported on in Study 1 was used in Study 2. Thus, PM and general cognition data from Study 1 were used in Study 2. Because the level of PM performance was consistent across the different types of PM tasks, an overall measure of PM (i.e., the proportion of missed PM responses) was used in Study 2. Additional data for Study 2 were collected at a separate time, which included self-care behaviours, assessed with the Self-care Heart Failure Index (Riegel, Lee, et al., 2009), medication adherence, and functional independence. A secondary aim of Study 2 was to assess whether self-care behaviours were related to more general cognitive abilities such as global cognition, verbal memory, and executive function. As presented in the literature review in Chapter 2, similar relationship were supported by a recent review (Currie et al., in press), but an understanding of whether cognitive processes are differentially related to specific aspects of self-care remains inconclusive.

## Study 2

Habota, T., Cameron, J., Ski, C. F., McLennan, S. N., Rendell, P. G., & Thompson, D. R. *Journal of Cardiovascular Nursing* 

**Title:** An investigation into the relationship between prospective memory and chronic heart failure self-care

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#### **Abbreviations:**

ACE-R: Addenbrooke's Cognitive Examination – Revised; CHF: Chronic heart failure; HADS: Hospital Anxiety and Depression Scale; IADL: Instrumental Activities of Daily Living; MMSE: Mini Mental State Examination; NYHA: New York Heart Association; PM: Prospective memory; RAVLT: Rey Auditory Verbal Learning Test; SCHFI: Self-care Heart Failure Index; TMT: Trail Making Test.

Keywords: Chronic heart failure, cognitive function, prospective memory, self-care

## Tables:

- Table 1. Demographic and Clinical Characteristics of the Sample
- Table 2. Descriptive Statistics for Cognitive Measures and Mental Health Symptoms
- Table 3. Correlations Between Cognitive Measures and Self-Care Maintenance and

   Management

#### 6.1.1 Abstract

**Background:** Cognitive deficits are common in patients with chronic heart failure (CHF), and at least some aspects of cognition are related to poor CHF self-care. Emerging evidence shows that CHF patients also have deficits in a specific cognitive process – remembering to perform tasks in the future (prospective memory, PM).

**Objectives:** The aims of this study were to investigate whether PM and more general cognitive abilities were associated with self-care.

**Methods:** 30 CHF patients (mean age = 70.03 years, SD = 3.44) were tested during the sub-acute phase. Self-care was assessed with the Self-care Heart Failure Index (SCHFI). A laboratory measure that closely simulates tasks in daily life (Virtual Week) was used to assess PM. Global cognition, executive functions, and verbal memory were also measured.

**Results:** The mean SCHFI scores indicated adequate self-care: maintenance M = 68.14, SD = 15.10; management M = 65.87, SD = 13.76; confidence M = 69.91, SD = 17.79. There were weak-to-moderate non-significant trends in the expected direction between self-care management and cognitive function: PM (r = -.22, p = .319), global cognition (r = .36, p = .103), executive functions (r = .38, p = .085), and verbal memory (r = .32, p = .144). The associations between self-care maintenance and cognitive function were less consistent and non-significant.

**Conclusion:** In a clinically stable, sub-acute group of CHF patients, cognition and PM were not strongly associated with self-care. The findings may reflect the select sample who had high cognitive abilities and were in relatively good physical and emotional health.

#### **6.1.2 Introduction**

Cognitive impairment is common in patients with CHF (Pressler, 2008; Vogels, Scheltens, Schroeder-Tanka, & Weinstein, 2007), with the most affected areas including memory, executive function, concentration and attention, and psychomotor speed (Alosco et al., 2013; Vogels, Oosterman, et al., 2007; Vogels, van der Flier, et al., 2007). The existing evidence shows that at least some aspects of selfcare are related to particular domains of cognition (Cameron et al., 2010; Currie, Rideout, Lindsay, & Harkness, in press). When cognitive impairment occurs in people with CHF, it consequently contributes to poor self-care and quality of life, and disease burden increases (Clark, McLennan, Dawson, Wilkinson, & Stewart, 2004; Lee, Chavez, Baker, & Luce, 2004; Smith et al., 2012). Therefore, it is essential to further investigate cognitive factors that may be impacting on self-care adherence.

One area of cognitive functioning that has only recently been investigated in patients with CHF is prospective memory (PM); the ability to remember to perform tasks at some point in the future. PM is a critical determinant of functional independence (Ellis & Freeman, 2008); lapses in PM can be momentarily frustrating, but some can be lethal (i.e., forgetting to turn-off dangerous appliances). Only one study has investigated PM performance in patients with CHF. Habota et al. (2015) found that compared to a group of demographically matched controls, patients with CHF had pervasive impairments in PM. It is surprising that research on PM has been neglected in the CHF population given that PM is implicated in a wide variety of important functional behaviours. In particular, PM may be important for patients with CHF because many of the tasks involved in self-care behaviours (e.g., medication adherence) place a heavy load on this particular cognitive ability (Habota et al., 2015).

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This has been supported in studies with other clinical groups (for review see, Zogg, Woods, Sauceda, Wiebe, & Simoni, 2012).

The main aim of this study was to investigate whether PM performance is associated with self-care practice. It was predicted that poorer PM ability would be correlated with lower self-care maintenance and management. A secondary aim was to clarify the nature of the relationship between more general cognitive abilities and self-care. It was predicted that lower global cognition, verbal memory, and executive function would be associated with worse self-care behaviours.

#### 6.1.3 Methods

We conducted a descriptive and correlation study using 3-month follow-up data that were collected for a separate intervention study. This research was approved by the Human Research Ethics Committees at Eastern Health and the Australian Catholic University. A detailed study protocol is described elsewhere (Habota et al., 2013).

#### **Participants**

Participants (described previously in Habota et al., 2015) were 30 patients who had a documented diagnosis of CHF (cardinal symptoms and clinical features of congestion, and objective evidence of cardiac impairment from an echocardiogram; Krum et al., 2006). All participants were outpatients actively engaged in a nurse-led CHF management program or CHF clinic, in one of three public hospitals in metropolitan Melbourne, Australia. Exclusion criteria were: aged high-care facility resident; terminal diagnosis; documented history of dementia; inability to read English; and cognitive assessment indicative of dementia (score of < 82 on the Addenbrooke's Cognitive Examination – Revised (Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000)).

#### Materials

### **Descriptive measures**

The *National Adult Reading Test* (NART) (Nelson, 1982) was used as an index of premorbid intelligence. Standardised IQ scores were calculated using the formula in the administration manual (Nelson, 1982).

The *New York Heart Association* classification (NYHA) was used as an index of functional status. The NYHA is an extensively used and validated clinical measure (Bennett, Riegel, Bittner, & Nichols, 2002). Classification I indicates no limitations and classification IV indicates the worst functional status.

The *Charlson Co-morbidity Index* was used to assess the severity of comorbid conditions. The weighted index of co-morbidity has proven to be a predictor of mortality (Charlson, Pompei, Ales, & MacKenzie, 1987). Overall index scores are categorised as mild, moderate, or severe; higher scores indicate more severe comorbidity.

The *Medication Adherence Scale* (Wu, Chung, Lennie, Hall, & Moser, 2008) was used to assess knowledge and attitudes to medication regiments. This measure has been validated on CHF populations and it has good psychometric properties (Wu et al., 2008). Subscale scores range from 0 to 30 for knowledge, and 0 to 40 for attitudes; higher scores indicate better knowledge and attitudes.

The *Instrumental Activities of Daily Living* (IADL) (Lawton & Brody, 1970) was used to assess functional independence. The IADL has good internal consistency, but additional psychometric data is limited (Sikkes, De Lange-de Klerk, Pijnenburg, & Scheltens, 2009). Scores range from 0 to 16; higher scores indicate a greater degree of functional dependence.

The *Hospital Anxiety Depression Scale* (HADS) (Zigmond & Snaith, 1983) was used to screen for symptoms of anxiety and depression, separately. The HADS has been validated in cardiac patients (Johnston, Pollard, & Hennessey, 2000). Higher scores indicate more emotional symptomology.

#### Self-care assessment

The *Self-care Heart Failure Index* (SCHFI) (v6) (Riegel, Lee, Dickson, & Carlson, 2009) was used as a measure of CHF self-care. This is the most commonly used measure to assess self-care skills and behaviours, and it has been extensively validated among CHF populations (Cameron, Worrall-Carter, Driscoll, & Stewart, 2009). Scores from each of the three self-care scales were transformed to 100-point scales; higher scores reflect better self-care.

#### **Cognitive measures**

The *Addenbrooke's Cognitive Examination – Revised* (Mathuranath et al., 2000) was used as a measure of global cognition. It is a validated screening test that is sensitive to early cognitive dysfunction (Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006). Scores range from 0-100; higher scores reflect better cognitive function.

The *Mini-Mental State Examination* (MMSE) is embedded in the ACE-R and was reported to allow direct comparisons with other published studies. Compared to the ACE-R, the sensitivity and specificity of the MMSE is low (Pendlebury, Mariz, Bull, Mehta, & Rothwell, 2012).

Verbal memory

The *Rey Auditory Verbal Learning Test* (RAVLT) (Rey, 1958) is a sensitive test of verbal learning and memory (Strauss, Sherman, & Spreen, 2006), and was used to measure immediate and delayed recall. A single composite score for the first five trials was used as the measure of immediate recall. The total number of correctly recalled words after a 20-minute delay was used as the measure of delayed recall. Higher scores indicate better performance.

#### Executive function – cognitive flexibility

The *Trail Making Test* (TMT) (Reitan, 1992) is a validated measure of executive control (Sánchez-Cubillo et al., 2009) that was used to assess cognitive flexibility. The Trails B minus Trails A difference score was used as an index of this construct (Lamberty, Putnam, Chatel, Bieliauskas, & Adams, 1994). Lower scores indicate better performance.

#### Executive function – cognitive inhibition

The *Hayling Sentence Completion* test (Burgess & Shallice, 1997) was used to assess cognitive inhibition. High reliability coefficients for this measure have been reported for a clinical sample (Burgess & Shallice, 1997). A total score was obtained by tallying errors and time taken (in seconds) to complete the task. Scaled scores were computed and higher scores indicate better performance.

#### Prospective memory

The *Virtual Week* (Rendell & Craik, 2000) measure was used to assess prospective memory. Virtual Week has been used extensively with clinical and nonclinical groups and has robust psychometric properties (Rendell & Henry, 2009). Virtual Week is a computerised board game that simulates a week of daily activities. Participants had eight PM tasks to complete each virtual day (e.g., take medication with breakfast and dinner). Prospective memory performance was measured as the proportion of *missed* PM tasks (i.e., tasks that participants had forgotten to perform altogether). Responses were coded as a proportion ranging from 0-1; higher scores reflect worse PM performance. A detailed description of this measure has been provided elsewhere (Habota et al., 2013).

#### Procedure

At the time of recruitment into the parent study, demographic and health characteristics were collected using patient self-report and reviewing medical records. Cognitive function was assessed during the sub-acute phase, approximately three months after recruitment, to ensure that participants were medically stable. The cognitive, self-care, and health-related measures were administered individually in a single session. All participants were provided standard care according to best-practice guidelines (Krum et al., 2006). This included interventions aimed at improving patient responsiveness and proactive management, establishing cohesion between different service providers, and providing psychosocial care and pharmacological management on a needs basis. Furthermore, patients received: self-care education to assist them in developing adequate self-management skills; and self-care support, such as monitoring and evaluating signs and symptoms to enable identification of CHF decompensation. Patients were also encouraged to engage in activities that protect and promote health, such as following lifestyle management advice (i.e., smoking cessation, physical activity and exercise programs, nutrition, and limiting alcohol use). Behavioural strategies were used to support patients in modifying risk factors and adhering to their management plans.

#### **Data Analysis**

All variables were assessed for normality and were normally distributed. Descriptive statistics were computed for all variables. Continuous data are presented as means and standard deviations, and categorical data are presented as percentages. Pearson bivariate correlations were conducted to examine relationship between cognitive function and health outcomes. Before conducting any analyses, data were screened for missing values. Little's MCAR test indicated that data were missing at random,  $\chi^2$  (316) = 306.31, p = .642. Therefore, expectation maximisation was used to replace missing values, except for one variable: self-care management. Eight patients did not report symptoms of breathlessness or oedema in the previous month (as per the SCHFI), meaning that the self-care management scale could only be analysed for 22 cases (instead of n = 30). A post-hoc power analysis showed that the study power was .55 for a medium effect size (r = .38; the strongest correlation observed).

To reduce the possibility of Type I error, a composite executive function score was created. The two measures of executive function (TMT, Hayling) were correlated (r = -.40, p = .027). The composite score was created by converting scores on these measures to *z* scores, reverse-coding TMT such that higher scores indicated higher performance, and then calculating a mean *z* for each participant. The two measures of verbal memory (immediate and delayed recall, RAVLT) were also correlated (r = .76, p < .001) so we created a composite verbal memory score using the same approach. Both composite scores were normally distributed.

#### 6.1.4 Results

#### **Demographic and clinical characteristics**

Participants were aged between 40 to 86 years (M = 70.03, SD = 11.88), predominantly male, and had a mean total number of 11.13 years (SD = 3.44) of education (Table 1). Most participants had relatively mild heart failure symptoms as assessed with the NYHA functional classification. Participants with left ventricular dysfunction (i.e., systolic) and ischaemic heart failure were dominant in the group, and hypertension was the most frequently reported cardiac risk factor. Participants had a moderate level of comorbid disease burden (Charlson Comorbidity Index mean = 3.17), time since initial diagnosis was almost three years (M = 33.19 months, SD =55.03), and only a few reported depressive symptoms. The majority of patients had been prescribed pharmacotherapy considered to be the gold standard treatment of CHF.

(Insert Table 1 about here)

### **Descriptive statistics**

Means and standard deviations for the cognitive measures are reported in Table 2. The sample had high global cognition; the mean average on the MMSE was in the normal range. On average, attitudes toward medication adherence were positive (M = 37.19, SD = 6.20), and medication knowledge was high (M = 23.47, SD = 5.86). Medication barriers could not be reported because only two participants reported that they had skipped medications. On average, self-care scores were: maintenance M =68.14, SD = 15.10, management M = 65.87, SD = 13.76, and confidence M = 69.91, SD = 17.79; the proportion of patients who were assessed as adequate  $(70 \ge)$  on each of the self-care scales were 47%, 33%, and 57%, respectively. Patients reported a high level of functional independence on the IADL scale (M = 2.03, SD = 2.46). Only 10% reported requiring some degree of assistance with medication management.

(Insert Table 2 about here)

#### **Correlations between self-care and cognitive function**

There were no significant correlations between any of the variables (Table 3), but there were several notable trends in the expected direction. There was a weak trend for an association between self-care maintenance and global cognition (r = .20, p = .292) and executive function (r = .24, p = .196), but not between self-care maintenance and PM (r = .04, p = .848) or verbal memory (r = .03, p = .877). There were also stronger and more consistent non-significant trends in the expected direction between self-care management and all cognitive variables. There were weak trends in the expected direction between self-care management and PM (r = .22, p =.319) and verbal memory (r = .32, p = .144). There was a moderate non-significant relationship between self-care management and global cognition (r = .36, p = .103) and executive function (r = .38, p = .085). In each case, the findings indicated that patients who had better self-care also had better cognitive functioning.

(Insert Table 3 about here)

#### 6.1.5 Discussion

This is the first study to investigate associations between PM performance and self-care in a group of CHF outpatients. On average, participants had relatively adequate self-care scores. Medication barriers could not be analysed, but participants reported positive attitudes toward medication adherence, and high knowledge of prescribed medication. Overall, a high degree of functional independence was reported.

Ultimately, in this high functioning CHF group, the results of this study did not support a statistically significant association between self-care and PM, verbal memory, or executive function, but a number of non-significant trends are notable. For self-care maintenance, there were weak to moderate associations with global cognition and executive function, respectively, but not with verbal memory. Self-care management was more consistently related to each of the cognitive domains assessed, with weak to moderate relationships. In each case, the non-significant correlations were in the expected direction. That is, patients who were more likely to have better cognitive functioning were also better at self-care behaviours.

These findings are consistent with the literature examining cognition and selfcare in the CHF population. A systematic review by Currie et al. (in press) reported that participants with higher cognitive abilities also had better self-care practice. Furthermore, whilst the relationship between PM and functional outcome has not previously been investigated in the CHF population, studies involving normal ageing (Woods, Weinborn, Velnoweth, Rooney, & Bucks, 2012) and other groups who are affected by chronic disease (Zogg et al., 2012) have reported that PM is an important contributor to general functional behaviours and medical adherence. The investigation of the relationship between PM and self-care deserves further attention. Problems with PM cause more difficulties in daily living than other memory failures (McDaniel & Einstein, 2007). This is particularly relevant to this patient population due to the numerous and concurrent tasks involved in CHF selfcare, such as taking medications, daily weighing, sodium intake monitoring, and initiating an appropriate response to deteriorating symptoms – all of which place a high load on one's cognitive ability. Even in a high functioning CHF sample, pervasive deficits in PM were evident as reported by Habota et al. (2015). These are important considerations given that in the wider population of people diagnosed with CHF, those who are more symptomatic and more cognitively impaired (Cannon, McMurray, & Quinn, 2015) are likely to have greater PM deficits.

The study findings need to be considered in the context of participant characteristics, as this was a clinically stable outpatient group. Global cognition as assessed by the MMSE was high, which contrasts with previous studies assessing patients during their hospital admission where, between 33% to 73% had impaired MMSE scores (Cameron et al., 2010; Harkness et al., 2014; Hawkins et al., 2012; Lee et al., 2013). Further, patients were relatively stable; 70% were NYHA functional classification I or II, and only 10% of patients reported depressive symptoms. Functional impairment and co-morbidities such as depression, which were present in few participants from this sample, may contribute to cognitive impairment (Cannon, McMurray, & Quinn, 2015). Additionally, over the short-term (i.e., up to 1 year), cognitive function may stabilise or improve with treatment (Hajduk, Kiefe, Person, Gore, & Saczynski, 2013).

The study had a small sample size and was underpowered to detect a relationship between PM and self-care. Additionally, because our sample was

predominantly high functioning, the study had a restricted range of cognitive function. Therefore, it remains unclear if, and how, PM might be related to self-care in lower functioning CHF samples.

In conclusion, the lack of associations between several different cognitive abilities and self-care might reflect this CHF sample, which had high cognitive abilities, and was in relatively good physical and emotional health when tested. Cognitive function may be a key factor in clinical success in the CHF population. Future research is needed to clarify the nature of the relationship between cognition and self-care, particularly in more symptomatic CHF populations.

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## Table 1:

## Demographic and Clinical Characteristics of the Sample

	%/M	n / SD
Socio demographic		
Male	63	19
Living alone	43	13
Retired	63	19
Completed > 12 years of education	53	16
Estimated IQ (M, SD)	112	6.67
Clinical data		
New diagnosis (< 2 months)	23	7
NYHA I & II	70	21
NYHA III & IV	30	9
Systolic heart failure	67	20
Ischaemic heart disease	50	15
Hypertension	73	22
Smoking history	63	19
Moderate to severe renal disease	13	4
Either on ACEI or ARB	67	20
Prescribed diuretic	83	25
Prescribed aldosterone antagonist	33	10
Prescribed beta blocker	77	23
Mild to moderate anxiety symptoms	37	11
Mild to moderate depression symptoms	10	3
Anxiety (HADS) (M, SD)	6.10	3.52
Depression (HADS) (M, SD)	5.00	2.83

*Notes.* ACEI = Angiotensin Converting Enzyme Inhibitor; ARB = Angiotensin II Receptor Antagonists; HADS = Hospital Anxiety Depression Scale; NYHA = New York Heart Association.

### Table 2:

Descriptive Statistics for Cognitive Measures

Measure	М	SD
Global cognition (ACE-R)	90.90	4.56
Global cognition (MMSE)	28.74	1.07
Prospective memory (Virtual Week)	0.26	0.24
Immediate recall (RAVLT)	42.06	8.81
Delayed recall (RAVLT)	8.90	2.47
Cognitive flexibility (TMT)	74.79	33.14
Cognitive inhibition (Hayling)	3.28	2.13

*Notes.* ACE-R = Addenbrooke's Cognitive Examination – Revised; NART = National Adult Reading Test; MMSE = Mini Mental State Examination; PM (missed responses); TMT = Trail Making Test (B minus A); RAVLT = Rey Auditory Verbal Learning Test.

## Table 3:

## Correlations Between Cognitive Measures and Self-Care Maintenance and

## Management

	Maintenance	Management
	( <i>n</i> = 30)	( <i>n</i> = 22)
Prospective memory	04 ( <i>p</i> = .848)	22 ( <i>p</i> = .319)
ACE-R	.20 (p = .292)	.36 ( <i>p</i> = .103)
Composite VM	.03 ( <i>p</i> = .877)	.32 ( <i>p</i> = .144)
Composite EF	.24 ( <i>p</i> = .196)	.38 ( <i>p</i> = .085)

*Notes.* ACE-R = Addenbrooke's Cognitive Examination – Revised; <math>EF = Executive function; VM = Verbal memory.

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# CHAPTER 7: Introduction Into the Investigation of Emotion Recognition and Theory of Mind in People with Chronic Heart Failure

The studies presented in this thesis have thus far focused on PM function in patients with CHF, an area of cognition that has not previously been investigated in this population. This next chapter focuses on social cognition, the second focus area of this thesis. This chapter presents a published manuscript, and the final study of the thesis.

The main objective of Study 3 was to assess two of the most basic and most widely studied social cognitive constructs – emotion recognition and ToM, in a group of CHF patients compared to demographically matched controls. To assess this, the most validated and widely used measures of emotion recognition (Ekman 60 Faces test; Ekman & Friesen, 1976) and ToM (Mind in the Eyes test; Baron-Cohen et al., 2001) were used. A secondary aim was to assess whether these social cognitive constructs were related to more general cognitive abilities. Such a relationship has been reported in other clinical groups, but a clear theoretical account of which aspects of general cognition are most salient to social cognition remains unclear. To achieve this second aim, a cognitive test battery involving measures of global cognition, verbal memory, and executive functions was also administered. Study 3 used a larger sample, but a subset of the final sample in Study 3 is the same as Study 1 and Study 2.

## Study 3

The following chapter is a manuscript that has been published in *PLoS ONE*.

Habota, T., McLennan, S. N., Cameron, J., Ski, C., F., Thompson, D. R., & Rendell, P. G. (2015). An investigation of emotion recognition and theory of mind in people with chronic heart failure. *PLoS ONE*, 10, e0141607. doi:10.1371/journal.pone.0141607
**Title:** An investigation of emotion recognition and theory of mind in people with chronic heart failure

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#### **Abbreviations:**

ACE-R: Addenbrooke's Cognitive Examination – Revised; CHF: Chronic heart failure; NART: National Adult Reading Test; RAVLT: Rey Auditory Verbal Learning Test; TMT: Trail Making Test; ToM: Theory of mind.

**Keywords:** Chronic heart failure; cognitive function; emotion recognition; social cognition; theory of mind

## Tables:

Table 1. Clinical Characteristics of the CHF Group

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 Table 3. Relationships Between Emotion Recognition and ToM Scores and Cognitive

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Figure 1. Mean number of correct responses for each emotion type on the Ekman

Faces test for the CHF and control groups.

#### 7.1.1 Abstract

**Objectives:** Cognitive deficits are common in patients with chronic heart failure (CHF), but no study has investigated whether these deficits extend to social cognition. The present study provided the first empirical assessment of emotion recognition and theory of mind (ToM) in patients with CHF. In addition, it assessed whether each of these social cognitive constructs was associated with more general cognitive impairment.

**Methods:** A group comparison design was used, with 31 CHF patients compared to 38 demographically matched controls. The Ekman Faces test was used to assess emotion recognition, and the Mind in the Eyes test to measure ToM. Measures assessing global cognition, executive functions, and verbal memory were also administered.

**Results:** There were no differences between groups on emotion recognition or ToM. The CHF group's performance was poorer on some executive measures, but memory was relatively preserved. In the CHF group, both emotion recognition performance and ToM ability correlated moderately with global cognition (r = .38, p = .034; r =.49, p = .005, respectively), but not with executive function or verbal memory. **Conclusion:** CHF patients with lower cognitive ability were more likely to have difficulty recognising emotions and inferring the mental states of others. Clinical implications of these findings are discussed.

#### 7.1.2 Introduction

Chronic heart failure (CHF) is a complex condition characterised by an underlying structural abnormality that impairs the function of the heart to deliver sufficient blood flow to meet the metabolic needs of the body and brain (Krum et al., 2006). In many patients with CHF, accumulated ischaemic damage to the brain results in secondary cognitive impairment (Vogels, van der Flier, et al., 2007; Vogels, Scheltens, Schroeder-Tanka, & Weinstein, 2007). The level of cognitive impairment varies from patient to patient, but some degree of dysfunction is seen in up to 80% of patients in select CHF populations (Cameron et al., 2010; Cannon, McMurray, & Quinn, 2015). Over the past few decades, multiple neuropsychological studies have established that people with CHF are affected by deficits in cognitive processes such as executive function, memory, and attention (for review see, Cannon et al., 2015). However, no study has assessed social cognition in this group.

Core aspects of social cognition are emotion recognition, which is the ability to perceive and correctly distinguish emotions displayed by others (Adolphs, 2002), and Theory of Mind (ToM), which is the ability to make inferences about the mental states of others (Frith & Frith, 2005). These two processes of social cognition are vital because they facilitate effective social interaction and allow people to form and maintain strong relationships with others (Grossmann, 2010) by enabling them to understand subtle social cues (Radice-Neumann, Zupan, Babbage, & Willer, 2007). Profound examples of deficits in these processes are seen in people with autism spectrum disorders (Harms, Martin, & Wallace, 2010) and schizophrenia (Kohler, Walker, Martin, Healey, & Moberg, 2009; Sprong, Schothorst, Vos, Hox, & Van Engeland, 2007). In clinical groups, deficits in social cognition have been linked to poor functional outcomes, for example poor community and/or psychological functioning (Fett, Viechtbauer, Penn, van Os, & Krabbendam, 2011; Schmidt, Mueller, & Roder, 2011). Therefore, social cognition may be particularly important for patients with CHF who experience debilitating physical symptoms that impact on their physical and emotional wellbeing, thereby increasing their need for support from others (O'Loughlin et al., 2010; Volz et al., 2011). Social cognitive impairment may also contribute to isolation through poor social functioning (Fett et al., 2011). This is important because social isolation is a significant predictor of mortality in CHF, while social support increases overall quality of life (Årestedt, Saveman, Johansson, & Blomqvist, 2013).

The overarching aim of this study was to examine emotion recognition and ToM in patients with CHF. It is possible that the deficits CHF patients experience with other cognitive abilities also extend to deficits in social cognition. This is because the neuropathology observed in these patients involves white matter hyperintensities and reduced grey matter (Vogels, van der Flier, et al., 2007; Woo, Macey, Fonarow, Hamilton, & Harper, 2003) in regions of the brain that are implicated in emotion recognition and ToM, including the prefrontal cortex and the limbic system (temporal lobe) (Carrington & Bailey, 2009; Phan, Wager, Taylor, & Liberzon, 2002). In particular, the observed white matter pathology is associated with disconnection within fronto-subcortical brain tracts (Jokinen et al., 2006) known to be involved in the processing of emotional signals (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000; Ruffman, Henry, Livingstone, & Phillips, 2008).

The second aim of the study was to assess whether deficits in emotion recognition and ToM were associated with more general cognitive impairment.

Although general cognition and social cognition are supported by different neural circuits (Alvarez & Emory, 2006; Binder, Desai, Graves, & Conant, 2009; Pinkham, Penn, Perkins, & Lieberman, 2003), the process of understanding others' thoughts and emotions has been shown to make substantial demands on cognitive control processes, such as inhibition and mental flexibility (Apperly, Samson, Chiavarino, & Humphreys, 2004; Bailey & Henry, 2008; Decety & Jackson, 2004). Given that executive control mechanisms are supported by frontal brain regions (Alvarez & Emory, 2006), which are amongst the most affected in CHF, it might be that in the context of CHF, any observed deficits in emotion recognition and ToM are related to more general cognitive difficulties. Indeed, a relationship between emotion recognition and/or ToM and general cognition has been observed in other clinical populations (Henry et al., 2009; Henry, Phillips, Crawford, Ietswaart, & Summers, 2006).

To address each of these aims, a group of CHF patients was compared to a group of matched controls. It was hypothesised that the CHF group would show deficits in emotion recognition and ToM compared to the group of healthy controls. It was also predicted that within the CHF group, emotion recognition and ToM would positively correlate with global cognition, executive function, and verbal memory.

#### 7.1.3 Methods

This research was approved by the Human Research Ethics Committees at Eastern Health and the Australian Catholic University. All participants provided written informed consent.

#### **Participants**

The CHF group was recruited from a pool of participants taking part in a larger study (n = 72); 13 participants were paid AUD \$10 per hour, and the rest were volunteers. To be eligible for the parent study participants had to be aged over 18, and actively engaged in a nurse-led CHF management program at one of three public hospitals in metropolitan Melbourne, Australia. All recruited participants had a confirmed diagnosis of CHF. Specifically, cardinal symptoms and clinical features of congestion, and objective evidence of cardiac impairment on echocardiogram (Krum et al., 2006).

Participants with CHF were excluded if they resided in a high care residential aged facility, had a terminal diagnosis, a documented history of dementia, or could not read English. All 72 participants were approached from the parent study; 25 declined, and five were unreachable. No participants had head injury or psychiatric illness. We screened participants' global cognition. Initially, we recruited 42 participants but excluded six who could not complete the primary measures because they either declined or ran out of time. Another five participants were excluded who showed signs of potential dementia as operationalised by a score lower than 82 on the Addenbrooke's Cognitive Examination – Revised (ACE-R) (Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000). The final sample of CHF patients included 31

adults. A subset of this final sample has been reported on previously (Habota et al., 2015), but not with regards to social cognitive performance.

The control group was recruited from the general community; 13 participants were paid AUD \$10 per hour, the rest were volunteers. Participants in the control group were excluded if they reported a history of CHF or neurological disease, had recent treatment (past three months) for an acute cardiovascular problem, or could not read English. We initially recruited 43 participants, but excluded four who could not complete the primary measures, and one who had an ACE-R score below the cut off. The final control group included 38 adults.

#### **Materials**

#### Health

The *New York Heart Association* (NYHA) classification (Bennett, Riegel, Bittner, & Nichols, 2002) was used as an index of functional status. The NYHA is an extensively used and validated clinical measure. Classification I indicates no limitations and classification IV indicates the worst functional status.

The *Charlson Co-morbidity Index* (Charlson, Pompei, Ales, & MacKenzie, 1987) was used to assess the severity of co-morbid conditions. Overall index scores are categorised as mild, moderate, or severe; higher scores indicate more severe co-morbidity.

#### Global cognition

The *Addenbrooke's Cognitive Examination – Revised* (Mathuranath et al., 2000) is a test of global cognition. The ACE-R is a reliable and sensitive test of early

cognitive dysfunction (Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006) and was used to identify and exclude participants with possible dementia (scores < 82). Higher scores indicate better cognitive functioning.

#### General intelligence

The *National Adult Reading Test* (NART) (Nelson, 1982) was used as an index of premorbid intelligence. Standardised IQ scores were calculated using the formula in the administration manual (Nelson, 1982).

#### Psychopathology

The *Hospital Anxiety and Depression Scale* (Zigmond & Snaith, 1983) was used to screen for symptoms of anxiety and depression. The level of emotional symptomology was assessed separately for anxiety and depression (seven items each). Higher scores indicate higher levels of symptomology.

#### Executive function – cognitive flexibility

The *Trail Making Test* (TMT) (Reitan, 1992) was used to assess cognitive flexibility. The Trails B minus Trails A difference score was used as an index of cognitive flexibility (Lamberty, Putnam, Chatel, Bieliauskas, & Adams, 1994). Lower scores indicate better performance.

#### Executive function - inhibition

The *Hayling Sentence Completion* test (Burgess & Shallice, 1997) was used to assess cognitive inhibition. A total score was obtained by tallying errors and time

taken (in seconds) to complete the task. Standardised scores were calculated; higher scores indicate better performance.

#### Executive function – initiation

The final measure of executive functioning was *verbal fluency*, which was extracted from the ACE-R and used to assess cognitive initiation. Two types of verbal fluency were assessed; phonemic and categorical. In the phonemic task, participants were given one minute to orally generate as many words beginning with the letter 'P' as they could, excluding proper nouns and the same word with a different suffix. In the categorical task, participants were given one minute to name as many animals as they could. A composite verbal fluency score was used in the present study. Higher scores indicate better performance.

#### Verbal memory

The *Rey Auditory Verbal Learning Test* (RAVLT) (Rey, 1958) was used to measure verbal memory. A single composite score for the first five trials was used as the measure of immediate recall. The total number of correctly recalled words after a 20-minute delay was used as a measure of delayed recall. Higher scores indicate better performance.

#### **Primary Measures**

#### Emotion recognition

The *Ekman 60 Faces* test (Ekman & Friesen, 1976) was used to assess recognition of six basic human emotions; happy, anger, sadness, disgust, surprise, and fear. Participants were presented with 60 slides, featuring extensively and universally validated photographs of human faces (Edwards, Jackson, & Pattison, 2002). Participants were asked to choose one of six emotions that best described the emotion that the person in the picture displayed. This measure takes approximately 15 minutes to administer, and it has been used extensively to assess emotion recognition in various groups.

#### Theory of Mind

The *Reading the Mind in the Eyes* test (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001) was used to assess ToM. Participants were presented with 36 black and white images of the eye region of human faces, and asked to indicate which of four given emotional states each image best represents. In comparison to measures of emotion recognition, which require participants to identify basic facial expressions, this task required participants to identify more complex and finely nuanced mental states (e.g., "perplexed", "flirtatious"). This measure is administered in approximately 10 minutes. It is a reliable and valid measure of social cognitive dysfunction, and it is commonly used to assess ToM in various clinical and non-clinical groups (Vellante et al., 2013).

#### Procedure

Participants with CHF were tested approximately three months after recruitment into the parent study. The delay of three months was built in to ensure that participants were medically stable when they completed the neuropsychological assessment. Participants were tested in a quiet room, either at their residences, in a hospital consultation room, or in a university-testing lab in a single session, lasting approximately two hours.

#### **Design and data analysis**

This study used a matched-group comparison design. Missing value analysis was conducted, which showed that data were missing at random. Therefore missing data were not substituted. Descriptive statistics were generated for all variables. Univariate analyses were conducted to assess group differences on the background cognitive measures, and the ToM task. A mixed two-way ANOVA was used to examine differences in performance on the emotion recognition measure.

Pearson correlations were used to examine associations between the social cognitive measures and each of the other cognitive measures. Before undertaking the correlational analyses, all variables were assessed for normality. In the CHF group, all variables were normally distributed. In the control group, the Ekman Faces score was negatively skewed. Skewness was corrected by adjusting one outlier (which was 3 standard deviations below the mean) to two standard deviations below the mean (Tabachnick & Fidell, 2001).

To reduce the possibility of Type I error, we created a composite executive function score given that the three measures of executive function (TMT, Hayling, verbal fluency) were correlated: TMT with Hayling (r = -.38, p = .003), TMT with verbal fluency (r = -.25, p = .048), and Hayling with verbal fluency (r = .41, p = .001). The composite executive function score was created by converting scores on the three measures of executive function to z scores, reverse-coding the TMT such that higher scores indicated higher performance, then calculating a mean z of the three scores for each participant. The two measures of verbal memory (immediate and delayed recall, RAVLT) were also correlated (r = .79, p < .001) so a composite verbal memory score was created using the same approach. Both composite scores were normally distributed.

#### 7.1.4 Results

#### **CHF group characteristics**

The CHF group consisted of adults aged 40 to 86 (M = 69.77, SD = 11.23) who were predominantly male (65%). Table 1 shows that the majority of the CHF sample was classified as functional classification II on the NYHA. Systolic and ischaemic CHF were the most common aetiologies in this group, and hypertension was the most frequently reported risk factor. On average, participants had a moderate level of comorbid disease burden (Charlson Comorbidity Index mean = 3.48, SD = 2.03), and the average length of time living with CHF was three years (M = 36.17 months, SD = 55.49).

(Insert Table 1 about here)

#### Group comparisons on demographics and cognition

Table 2 shows that there was a trend towards higher proportions of cardiac risk factors in the CHF group, but these group differences were not significant (all *ps* > .060). Table 2 also shows that the two groups were closely matched in gender distribution, age, education, and estimated IQ as indexed by the NART. Independent samples *t*-tests were conducted to examine differences between groups on cognitive measures (Table 2). The control group performed significantly better on two of the three measures of executive function; cognitive flexibility t(62) = 3.07, p = .003, and cognitive inhibition t(61) = 5.88, p < .001, but not on either measures of verbal memory. The control group reported more symptoms of anxiety t(67) = 2.23, p = .029.

(Insert Table 2 about here)

#### Group comparisons on measures of emotion recognition and ToM

Emotion recognition: Ekman Faces test

Figure 1 shows the results of the Ekman Faces test as a function of *group* (CHF, control) and *emotion type* (happiness, surprise, anger, disgust, sadness, fear). These data were analysed with a mixed 2 x 6 ANOVA with the between-groups variable of group and the within-groups variable of emotion type. Mauchly's test indicated that the sphericity assumption was violated; therefore the Huynh-Feldt correction was used. Of primary interest, there was no significant main effect of group  $F(1, 67) = 0.01, p = .932 \eta_{p}^{2} < .001$ , and no interaction effect F(4.38, 293.15) = 0.76, p = .566,  $\eta_p^2 = .011$ , which indicates that recognition of basic emotions did not differ as a function of group status. Of secondary interest was the main effect of emotion type, F(4.38, 293.15) = 99.99, p < .001,  $\eta_p^2 = 0.60$ . Post hoc revealed that for all participants, the recognition accuracy significantly differed for each comparison of each type of emotion, with the order from best to worst recognised being: happiness (M = 9.91, SD = 0.33), surprise (M = 9.04; SD = 1.14), sadness (M = 7.99; SD = 1.82), disgust (M = 7.87; SD = 1.62), anger (M = 6.94, SD = 1.91), and fear (M = 4.99, SD = 1.91)2.17). The one exception was that recognition accuracy did not differ for the comparison of sadness and disgust.

#### Theory of Mind: Mind in the Eyes test

An independent samples *t*-test revealed that the groups did not significantly differ on their ability to accurately infer the mental states of others, t(66) = 0.63, p = .450, d = 0.18 (CHF M = 23.87, SD = 4.39; controls M = 23.08, SD = 4.23). The effect size was less than the cut off for a small Cohen's d(0.2) (Cohen, 1988).

# Correlations between emotion recognition and ToM with other cognitive measures

Pearson correlations were computed separately for the CHF group and controls to assess the relationship between emotion recognition and ToM and the other cognitive measures. Separate correlations were run for the Ekman Faces test and the Mind in the Eyes test (Table 3). All correlations were in the expected direction for both groups with better cognitive performance associated with better social cognition performance. In the CHF group, both emotion recognition and ToM showed significant moderate positive correlations with global cognition ( $r = .38 \ p = .034$ ;  $r = .49 \ p = .005$ , respectively). However, neither emotion recognition nor ToM significantly correlated with executive function or verbal memory. In the control group, neither executive function nor verbal memory significantly correlated with the Ekman Faces test and the Mind in the Eyes test, however there was a significant correlation between the Ekman Faces test and the Mind in the Eyes test (r = .45, p = .004), as might be expected.

(Insert Table 3 about here)

#### 7.1.5 Discussion

A large body of research has shown that people with CHF present with deficits in a range of cognitive abilities (Pressler, 2008; Vogels, Scheltens, et al., 2007). In the present study the CHF group's cognitive performance varied across cognitive domains. People with CHF showed deficits in some, but not all, cognitive functions, with relatively preserved memory function. No previous studies have investigated whether these deficits might extend to social cognition. The present study compared the emotion recognition and ToM abilities of people with CHF to a group of demographically matched controls. Contrary to expectations, the findings indicated that the performance of the two groups did not differ on either aspect of social cognition. This is also the first study to examine the association between social cognition and more general cognition. Importantly, in the CHF group, people with lower global cognitive ability were more likely to have difficulty recognising emotions and inferring the mental states of others, as expected. However, contradictory to our prediction, emotion recognition and ToM were not significantly correlated with measures of executive function or verbal memory.

The absence of group differences in emotion recognition and ToM is surprising because people with CHF are affected by diffuse damage to neural structures, including frontal and temporal regions (Vogels, van der Flier, et al., 2007; Woo et al., 2003), which have specifically been implicated in both of these social cognitive processes (Carrington & Bailey, 2009; Phan et al., 2002). The lack of group differences is further surprising because similar diffuse neural damage and widespread cognitive impairment is seen in other neurocognitive disorders, including people with traumatic brain injury (Babbage et al., 2011; Henry et al., 2006; Martín-Rodríguez & León-Carrión, 2010), autism spectrum disorders (Baron-Cohen, 2000, p. -; Harms et al., 2010), and multiple sclerosis (Henry et al., 2009; Phillips, Henry, Scott, Summers, & Whyte, 2011; Pöttgen, Dziobek, Reh, Heesen, & Gold, 2013). Each of these groups has shown significant deficits in general cognition, but also in emotion recognition and ToM. Furthermore, social cognition deficits have also been observed in a range of neuropsychiatric disorders, most commonly schizophrenia (Kohler et al., 2009; Sprong et al., 2007), but also mood disorders, such as major depression and anxiety (for review see, Kret & Ploeger, 2015). Thus, the common finding that CHF patients are affected by elevated rates of depression and anxiety (Yohannes, Willgoss, Baldwin, & Connolly, 2010), might have been expected to further increase their vulnerability to social cognition deficits.

There are several likely explanations for the null findings of this study. In the CHF group, correlations between emotion recognition and ToM with variables that had missing data (i.e., composite verbal memory n = 24; executive function n = 26) were underpowered; a post-hoc power analysis showed that the study power was .42 for a medium effect size (r = .30; the strongest correlation observed with a reduced sample size). Additionally, participants were a select and relatively high functioning group, cognitively and symptomatically. Specifically, we were interested in the performance of non-demented participants and therefore excluded anyone who showed signs of dementia. In addition, 64.6% of the CHF sample had no, or only mild, heart failure symptoms, and the overall subjective rating of depression was within the normal range. Thus, in the wider CHF population, where medical (Gaviria, Pliskin, & Kney, 2011; Mapelli et al., 2011; Pressler et al., 2010) and emotional (Hawkins et al., in press; Insel & Badger, 2002; Li, Meyer, & Thornby, 2001) symptoms are often more severe, brain pathology may also be more severe.

about the mental states of others is likely to be more impaired in CHF patients with greater comorbidity and worse functioning.

Finally, we chose measures of emotion recognition and ToM that have been used extensively with other clinical groups. However, they may not have been sensitive enough to detect subtle group differences because the CHF group was high functioning. Other studies have found that traditional and static measures of emotion recognition and ToM, like those used in the present study, do not always detect deficits that are picked up by dynamic measures (Golan, Baron-Cohen, & Hill, 2006; Golan, Baron-Cohen, Hill, & Rutherford, 2007; Rutherford, Baron-Cohen, & Wheelwright, 2002). Thus, future research could extend this study by using dynamic and/or morphed images (emotionally neutral expressions that are morphed into expressions of a specific emotion; e.g., Isaacowitz, Wadlinger, Goren, & Wilson, 2006) and include measures of reaction time. These measurement approaches could be more sensitive to subtle deficits in emotion recognition in high functioning groups.

Although preliminary, the significant correlations between global cognition and emotion recognition and ToM suggest that CHF patients with lower cognitive functioning are also more likely to have social cognitive deficits. If these findings are confirmed by other studies, then patients with poor cognitive function might require tailored intervention that focuses on improving psychosocial functioning. This is an important consideration because a key factor in successful CHF self-care is social support (Moser & Watkins, 2008). The available evidence has shown that social isolation and lack of social support are associated with increased risk of rehospitalisation and death (Friedmann et al., 2006; Luttik, Jaarsma, Moser, Sanderman, & van Veldhuisen, 2005; Murberg, 2004). Therefore, for patients with low global cognition, emotion recognition and ToM may indirectly impact self-care

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decision-making and quality of life through impoverished relationships or social isolation. Indeed, this indirect effect has been reported in people with schizophrenia where general cognitive abilities affected social abilities, which consequently exerted a negative influence on general functioning and quality of life (Fett et al., 2011; Schmidt et al., 2011).

In conclusion, in this group of high functioning CHF patients, which was matched to the control group on many important characteristics, capacity for emotion recognition and ToM was not found to be impaired, but each social cognitive construct was related to global cognition. Considering these preliminary findings, it seems likely that people with CHF who present with low general cognitive ability may also be affected by difficulties with accurately recognising emotions and inferring the mental states of others. This information is important given that psychosocial status, including social support and isolation are important influences of CHF self-care (Moser & Watkins, 2008).

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## Table 1:

# Clinical Characteristics of the CHF Group

Health characteristics	п	%
NYHA classification		
Class I	2	6.5
Class II	18	58.1
Class III	10	32.3
Class IV	1	3.2
Heart failure type		
Systolic	22	71.0
Diastolic	4	12.9
Mixed	3	9.7
Unspecified	2	6.5
Heart failure aetiology		
Ischaemic	17	54.8
Non ischaemic	8	25.8
Idiopathic	1	3.2
Other	5	16.1

*Note.* NYHA = New York Heart Association.

## Table 2:

# Participant Characteristics

	CHF group			Control group				
	п	%		n	%		$\chi^2$	
Proportion of men (%)	20	65.0		27	71.0		0.34	
Cardiac risk factors (%)								
Hypercholesterolemia	13	41.9%		15	39.5%		0.04	
Hypertension	21	67.7%		18	47.4%		2.88	
Smoking	13	41.9%		8	21.1%		3.52	
Diabetes	7	22.6%		4	10.5%		1.85	
Obesity	5	16.1%		2	5.3%		2.21	
Demographic (M)		М	SD		М	SD	t	d
Age (years)	31	69.77	11.23	38	67.13	7.53	1.12	0.28
Education (years)	31	11.65	3.74	38	13.07	3.57	1.61	0.39
Estimated IQ	30	112.54	5.89	38	114.33	6.38	1.19	0.29
Global cognition and mental h	ealth							
Global cognition (ACE-R)	31	91.00	4.89	38	92.08	4.55	0.95	0.23
Anxiety (HADS)	31	6.03	3.73	38	8.29	4.51	$2.23^{*}$	0.55
Depression (HADS)	31	5.19	2.91	38	5.55	3.29	0.48	0.12
Executive functions								
Cognitive flexibility (TMT)	27	74.83	35.17	37	49.19	31.35	3.07**	0.77

Inhibition (Hayling)	28	2.89	2.01	35	5.57	1.61	$5.88^{***}$	1.47
Initiation (Verbal fluency)	31	29.94	6.51	38	32.21	7.85	1.29	0.31
Verbal memory (RAVLT)								
Immediate recall	26	41.58	8.89	38	45.00	8.96	1.51	0.38
Delayed recall	24	8.83	2.51	38	9.13	2.84	0.42	0.11

 $\overline{d}$  = Cohen's d index of effect size. Effect sizes: small = 0.2; medium = 0.5; large = 0.8 (Cohen, 1988). \*p < .05 \*\*p < .01 \*\*\*p < .001

*Notes.* ACE-R = Addenbrooke's Cognitive Examination – Revised; HADS = Hospital Anxiety Depression Scale; RAVLT = Rev Auditory Verbal Learning Test; TMT = Trail Making Test (B minus A).



Figure 1. Mean number of correct responses for each emotion type on the Ekman Faces test for the CHF and control groups.

## Table 3:

## Relationships Between Emotion Recognition and ToM Scores and Cognitive Measures

	Ekman Faces					Mind in the Eyes				
	CHF		Controls		CHF		Controls			
	n	r (p)	n	r (p)	n	r (p)	п	r (p)		
Global cognition (ACE-R)	31	.38 (.034)*	38	.10 (.565)	31	.49 (.005)**	38	.07 (.659)		
Executive function	26	.02 (.957)	34	.15 (.410)	26	.14 (.495)	34	.25 (.158)		
Verbal memory	24	.30 (.154)	38	.21 (.208)	24	.21 (.327)	38	.11 (.530)		
Mind in the Eyes	31	.29 (.104)	38	.45 (.004)**		-		-		

p < .05 p < .01

*Note.* ACE-R = Addenbrooke's Cognitive Examination – Revised; Executive function and verbal memory are both composite scores.

#### 7.1.7 References for Study 3

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#### **CHAPTER 8: Review and Discussion**

#### 8.1 Chapter Overview and Summary of Key Findings

The studies presented in this thesis were designed to examine a series of questions pertaining to two areas of cognition that have not previously been researched in the CHF population: prospective memory and social cognition. The first major contribution of this thesis was that it demonstrated that people with CHF, at least the sample examined, are affected by pervasive but modest PM deficits (Study 1). Despite this decline, PM was not significantly associated with self-care behaviours (Study 2). This thesis also showed that social cognition in this sample was preserved (Study 3).

A major feature to emerge in the sequence of studies was that compared to existing CHF studies, this CHF group had high abilities in three important domains. The sample had modest or no deficits in other more general cognitive domains, thus the group had relatively high cognitive ability (Study 1 and Study 3). The sample also had good physical and emotional health status (Study 1, Study 2, and Study 3). The final feature of the sample was that it had high day-to-day management, such as medication adherence, functional independence, and self-care (Study 3).

In this final chapter, the research and clinical implications of these findings to the field of CHF are examined in detail. Methodological issues are also discussed. Because each of the individual studies included in the thesis have already addressed some of these issues, this chapter will discuss these issues from a broader perspective.

#### **8.2 Research Implications**

Before discussing the implications of the main findings and the clinical contributions of the findings that emerged in this thesis, it is important to highlight and discuss the areas the CHF sample in this thesis had better performance, compared to existing CHF studies.

#### 8.2.1 Cognitive performance.

The first notable feature of this CHF sample is that the group had high cognitive functioning. Compared to existing CHF studies, the sample in this thesis consistently performed better on measures of global cognition, and memory and executive function was either equivalent to, or better than, existing CHF studies. The effect sizes between CHF and controls on the background cognitive measures in the present thesis were either smaller than, or at least equivalent to, the effect sizes reported by existing CHF studies. When effect sizes were not reported by existing studies, a comparison of cognitive test scores also showed that this CHF sample consistently performed better. Each of these cognitive aspects is discussed in turn. Notably, it is difficult to directly compare all cognitive areas of existing studies to the results of this thesis due to differences in the measures used and the constructs assessed. For that reason, the following section has focused on a comparison of results of this thesis to other studies that have examined the same cognitive domains.

First, the sample in this thesis had high scores on measures of global cognition. As reported in Study 2, the MMSE score for the CHF participants was 28.74, which is considered to be within the normal cognitive range. Cut-offs between 21 to 24 are
typically used for mild cognitive impairment and  $\leq 20$  for dementia (Young, Meagher, & MacLullich, 2011). Further support that the sample had relatively high global cognition was observed from the results on the ACE-R, which is a more sensitive measure than the MMSE. In both Study 1 and Study 3, the mean scores on global cognition as assessed by the ACE-R were 90.79 (Study 1) and 91.00 (Study 3). The cut-off recommended for mild cognitive impairment is between 92 to 94 (Pendlebury, Mariz, Bull, Mehta, & Rothwell, 2012) and between 82 and 88 for dementia (Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006). The ACE-R has not previously been used in a CHF sample; however, scores for the MMSE, a frequently used measure in CHF research, were higher in the sample of this thesis than the vast majority of other studies. For example, a systematic review of 22 studies of cognitive functioning of patients with CHF by Vogels and Scheltens et al. (2007) reported that the mean score for global cognition on the MMSE was 24.84 for the pooled CHF participants. In subsequent studies that assessed cognitive performance in CHF, mean MMSE scores of 27.6 were reported in three studies (Bratzke-Bauer et al., 2013; Pressler, Subramanian, Kareken, Perkins, Gradus-Pizlo, Sauve, Ding, Kim, Sloan, Jaynes, et al., 2010; Vogels, Oosterman, van Harten, Scheltens, et al., 2007), and 23.5 in one recent study (Dodson et al., 2013), all of which are lower than the mean scores in the present thesis.

The CHF sample in this thesis also performed well on measures of retrospective memory. The mean for immediate recall on the RAVLT was 41.31 in Study 1 and 41.58 in Study 3, but the effect sizes were mixed. In Study 1, the size of the difference between the CHF and control groups was large (Cohen's d = .91), but it was small to moderate in Study 3 (Cohen's d = .38). For delayed recall (using the RAVLT), the mean scores were

8.96 and 8.83 in Study 1 and Study 3, respectively, with small differences between CHF and controls in each case (Cohen's d = .41 and .11, respectively). Importantly, performance on all memory measures was preserved in the CHF group compared to controls in Study 3. Although there were some mixed differences of effects between CHF and controls, the mean memory scores were consistently better than in existing CHF studies.

For example, using the same assessment approach as this thesis (i.e., immediate and delayed recall), pooled memory data from 13 studies (Vogels, Scheltens, et al., 2007) reported the size of effect between CHF and controls (standard mean difference (SMD)) was .43, which is either bigger than, or at least equivalent to, the present thesis. There was only one exception where the size of effect between CHF and control groups for memory was larger in the present thesis (immediate recall, Study 1) compared to the review by Vogels and Scheltens et al. (2007). Furthermore, a comparison of mean scores for immediate and delayed recall also showed that the CHF sample in this thesis performed better than samples of existing studies. Two subsequent studies that were not included in the review by Vogels and Scheltens et al. (2007) reported mean scores of 37.8 (Vogels, Oosterman, van Harten, Scheltens, et al., 2007) and 40.2 for immediate recall (Sauvé, Lewis, Blankenbiller, Rickabaugh, & Pressler, 2009), both which are lower than the scores in Study 1 and Study 3 in the present thesis (41.31 and 41.58, respectively). This pattern was consistent for delayed recall, with mean scores of 7.2 (Vogels, Oosterman, van Harten, Scheltens, et al., 2007) and 7.8 (Sauvé et al., 2009), both lower compared to the present thesis.

Furthermore, the CHF sample in this thesis also performed better than other CHF groups on executive function. This was observed when mean scores were compared, but mixed effect sizes were found, similar to memory. The mean scores for the TMT, which measures cognitive flexibility, was 71.8 in Study 1, with a small effect size of the difference between CHF and controls (Cohen's d = .40). Additionally, the mean score, for the same construct, was 74.83 in Study 3 with a medium to large effect size (Cohen's d = .77). The mean score for Digit Span, which taps working memory, and which was only assessed in Study 1, was 17.70. For the TMT, two recent studies reported higher mean scores (i.e., worse performance) of 96 (Vogels, Oosterman, van Harten, Scheltens, et al., 2007) and 84.6 (Pressler, Kim, Riley, Ronis, & Gradus-Pizlo, 2010), compared to this thesis. An examination of the effect size for the construct of cognitive flexibility revealed mixed findings. The results of Study 1 showed that the size of the effect between CHF and controls was equivalent to a review involving pooled data from nine studies (SMD = .42). However the effect between CHF and controls reported in Study 3 was larger (Vogels, Scheltens, et al., 2007). Additionally, a comparison of Digit Span performance showed that recent studies have consistently reported lower mean scores (i.e., worse performance) of 10.5 (Pressler, Kim, Riley, Ronis, & Gradus-Pizlo, 2010) and 12.4 (Vogels, Oosterman, van Harten, Scheltens, et al., 2007), compared to this CHF sample.

To summarise, the CHF sample reported in this thesis performed consistently better, or at least equally well, on measures of global cognition, retrospective memory, and executive function compared to existing research. A comparison of the difference in effect sizes between CHF and controls revealed mixed differences, but the pattern of findings favoured the performance by the CHF sample from this thesis. There were only two exceptions (retrospective memory from Study 1, and cognitive flexibility from Study 3). Here, the size of the effects between CHF and controls in this thesis were larger than existing research. However, a review of means scores, even in these cases of mixed effect sizes, showed a consistent pattern of better performance by this CHF cohort, across all cognitive domains, compared to existing CHF samples.

## 8.2.2 Health status.

The CHF group described in this thesis also had a better physical and emotional health status, compared to existing studies. First, the CHF sample in this thesis had less severe CHF symptoms, as measured by the NYHA functional classification, compared to a review of CHF severity data in other samples. In all of the studies included in this thesis, the majority of the sample (70%) reported no or only mild CHF symptoms (NYHA classification I and II) during moderate activities. By contrast, existing studies that have examined aspects of cognition and/or self-care in CHF, have consistently reported more severe symptoms of CHF with mild activities, or even when at rest. This was evident in several recent large studies where, between 50% to 76.5% of the CHF samples had moderate or severe CHF symptoms (NYHA functional classification III and IV (Bauer et al., 2012; Bratzke-Bauer et al., 2013; Cameron, Worrall-Carter, Page, Riegel, et al., 2010; Dickson et al., 2011; Huijts et al., 2013; Lee et al., 2013; Lee et al., 2015; Pressler, Subramanian, Kareken, Perkins, Gradus-Pizlo, Sauve, Ding, Kim, Sloan, & Jaynes, 2010; Pressler, Subramanian, Kareken, Perkins, Gradus-Pizlo, Sauve, Ding, Kim, Sloan, Jaynes, et al., 2010; Riegel, Moelter, et al., 2011; Riegel et al., 2007; Sauvé

et al., 2009). Methodological considerations that likely contributed to the CHF sample having low severity CHF are discussed in Section 8.3.

Further evidence that the CHF sample had better physical health, compared to existing research, is that self-care management in Study 2 could only be analysed for three quarters of the sample (22 out of 30 cases). This was because eight patients (26.6%) reported that they did not have symptoms of breathlessness or oedema in the previous month. By contrast, recent studies (Cameron, Worrall-Carter, Page, Riegel, et al., 2010; Harkness et al., 2014; Lee et al., 2013; Lee et al., 2015; Riegel et al., 2007) that examined the relationship between cognition and self-care reported self-care management scores for 100% of their sample. That is, 100% of participants in other recent studies experienced symptoms of worsening heart failure in the previous month. There was only one study that reported a similar proportion (22%) of patients who did not experience symptoms of worsening heart failure in the preceding three months (Dickson et al., 2011).

In addition to the particularly good physical health status of the CHF sample, participants also had good mental health, as evidenced by no, or only mild, symptoms of depression. More specifically, the mean scores on the HADS were 5.00 (Study 1) and 5.19 (Study 3), which falls within the normal range. Additionally, the effect size of the difference between CHF and controls was small (Cohen's d = .28 and .12, respectively). Furthermore, in Study 2, only 10% of patients reported *mild to moderate* depressive symptoms.

Emotional symptomology is consistently higher in the wider CHF literature, although varying rates have been reported. This was observed when a comparison of effect sizes, mean scores, and proportions of depressive symptoms were compared; for example, the size of the difference between CHF and controls reported in the present thesis was smaller compared to the medium effect (SMD = .48) reported by pooled data involving 11 studies (Vogels, Scheltens, et al., 2007). A separate review paper involving 27 studies reported that *clinically significant* depression was seen in approximately 21.5% of the CHF population (Rutledge et al., 2006). Furthermore, a Cochrane review (Lane, Chong, & Lip, 2005) that evaluated eight studies reported varying prevalence rates, but concluded that *major clinical depression* was present in up to 26% of the CHF participants. The most recent review paper (Yohannes, Willgoss, Baldwin, & Connolly, 2010) involving 33 studies also found varied rates of depression (between 10% to 60%), however the use of a wide range of diagnostic tools made it difficult to reach a consensus on the prevalence.

Notably, three studies have used the same depression tool (HADS) as the present thesis. In each of these studies, higher mean scores or proportions of depressive symptoms have been reported, compared to this thesis. Two studies (Jünger et al., 2005; Yu, Thompson, Yu, & Oldridge, 2009) reported means scores within a normal range (6.1 and 6.31), but still higher than in the present thesis. One of these studies reported the same proportion (10%) of depression (Yu et al., 2009), while the other study reported a higher proportion (30%) (Jünger et al., 2005), compared to this thesis. The most recent study of cognition in CHF that also used the same measure of depression also reported more severe symptoms: 21.7% of the sample was described as having *clinically significant* depression (Almeida et al., 2013).

A factor that likely contributed to the good health status (i.e., clinical stability) and high cognitive performance of this sample was that participants were managed using

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gold standard pharmacological treatment. Study 2 reported that 67% of patients were prescribed either an ACEI or ARB, 77% were prescribed a beta-blocker, and 83% were prescribed a diuretic. These findings are important because common neurohormonal antagonists include ACEI or ARB and beta-blockers, which are commonly used in conjunction with a diuretic to relieve the symptoms and signs of congestion (McMurray et al., 2012). Notably, meta-analyses of key randomised controlled trials involving ACEI (Flather et al., 2000) and beta-blockers (Foody, Farrell, & Krumholz, 2002; Shibata, Flather, & Wang, 2001) have shown that gold standard treatment improves health outcomes for worsening heart failure within approximately one year of starting treatment. Furthermore, in support of the relationship between gold standard pharmacological treatment and cognitive performance, a recent systematic review involving 15 studies found that after interventions to improve cardiac function, such as medications, cognitive function stabilised or improved in patients with CHF (Hajduk, Kiefe, et al., 2013).

In summary, this section highlighted several important aspects of the CHF sample's health that are known to impact on cognitive performance. More specifically, this section demonstrated that the CHF sample included in this thesis had better physical health compared to existing studies. Additionally, the sample reported no, or only mild symptoms of depression, whereas in the wider population of people affected by CHF, higher rates of depression, including clinically significant depression are frequently reported.

## 8.2.3 Day-to-day management.

The final feature of this CHF sample that sets it apart from other samples is that the group had moderate to high abilities to manage day-to-day tasks. This was demonstrated from data related to medication adherence, functional independence, and self-care behaviours. First, in Study 2, medication barriers could not be analysed because only three participants (10%) reported skipping medications. By contrast, in the wider literature, medication non-adherence rates continue to be high (Riles, Jain, & Fendrick, 2014), and are frequently higher than that reported in this thesis. More specifically, a review paper involving 50 studies concluded that most studies reported medication nonadherence rates to be between 40% to 60% (Wu, Moser, Lennie, et al., 2008), depending on how adherence was measured and defined.

Additionally, in Study 2, a high degree of overall functional independence was found. The mean IADL total score in this thesis was 2.03 (out of 16; lower scores represented more functional independence), two points from total independence. A comparison to existing studies showed that the degree of functional independence in the CHF sample examined in this thesis was relatively similar to other studies. The results of two recent studies (Alosco et al., 2012; Alosco, Spitznagel, et al., 2013) reported mean scores of ~13.5 (out of 16; with higher scores representing greater functional independence) on the same measure of functional independence. Notably, although the scoring of the IADL scale is reversed in Study 2 compared to existing studies, the CHF sample in this thesis had a mean score within a 1-point difference (in the direction towards total functional independence) of the existing literature.

The final aspect of the CHF sample's day-to-day management was self-care, which was mixed. In Study 2, the average self-care maintenance score on the SCHFI was 68.14 (47% adequate), management was 65.87 (33% adequate), and confidence was 69.91 (57% adequate). A comparison to existing studies showed that self-care confidence was consistently higher in the CHF sample of this thesis compared to other studies, with one study reporting a mean score of 63.9 for confidence (Lee et al., 2013), and another reporting that 44% of the sample had adequate confidence (Cameron, Worrall-Carter, Page, Riegel, et al., 2010). Self-care management scores were generally higher in the present thesis. Two existing studies reported substantially lower mean management scores of 55.5 (Lee et al., 2015), or between 45.6 to 59.3 (Harkness et al., 2014), and one study reported that 27% of the sample had adequate management (Cameron, Worrall-Carter, Page, Riegel, et al., 2010). An additional two studies, however, reported higher mean management scores of 67.3 (Lee et al., 2013) and 71.28 (Dickson et al., 2011). Compared to Study 2, self-care maintenance scores of existing studies were also mixed; they were either similar to this thesis, or only marginally higher. More specifically, one study reported a mean maintenance score of 69.8 (Lee et al., 2013), another reported a higher mean score of 71.54 (Dickson et al., 2011), and one reported that 53% of the sample had adequate maintenance (Cameron, Worrall-Carter, Page, Riegel, et al., 2010).

Taken together, this section has showed that compared to existing samples, this CHF sample had high abilities to manage day-to-day tasks. Medication adherence and functional independence were high and consistently better in this thesis, but the results involving self-care were mixed. More specifically, the CHF sample in this thesis consistently had higher confidence scores, management was largely better in this thesis, but maintenance scores were either similar to, or marginally better in existing samples.

In summary, Section 8.2 discussed several aspects of the CHF sample's functioning, including cognitive performance, health status, and the cohort's day-to-day management. This section demonstrated that in each of these domains, the CHF cohort from this thesis had higher cognitive performance, better physical and emotional health, and management of day-to-day tasks was mixed but generally higher in this sample, compared to other studies.

# 8.3 Methodological Considerations

Thus far, this chapter has focused on describing features of the CHF sample's performance. The next section focuses on methodological and sampling processes that likely contributed to the sample having relatively high cognitive performance, good health status, and high abilities to manage day-to-day tasks.

#### **8.3.1** Methodological limitations.

The studies in this thesis excluded anyone with acute CHF. For this reason participants were outpatients who were tested three months after recruitment into the parent study. Anyone with possible dementia was also excluded. These factors likely contributed to this sample having good health status and relatively high cognitive performance.

A consideration of the timing of testing is important because participants at the acute stage of CHF are likely to experience symptoms, such as shortness of breath, which

can diminish cognitive performance. One study tested the cognitive performance of patients who were admitted due to decompensated CHF; these patients' performance was compared to a group of stable outpatients engaging in a heart failure clinic who had no signs of decompensation (i.e., symptoms of breathlessness, oedema) for at least three months before inclusion in the study (Kindermann et al., 2012). The study reported that, compared to stable CHF, the cognitive performance of patients suffering from decompensated CHF was poorer, particularly with respect to memory, processing speed, and executive function. These findings suggest that symptomatic CHF can result in poorer cognitive impairment. Similarly, depression appears to be up to three times more prevalent in acutely unwell CHF samples, compared to outpatients (Rutledge et al., 2006).

Furthermore, it is likely that eligible participants who declined were too fatigued to commit to participation in the studies of this thesis. This thesis involved a two-stage screening and recruitment process, and large proportions of participants declined to take part in the study. During the first-stage of the recruitment process, a total of 407 participants were screened for eligibility from the parent study. Out of this pool of potential participants, 188 (46%) were ineligible for enrolment into the parent study. Reasons for ineligibility included being referred to the CHF management program but not having a confirmed diagnosis of CHF, having a confirmed diagnosis of CHF but also a terminal illness, a documented history of dementia, poor English proficiency, or living in a high care residential facility and therefore not self-managing (i.e., their self-care). A further 45 (11%) were not approached, mainly because they could not be contacted, and a further 78 (20%) patients declined to take part in the study. Thus, over a quarter of the

initial *eligible* participants either declined or could not be contacted. These proportions are consistent with a study by (Pressler et al., 2008) which discussed the challenges in recruitment of people with serious, life-threatening chronic conditions like CHF. Indeed, Pressler et al. (2008) argued that given the highly symptomatic condition of CHF, it is likely that some patients may have been too fatigued to commit to participating in the study (Pressler et al., 2008).

Additional participants who were eligible were lost during the second-stage recruitment. This included participants who were already engaging in the parent study, and were possibly too fatigued to commit to participation in additional research. Out of the 96 participants that were recruited into the parent study, only 72 were available for cognitive testing during the time that recruitment for studies included in this thesis was being conducted. Figure 1 in Study 2 showed that out of 72 approached participants, 25 (35%) declined, five (7%) were not contactable, and seven (10%) withdrew before completing the primary measure of PM. This meant that, out of the 72 participants that could be approached from the parent study, a total of 37 (51%) were lost during the recruitment process. Notably, another five (7%) participants were excluded because of possible dementia. Thus, out of the total number of eligible participants at both recruitment stages, 160 (39%) were lost at either the point of recruitment into the parent study, or at the point of recruitment into the studies for this thesis.

To summarise, the recruitment of outpatients and exclusion of people with dementia contributed to this thesis capturing participants with better health status and higher cognitive performance than prior studies. Additionally, the challenge in recruitment also likely contributed to the sample having good health status. This is

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because the large proportion of participants who declined were probably more symptomatic, although data to confirm this were not available. Thus, the findings of this thesis cannot be generalised to all CHF patients. Although, in one sense this might be viewed as a limitation, the relatively high functioning sample provided an opportunity to investigate a portion of CHF patients that has rarely been examined in the published literature. The clinical implications of this are discussed in Section 8.5 of this chapter.

A final limitation of this thesis was that Study 2 and Study 3 were underpowered. A post-hoc power analyses for Study 2 showed that with a small sample (n = 30), the power was .55 for a medium effect size, which means that there was insufficient power to detect a relationship between PM and self-care. Furthermore, Study 3 had missing data on some background cognitive measures (i.e., verbal memory, executive function). A posthoc power analysis in this study showed that power was .42 for a medium effect size. Thus, in the CHF group, correlations between each of the social cognitive measures and general cognitive measures were not sufficiently powered to reach statistical significance.

### 8.3.2 Methodological strengths.

The strongest aspect of the methodology was the thorough approach to the assessment of cognitive performance. This included measures of global cognition, as well as a large cognitive test battery including measures of retrospective memory, working memory, and executive functions. Many prior studies that have assessed cognition in CHF are limited because the assessment of cognitive performance has been determined using brief screening measures, such as the MMSE. In CHF research, it is rare for studies to include a comprehensive cognitive assessment. A recent review paper (Davis & Allen, 2013) involving 23 studies found that the MMSE was used most often in CHF research, with only three studies incorporating other screening measures (Davis & Allen, 2013). The findings in existing studies that have used this superficial approach to cognitive assessment are problematic because the MMSE has been shown to have poor sensitivity in detecting mild levels of cognitive impairment (Mitchell, 2009), and it does not detect cognitive impairment in the domains frequently affected in CHF patients (i.e., executive function) (Cameron, Worrall-Carter, Riegel, et al., 2009; Riegel et al., 2002).

In the present thesis, a more thorough assessment of global cognition (ACE-R) was used, instead of the MMSE, albeit scores on the MMSE were also reported in Study 2 to allow comparisons with existing research. Compared to the MMSE, the ACE-R is more sensitive to mild forms of cognitive impairment (Pendlebury et al., 2012). In addition to the ACE-R, a comprehensive cognitive test battery was included in this thesis with measures that have been extensively validated in detecting cognitive decline. The use of sensitive cognitive measures is especially important in samples with high cognitive performance, where deficits in some aspects of cognition are only mild.

In addition to conducting a systematic cognitive assessment, the sample described in this thesis was also thoroughly characterised, and a comprehensive clinical history was collected and reported. This provides contextual information and will allow researchers to consider the relevance of the findings to other CHF groups.

#### **8.4 Implications of Main Thesis Findings**

Prior to this thesis, there was clear evidence that people with CHF experience increased rates of cognitive impairment. However, the degree of cognitive impairment, and the patterns of cognitive performance in samples that have higher cognitive abilities and better health status were not understood. Indeed, in the broader CHF literature, the type and severity of cognitive impairment varies within- and between studies (Alosco, Spitznagel, et al., 2013; Bauer et al., 2012; Bratzke-Bauer, Pozehl, Paul, & Johnson, 2013; Hjelm et al., 2012; Kindermann et al., 2012; Pressler, Kim, Riley, Ronis, & Gradus-Pizlo, 2010; Vogels, Oosterman, van Harten, Scheltens, et al., 2007; Vogels, Scheltens, et al., 2007). Nonetheless, large meta-analyses have reported that CHF is associated with a pattern of generalised cognitive impairment (Vogels, Scheltens, et al., 2007), and that cognitive decline is a substantial problem in all CHF cases, even in patients with asymptomatic CHF (Cannon et al., 2015). Using a methodologically rigorous approach to the assessment of cognitive function, the original research in this thesis found that a mixed cognitive profile was observed in this relatively healthy CHF sample, with deficits in some, but not all cognitive domains.

## **8.4.1** Prospective memory.

The first finding to emerge in this thesis showed that the CHF sample had pervasive deficits in PM (Study 1). Given that there was a consistent PM deficit, in real life, everyday lapses of intention in people with CHF are probably broad-based, rather than specific to a particular type of task. Notably, there is some evidence that laboratory measures may not accurately reflect the performance of older adults in everyday life (Bailey, Henry, Rendell, Phillips, & Kliegel, 2010; Henry et al., 2004; Niedźwieńska & Barzykowski, 2012). PM measures are often criticised for having poor ecological validity (Phillips et al., 2008). As this thesis used Virtual Week, a laboratory measure of PM, some caution should be taken when predicting this CHF group's PM performance in naturalistic settings. Nonetheless, as discussed in Chapter 3, Virtual Week was designed to overcome the limitations of other laboratory measures by simulating activities in daily life. Thus, the results reported in Study 1 are thought to closely represent the everyday patterns of PM performance in people who are affected by CHF. Additionally, an important finding from Study 1 was that the PM deficits in the CHF sample were mild. These findings suggests that CHF groups such as the sample in this thesis might not have frequent or obvious PM lapses, but are likely to have occasional lapses of PM in everyday tasks. Although once-off lapses of intention might not have any major consequences for the individual, an accumulation of lapses over time are likely to cause annoyance and frustration.

Additionally, this thesis showed that, compared to other more general cognitive processes, PM decline might be particularly sensitive to CHF-related pathology. As discussed, Study 1 found that in the CHF group, there was a pervasive PM deficit across four different types of PM tasks (time- and event-based, regular, and irregular). By contrast, deficits in general cognitive constructs were mixed, with decline in some, but not all cognitive domains. For instance, Study 1 found that the CHF sample was impaired on two (i.e., inhibition and initiation) out of four executive functions, compared to the control group. Study 1 also found that the CHF group had a poorer performance on two (i.e., immediate and delayed recall) out of three indices of verbal memory, compared to the control group. Similar mixed findings were reported in Study 3; for instance, the CHF group had deficits in two (i.e., cognitive flexibility and inhibition) out of three executive functions compared to the control group, but memory was entirely preserved. Taken

together, these findings demonstrate that aspects of more general cognition were sometimes impaired and sometimes not, whereas *all* aspects of PM function were impaired in this CHF group.

### 8.4.2 Social cognition.

The second part of this thesis showed that, unlike PM function, emotion recognition abilities and ToM were preserved in this CHF group. Study 3 also showed that as CHF patients' global cognition (as assessed with the ACE-R) declined, social cognitive abilities also reduced. The significant correlations between the ACE-R and emotion recognition and ToM suggests that any social cognitive decline may be the result of CHF-related pathology. It is possible that in Study 3 a deficit in social cognition in the CHF group was not observed compared to the control group because the CHF group had relatively high ACE-R scores, as demonstrated in Section 8.2.1; therefore, the few CHF patients with low ACE-R scores did not offset those with high ACE-R scores. Future studies should assess emotion recognition abilities and ToM in CHF groups that have lower scores on global cognition than what was observed in this thesis. Future research should also assess the specificity of social cognitive decline compared to other general cognitive tasks in people with CHF.

### 8.4.3 Impact of cognitive impairment.

Prior to this thesis, the significance of cognitive deficits in samples that have relatively high cognitive performance and good health status was not understood. The original research presented in this thesis shows that it cannot be assumed that any degree

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of cognitive impairment will have an adverse impact on an individual's management of day-to-day tasks. In the broader CHF population, there is clear and strong evidence of an association between cognitive impairment and poor CHF management (Alosco et al., 2012; Alosco, Spitznagel, et al., 2013; Cameron, Worrall-Carter, Page, Riegel, et al., 2010; Currie et al., in press; Harkness et al., 2014; Hawkins et al., 2012; Lee et al., 2013; Riegel, Moelter, et al., 2011). However, Study 2 of this thesis found that cognitive processes such as executive functions and/or verbal memory, which in other studies have been shown to impact self-care, were not related to self-care behaviours in this CHF sample. These findings show that in CHF groups who have relatively high cognitive performance and good health status, such as the sample in this thesis, even when some cognitive decline is present, this degree of impairment does not adversely affect abilities to manage day-to-day behaviours, as is often the case in the wider CHF population.

An alternative explanation for the lack of association between cognition and selfcare is that self-care was assessed using self-report (SCHFI), which could have resulted in socially desirable responses by patients. However, this CHF sample still had relatively good physical health, with no or only mild symptoms of CHF, as demonstrated in Section 8.2.2. This finding suggests that the CHF sample was able to effectively follow treatment recommendations, and that the PM deficits did not impact the ability to perform self-care tasks. If patients were not successfully adhering to self-care behaviours, the CHF sample's health would have, presumably, been poorer than was observed in this thesis.

It seems likely that this CHF sample had high general abilities, or more specifically, high premorbid functioning, which enabled the group to withstand the effects of brain pathology. The CHF group's high premorbid ability may have facilitated

the use of strategies to compensate for cognitive difficulties that were present. The notion of cognitive reserve suggests that people's higher education level and higher estimated IQ can serve as a protective factor and optimise performance by drawing on differential brain networks (Stern, 2002). That is, in people with high cognitive reserve, tasks are processed more efficiently through the use of alternative cognitive strategies. It is possible that the CHF sample examined in this thesis had high cognitive reserve, with the majority of CHF participants having above average estimated IQ, as assessed with the NART; for instance, in Study 1 and Study 2, estimated IQ for the CHF sample was 111.93, and the average years of education was 11.13 (53% with > 12 years of education); for Study 3, estimated IQ was 112.54, and the average years of education was 11.65. Thus, from a cognitive reserve perspective, it could be argued that in this CHF sample, general cognitive processes that were preserved provided differential coping strategies to compensate for aspects of cognition that were affected. It is possible that the PM decline in this CHF sample could be withstood; this meant that performance of dayto-day tasks was optimised.

### **8.4.4** Clinical implications.

Taken together, the findings of this thesis show that there are subgroups of people with CHF whose cognitive abilities are not compromised, or are only marginally impaired, and that the impact of cognitive decline is not significant in all CHF cases. Much of the literature involving people with CHF has focused on patients who have lower cognitive functioning, and who are affected by physical and emotional symptomology that are known to impact cognition. Despite the uniformity that is implied by umbrella terms like 'vascular cognitive impairment' and 'mild neurocognitive disorder' (described in the review in Chapter 2), the cognitive deficits of the sample reported in this thesis were not consistent, in severity, with other CHF samples. Indeed, little is known about the outcomes of people with CHF who have high cognitive functioning, such as the sample in this thesis.

Consistent with the findings of this thesis, emerging research has shown that the cognitive profiles of people with CHF are more heterogeneous than originally expected and cannot be simplified to a single profile. A study that assessed participants' cognitive profiles using a cluster analytic approach reported that three unique cognitive profiles emerged (Miller et al., 2012). These three profiles included people with intact cognitive performance, those with impaired memory performance, and people with globally impaired cognition (i.e., decreased performance in all cognitive domains). The presence of discrete clusters was later observed in a different and larger sample (Hawkins et al., 2015).

The current guidelines for the management of CHF involve a set of unitary recommendations (Krum et al., 2006) that do not account for individual differences in cognition, health status, or day-to-day management, such as self-care. The findings presented in this thesis highlight the need to consider different approaches to intervention, depending on the abilities and degree of impairment of the individual. Clearly, there needs to be further research on PM and social cognition in other CHF samples with poorer abilities in general cognitive domains and poorer health status. This is because in the wider CHF population where cognitive decline and physical and emotional symptoms are often more severe, PM difficulties are likely to be more substantial and could contribute to poor self-care behaviours that could lead to episodes of CHF decompensation. However, the three original studies of this thesis show that possibly, CHF samples that have relatively high cognitive function, good health status, and good abilities to manage day-to-day behaviours might not require high intensity CHF management. This idea is explored further in the next section, which focuses on factors that are likely to impact outcomes of CHF patients more broadly, and need to be considered in order to optimise management of this complex condition.

### 8.5 Broader Clinical Implications

### 8.5.1 Disease management programs.

CHF disease management programs are common in Australia, North America, and Europe (Savard, Thompson, & Clark, 2011) and focus on providing care to optimise management of CHF. Numerous studies have been conducted to investigate the efficacy of disease management programs, however the interventions provided were not selectively applied. Nevertheless, several meta-analyses of randomised controlled trials have shown that predominantly nurse-led, multidisciplinary programs of care significantly reduce the risk of rehospitalisation, improve quality of life, reduce health care costs, and prolong survival (McAlister, Lawson, Teo, & Armstrong, 2001; McAlister, Stewart, Ferrua, & McMurray, 2004; Savard et al., 2011; Stewart & Horowitz, 2002; Stewart, Marley, & Horowitz, 1999). Although, the mode of delivery of management programs varies, the key components of care are the same, and involve routine contact, clinical and physiological monitoring, education, self-care support/monitoring, exercise therapy, and carer support (Stewart, 2013). The findings of this thesis raise the possibility that high functioning CHF samples, like the one described in this thesis might not need high levels of CHF care because this subgroup of patients are less likely to have adverse health outcomes. Aspects of disease management programs such as clinical and physical monitoring, and/or self-care support, are resource intensive and patients who are managing well may require less support. More specifically, this CHF group had relatively high cognitive performance compared to existing studies, CHF severity was low in the group, self-care was moderate to adequate on average, and only three out of 30 participants reported having medication barriers. By contrast, CHF patients with more severe cognitive impairment that impact on management of day-to-day tasks, and patients with more severe physical and emotional symptoms, are likely to require more intensive disease management efforts to reduce adverse health outcomes.

The notion that standard disease management might not equally benefit all CHF patients has previously been reported. One large randomised controlled trial study compared the effectiveness of two different interventions (Jaarsma et al., 2008). This included a comparison of less intensive versus more intensive (home-based) support by a nurse, compared to a control group that received standard follow-up by a cardiologist. The study found a small non-statistically significant 15% reduction in all-cause mortality when the two intervention groups were compared to the control group. Notably, in the study by Jaarsma et al. (2008) intervention was not selectively applied. One likely explanation for the lack of significant differences between the intervention and control groups was that patients in the control group were on optimal management according to evidenced-based guidelines. Thus, it would have been difficult to further improve health

outcomes for that group (Jaarsma et al., 2008). The study by Jaarsma et al. (2008) highlights that CHF samples who are managing well, like the sample in this thesis may not require much attention from the perspective of CHF care.

Furthermore, in the context of the continued debate about the best approach to CHF, there has been increasing awareness of the need to conduct pragmatic trials of different forms of programs. However, no prior study has focused on assessing a patient's needs first, and then choosing the most appropriate intervention for that individual. The WHICH (Which Heart Failure Intervention Is Most Cost-Effective & Consumer Friendly in Reducing Hospital Care) trial is the first to investigate whether there might be important differences in the impact and patient acceptability of the two most common forms of management: home-based and clinic-based approaches (Stewart, Carrington, Marwick, et al., 2012). Importantly, the findings of the WHICH study showed that patients in the home-based intervention accumulated significantly fewer days of cardiovascular-related hospitalisations (37% less). It is likely that home-based intervention allowed informal assessment of a patient's clinical and psychosocial functioning, as well as their self-care abilities (Stewart, Carrington, Marwick, et al., 2012). Thus, these findings highlight the potential benefits of providing tailored intervention based on individual needs.

*Management programs and patient characteristics.* Although patients with certain characteristics may not derive the same benefit from CHF management programs as other patients, studies that have assessed CHF management programs rarely consider patient characteristics and heterogeneity. A recent meta-analysis of previous reviews of

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management programs concluded that the CHF populations and the program features were inconsistently and poorly described in the published literature (Savard et al., 2011). That is, interventions were described using general descriptors, and findings from interventions with very diverse characteristics and populations were pooled, and clinical or methodological heterogeneity were seldom taken into account in the analyses. Seven out of 15 reviews that were included in that meta-analysis reported no information on comorbidities, 10 out of 15 reported incomplete or no data on NYHA functional classification, and cognitive functioning was not taken into account (Savard et al., 2011). These findings are important because it remains unclear how patients with relatively high cognition and few clinical symptoms (i.e., NYHA functional classification, emotional symptoms), such as the group described in this thesis, might benefit differently from these programs. A recent review highlighted this gap in knowledge about "what works for whom", or more specifically, the relationship between patient characteristics and the likelihood of success of intervention (Bos-Touwen et al., 2015).

Furthermore, patients need experience in order to build tactical skills and improve their adherence to self-care. That is, skills in self-care evolved over time and with practice (Cameron, Worrall-Carter, Page, & Stewart, 2010; Dickson & Riegel, 2009; Riegel & Dickson, 2008; Riegel, Dickson, & Faulkner, in press). Thus, traditional education, which has been identified as the most common element of management programs (Savard et al., 2011), did not enhance self-care skill development (Dickson & Riegel, 2009). These findings suggest that patients classified as having no or only mild CHF symptoms (NYHA functional classification I or II), such as the sample in this thesis are unlikely to benefit from educational strategies. This is because this subgroup of patients would have either no or only limited experience managing CHF symptoms and thus, would not see the personal relevance of the education intervention.

In summary, the discussion in this section has highlighted the fact that, although there is extensive literature to support the efficacy of disease management programs, the relevance of the programs need to be considered in the context of the overall abilities of the individual. The CHF sample described in this thesis had predominantly low severity CHF as assessed with the NYHA functional class; depression was within a normal range; and cognitive functioning was higher than in existing studies. Additionally, medication barriers were minimal, and self-care was moderate to adequate. Patients with similar features to the CHF sample included in this thesis are unlikely to need intensive support from a traditional disease management program.

#### 8.5.2 Individualised treatment.

It is rare for disease management programs to selectively apply intervention based on the assessment of the needs of the patient. A systematic review involving educational strategies for people affected by CHF found that only four out of 19 studies conducted an assessment prior to implementing a strategy (Boyde, Turner, Thompson, & Stewart, 2011). Another review found that published trials involving disease management were rarely applied through explicit identification of subgroups, followed by allocation of tailored strategies (Bos-Touwen et al., 2015). In order to optimise the management of CHF, a shift needs to be made toward assessing a patient's needs, and then providing individualised and tailored education and support interventions that reflect the unique abilities of that person.

One approach to risk delineation is the Heart-FaST, which was developed by the parent study of this thesis (as noted in Chapter 1). It was developed specifically for use in CHF populations in order to assist clinicians in applying educational and support strategies based on self-care capacity (Cameron et al., 2014; Cameron, Ski, et al., 2013). As described in the Protocol Paper in Chapter 5, Heart-FaST comprises three key domains, including cognitive, emotional, and physical functioning; levels of functioning across each area is graded as low, medium or high. Psychometric validation of Heart-FaST is currently being conducted, but preliminary evidence supports its construct validity (Cameron et al., 2014). Thus, Heart-FaST has the potential to aid clinicians in tailoring disease management intervention. CHF care is based on nursing recommendations and guidelines that have been developed alongside this tool, and which are directed at applying individual educational and support strategies for each level of functioning (cognitive, emotional, physical). Using this approach to assessment and disease management, CHF samples that are high functioning in these three domains, such as the sample of this thesis, would require low priority and less intensive nursing care.

Another approach to individually assessing risk and need from disease management is the 'traffic-light' (Green, Amber, Red Delineation of Risk and Need; GARDIAN) system, which can also regulate the intensity of healthcare intervention (Carrington, Kok, Jansen, & Stewart, 2013). However, in comparison to Heart-FaST, the GARDIAN approach was not specifically developed for use in CHF populations. Rather, it has been applied in people at risk of CVD or patients who have established CVD. The GARDIAN approach to risk delineation and management includes: 1) assessment of clinical stability; 2) evaluation of treatment against gold-standard guidelines; and 3) holistic profile, which incorporates important behavioural, psychological, or social factors that can impact health. These might include factors such as self-care ability, cognitive function, mental health, social support, and patterns of treatment adherence.

Using the GARDIAN approach, an individual assessment of risk and need is conducted for interventions that are ranked in order of severity from 'green' to 'red' (Carrington et al., 2013). More specifically, a 'green' code is assigned to anyone who is: clinically stable, on gold-standard management, is meeting therapeutic targets, and presents with no individual issues that are likely to negatively impact on their health. For example, the CHF sample in this thesis had good performance on several important domains. Even when some decline was observed in general cognitive abilities and PM, specifically, the deficits were not severe enough to impact on self-care. Thus, the CHF sample in this thesis best reflects a group with low intervention needs. By comparison, an 'amber' code is assigned to anyone who is sub-optimally managed or has deficits in their holistic profile (i.e., isolation, cognitive impairment, incapable of self-care) without causing clinical instability. This level of need might apply to patients in the wider CHF population where cognitive impairment is more severe, compared to the sample in this thesis. Thus, in the broader population, PM deficits are also likely to be greater and would impact self-care abilities. Finally, a 'red' code is assigned to anyone who is clinically unstable and the focus is to address areas of concern to promote clinical stability. By providing tailored interventions, adherence to treatment recommendations and outcomes might be improved, when intervention is targeted to meet the specific needs of the individual.

Validation of the GARDIAN system is currently being conducted, with over 5000 individuals who have been assessed and profiled in a range of clinical settings (Carrington et al., 2013). Data about the success of using this approach of applying enhanced and tailored intervention is yet to be reported. However, preliminary findings from other chronic disease management studies (Chan et al., 2012; Stewart, Carrington, Swemmer, et al., 2012; Stewart, Carrington, Swemmer, Kurstjens, & Jennings, 2011) have provided promising findings about the use of structured treatment that is tailored to an individual's clinical stability and risk profile.

# **8.6 Concluding Comments and Future Directions**

The studies in the present thesis set out to examine PM and social cognition in patients with CHF who were not affected by dementia. The thesis did not specifically set out to assess people who were high functioning, but the studies have contributed to the current understanding of patients who have relatively high cognition and good health status, compared to existing CHF groups. This contribution is important because limited existing research has focused on samples with these features.

The key findings from this thesis showed that in a CHF sample, deficits in some, but not all cognitive domains were evident. The first aspect of the original research showed that the CHF sample had broad-based deficits in PM, but that the PM deficit was not severe enough to impact self-care behaviours. The second part of this thesis showed that social cognition was preserved. Even when some cognitive decline was evident, the CHF sample in this thesis had better cognitive performance, better health status, and good abilities to manage day-to-day tasks, compared to existing CHF studies. The original research in this thesis raises the possibility that samples that have high functioning in these important areas might not benefit from a "one size fits all" approach to disease management that is currently offered to the general CHF population. Currently, there is no research that has assessed the needs of the patient, and then selectively allocated disease management strategies to suit the need and risk profile of the individual. Thus, it remains unclear what component/s of CHF care are most effective and for whom.

Prospective studies are needed to assess potential differences in outcomes of individuals with heterogeneous cognitive and health profiles. Future studies are also needed to assess which component/s of programs are most beneficial to individuals whose cognitive impairment is mild and is not affecting their day-to-day management versus patients whose cognition is more compromised and thus substantially impacting self-care behaviours. Such research would make it possible to selectively allocate the most appropriate intervention to address an individual's specific risk and need, with potentially significant cost-benefits.

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# Appendices

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- A.5 Awards and Prizes

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#### Appendix A Research Portfolio

Appendix A.1 List of Manuscripts and Statement of Contributions

#### Published works by the candidate

- Habota, T., Cameron, J., McLennan, S. N., Ski, C., F., Thompson, D. R., & Rendell, P.
  G. (2013). Prospective memory and chronic heart failure. *BMC Cardiovascular Disorders*, *13*, 63–71. doi: 10.1186/1471-2261-13-63.
- Habota, T., McLennan, S. N., Cameron, J., Ski, C. F., Thompson, D. R., Henry, J. D., & Rendell, P. G. (2015). Prospective memory impairment in chronic heart failure. *Journal of International Neuropsychological Society*, 21, 183-192. doi: 10.1017/S1355617715000119
- Habota, T., McLennan, S. N., Cameron, J., Ski, C., F., Thompson, D. R., & Rendell, P. G. (2015). An investigation of emotion recognition and theory of mind in people with chronic heart failure. *PLoS ONE*, 10, e0141607.
  doi:10.1371/journal.pone.0141607

# **Protocol Paper**

Title: Prospective memory and chronic heart failure: Study protocol

Status: Published in BMC Cardiovascular Disorders

# **Statement of Contribution of Others:**

I acknowledge that my contribution to the above paper is 50%.

I acknowledge that my contribution to the above paper is 15%.

I acknowledge that my contribution to the above paper is 10%.

Juffun Dr Skye N McLennan

I acknowledge that my contribution to the above paper is 5%.

<u>\_\_\_\_</u>-

..... Association Professor Chantal F Ski

I acknowledge that my contribution to the above paper is 5%.

I acknowledge that my contribution to the above paper is 15%.

Rendell Professor Peter G Rendell .....

# Study 1

Title: Prospective memory impairment in chronic heart failure

Status: Published in Journal of the International Neuropsychological Society

# **Statement of Contribution of Others:**

I acknowledge that my contribution to the above paper is 50%.

I acknowledge that my contribution to the above paper is 10%.

...... Dr Skye N McLennan

I acknowledge that my contribution to the above paper is 5%.

I acknowledge that my contribution to the above paper is 5%.

Associate Professor Julie D Henry 

I acknowledge that my contribution to the above paper is 5%.

..... Association Professor Chantal F Ski

I acknowledge that my contribution to the above paper is 5%.

I acknowledge that my contribution to the above paper is 20%.

for the day

..... Professor Peter G Rendell

# Study 3

Title: An investigation into emotion recognition and theory of mind in people with chronic heart failure

Status: Published in PLoS ONE

# **Statement of Contribution of Others:**

I acknowledge that my contribution to the above paper is 55%.

I acknowledge that my contribution to the above paper is 10%.

..... Dr Skye N McLennan

I acknowledge that my contribution to the above paper is 5%.

JCameron Dr Jan Cameron

I acknowledge that my contribution to the above paper is 5%.

- Carple -

..... Association Professor Chantal F Ski

I acknowledge that my contribution to the above paper is 5%.

I acknowledge that my contribution to the above paper is 15%.

for the day

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Habota, T., Cameron, J., Ski, C. F., McLennan, S. N., Rendell, P. G., & Thompson, D.

R. Manuscript submitted for publication to the Journal of Cardiovascular

Nursing.

# Study 2

Title: An investigation into the relationship between prospective memory and chronic heart failure self-care

Status: Submitted for publication to the Journal of Cardiovascular Nursing

# **Statement of Contribution of Others:**

I acknowledge that my contribution to the above paper is 55%.

I acknowledge that my contribution to the above paper is 15%.

I acknowledge that my contribution to the above paper is 10%.

lafte-

..... Association Professor Chantal F Ski

I acknowledge that my contribution to the above paper is 10%.

...... Dr Skye N McLennan

I acknowledge that my contribution to the above paper is 5%.

for the day

..... Professor Peter G Rendell

I acknowledge that my contribution to the above paper is 10%.

#### Appendix A.2 List of Peer-reviewed Conference Presentations

# National and International conference abstracts presentations by the candidate relating to the Thesis

- Habota, T., McLennan, S. N., Cameron, J., Ski, C. F., Thompson, D. R., Rendell, P. G. (May 2014). *Prospective memory impairment in chronic heart failure patients*. Oral presentation at the 4th International Conference on Prospective Memory, Naples, Italy.
- Habota, T., Cameron, J., McLennan, S. N., Ski, C. F., Thompson, D. R., Rendell, P. G.
  (May 2014). *Prospective memory in chronic heart failure*. Oral presentation at the World Congress of Cardiology, Melbourne, Australia.
- Habota, T., Cameron, J., McLennan, S. N., Ski, C. F., Thompson, D. R., Rendell, P. G. (August 2014). *Prospective memory ability in patients with chronic heart failure*. Poster presentation at St Vincent's and St Andrew's Research Week, Melbourne, Australia.
- Habota, T., Cameron, J., McLennan, S. N., Ski, C. F., Thompson, D. R., Rendell, P. G.
  (October 2014). *An investigation of prospective remembering in people with chronic heart failure*. Poster presentation at the Victorian Association of Cardiac Rehabilitation, Melbourne, Australia.

# National and International conference abstract presentations by the candidate relevant to the thesis but not forming part of it

Cameron, J., Habota, T., Ski, C. F., McLennan, S. N., Rendell, P. G., Thompson, D. R. (2014). Factors associated with medication adherence among heart failure patients. Oral presentation at the Australian Cardiovascular Rehabilitation Association, Sydney, Australia.

Cameron. J., Habota, T., Ski, C. F., McLennan, S. N., Rendell, P. G., & Thompson, D.
R. (2014). Preliminary evaluation of the Heart Failure Screening Tool (Heart-FaST): Assessing for patient barriers to engagement in heart failure self-care (abstract). *Journal of Cardiac Failure, 20*, S11-S12. Oral presentation at the Heart Failure Society of America, Las Vegas, United States.

#### Appendix A.3 List of University Conference Presentations and Events

Presentations by the candidate relevant to chapters of the thesis

Australian Catholic University – School of Psychology Conference

Habota, T., McLennan, S. N., Cameron, J., & Rendell, P. G. (October 2012).
 Prospective memory and chronic heart failure: Study protocol investigating everyday memory deficits and its association to CHF self-care. Oral presentation at the 1<sup>st</sup> Inaugural School of Psychology Conference, Melbourne, Australia.

- Habota, T., McLennan, S. N., Cameron, J., & Rendell, P. G. (October 2013). *Chronic heart failure and prospective remembering: Preliminary findings*. Oral presentation at the 2<sup>nd</sup> School of Psychology Conference, Melbourne, Australia.
- Habota, T., McLennan, S. N., Cameron, J., & Rendell, P. G. (October 2014). An investigation of prospective memory in people with chronic heart failure. Oral presentation at the 3<sup>rd</sup> School of Psychology Conference, Melbourne, Australia.

Australian Catholic University – 3 Minute Thesis Competition

Habota, T. (July 2012). *Remembering to remember*. Melbourne, Australia.
Habota, T. (July 2013). *Remembering to remember*. Melbourne, Australia.
Habota, T. (July 2014). *Remembering to remember*. Melbourne, Australia.

# Appendix A.4 Additional Presentations and Events

# Invited guest speaker of research relevant to chapters of the thesis

# 2014

Ramsay Health care, Albert Road Clinic

Professorial (Psychiatrists') Unit Meeting

Melbourne, Australia

# 2015

St Vincent's Hospital

Cardiology and Cardiac Surgeon Meeting

Melbourne, Australia

# Appendix A.5 Awards and Prizes

### Prize awarded to candidate for research relevant to chapters of the thesis

# Winner

# 2014 Allied Health and Technologist's Affiliates Prize for best research

Prospective memory in chronic heart failure

Presented at the World Congress of Cardiology, Melbourne, Australia, May 2014

Prize awarded by the Cardiac Society of Australia and New Zealand

#### Winner

### **2014 Best Poster Award**

An investigation of prospective remembering in people with chronic heart failure Presented at the Victorian Association of Cardiac Rehabilitation State Conference, Melbourne, Australia, October 2014

#### Appendix B Ethics Approval

#### Appendix B.1Eastern Health – Original (CHF group)



5 Arnold Street, Box Hill Victoria 3128 Australia PO Box 94, Box Hill 3128 Tel (03) 9895 3281 Fax (03) 9895 4896 info@easternhealth.org.au ABN 68 223 819 017

www.easternhealth.org.au

Eastern Health Research and Ethics Committee Ph: 03 9895 3398

Fax: 03 9094 9610 Email: ethics@easternhealth.org.au

www.easternhealth.org.au/ethics

Website:

#### Human Research Ethics Committee - Scientific and Ethical Review

Ethical Approval – Granted

Commencement of Research at Eastern Health has been authorised

12 December 2011

Dr Jan Cameron Cardiovascular Research Centre VECCI Building Locked Bag 4115 Fitzroy MDC Vic 3065

Dear Dr Cameron

LR39/1112 Evaluation of an assessment tool to guide heart failure support

Principal Investigator: Dr Jan Cameron

Associate Investigators: A/Prof Chantal Ski, Prof David Thompson & Dr Gary Gordon

Other approved personnel (Eastern Health contacts): Mr Andrew Nixon, Ms Louise Roberts & Ms Janice Beale

Eastern Health sites: Box Hill, Maroondah & Angliss Hospitals

Thank you for the submission of the above project for review. Project has been reviewed by the Eastern Health Research and Ethics Committee. The project is considered of negligible risk in accordance with definitions given in the National Statement (2007). All queries have now been addressed and the project is accordingly **APPROVED**.

Documents submitted for review:

- Module 1 Application Form version 3 Revised sections 1.3, 1.8,1.9, 1.11, 1.14b and 1.20c
   Project Proposal version 1 dated May 2011
- Participant Information and Consent Form Version 2 dated 12 November 2011
- Clinical Data Form version 1 dated 14 June 2011
- Chronic Heart Failure Self-Care version 2 25 November 2011
- Self-efficacy to manage CHF version 1 dated 20 October 2011
- Self-Care of Heart Failure Index version dated 2010
- Your Health and Well-Being SF-12 version 2 dated 1994
- Medication Adherence version 1 dated 20 October 2011
- Curriculum Vitae Janette Cameron
- Curriculum Vitae Chantal Fraser Ski
- Curriculum Vitae David Robert Thompson
- Confidentiality Agreement Jan Cameron signed dated 11 November 2011
- Response to Ethics queries dated 28 November 2011
- Response to Ethics queries dated 09 December 2011

Angliss Hospital	Box Hill Hospital	Healesville & District	Maroondah Hospital	Peter James Centre	Wantima Health	Yarra Ranges Health	Yama Valley		
Tel (03) 9764 6111	Tel (03) 9895 3333	Hospital Tel (03) 5962 4300	Tel (03) 9871 3333	Tel (03) 9881 1888	Tel (03) 9955 1200	Tel (03) 9091 8888	Community Health Service Tel 1300 130 381		



5 Arnold Street, Box Hill Victoria 3128 Australia PO Box 94, Box Hill 3128 Tel (03) 9895 3281 Fax (03) 9895 4896 info@easternhealth.org.au ABN 68 223 819 017

www.easternhealth.org.au

**IMPORTANT**: A final progress report should be submitted on project completion. If the project continues beyond 12 months an annual progress report should be submitted in **December 2012**. Continuing approval is subject to the submission of satisfactory progress reports. Progress report template can be downloaded from our web-page: <a href="http://www.eastemhealth.org.au/research/ethics/progressreports.aspx">http://www.eastemhealth.org.au/research/ethics/progressreport.aspx</a>

Please quote our reference number LR39/1112 in all future correspondence.

Yours sincerely

Ms Lai Wan Reid Manager (Signed on behalf of the Eastern Health Research and Ethics Committee)

Copy to:

- Prof Chantal Ski
- Prof David Thompson
- Dr Gary Gordon
- Mr Andrew Nixon
- Ms Louise Roberts
- Ms Janice Beale

#### Confidentiality, Privacy & Research

Research data stored on personal computers, USBs and other portable electronic devices must not be identifiable. No patients' names or UR numbers must be stored on these devices.

Electronic storage devices must be password protected or encrypted.

The conduct of research must be compliant with the conditions of ethics approval and Eastern Health policies.

#### **Publications**

Whilst the Eastern Health Research and Ethics Committee is an independent committee, the committee and Eastern Health management encourage the publication of the results of research in a discipline appropriate manner. Publications provide evidence of the contribution that participants, researchers and funding sources make.

#### It is very important that the role of Eastern Health is acknowledged in publications.

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Angliss Hospital Tel (03) 9764 6111	Box Hill Hospital Tel (03) 9896 3333	Healesville & District Hospital Tel 1031 5962 4300	Maroondah Hospital Tel (03) 9871 3333	Peter James Centre Tel (03) 9881 1888	Wantima Health Tel (03) 9955 1200	Yarra Ranges Health Tel (03) 9091 8888	Yama Valley Community Health Service Tel 1300 130 381		

#### Appendix B.2Eastern Health – Modification (CHF group)



7 February 2012

Dr Jan Cameron Cardiovascular Research Centre VECCI Building Locked Bag 4115 Fitzroy MDC Vic 3065 5 Arnold Street, Box Hill Victoria 3128 Australia PO Box 94, Box Hill 3128 Tel (03) 9895 3281 Fax (03) 9895 4896 info@easternhealth.org.au ABN 68 223 819 017

www.easternhealth.org.au

Eastern Health Research and Ethics Committee Ph: 03 9885 3388 Fax: 03 9094 9610 Email: ethics@easternhealth.org.au Website: www.easternhealth.org.au/ethics

Dear Dr Cameron

LR39/1112 Evaluation of an assessment tool to guide heart failure support

Principal Investigator: Dr Jan Cameron

Associate Investigators: A/Prof Chantal Ski, Prof David Thompson & Dr Gary Gordon

<u>Other approved personnel</u> (Eastern Health contacts): Mr Andrew Nixon, Ms Louise Roberts & Ms Janice Beale

Eastern Health sites: Box Hill, Maroondah & Angliss Hospitals

The following documents have been reviewed and **approved** by the Sub-Committee at its meeting on 6 February 2012.

- Request for Approval of Amendment Form dated 05 January 2012
  - Change of Research Personnel Form Prof Peter Rendell, Kerry Rhodes & Ms Tina Habota
    - Declarations signed dated 05 January 2012
  - Curriculum Vitae Tina Hobota
  - Curriculum Vitae Peter Rendell
  - Curriculum Vitae Kerry Rhodes
  - Module One version 4
  - Participant Information and Consent Form version 3 dated 05 January 2012
  - Appendix 1 Cognitive Screen Tests dated 05 January 2012
    - Addenbroke's Cognitive Examination ACE-R version A dated May 2004
    - National Adult Reading Test (NART) version undated
    - Hospital Anxiety and Depression Scale (HADS) version dated 1983
    - Trail Marking Test version undated
    - Example of The Hayling Sentence Completion Test version undated
    - Example of Ekman's Picture of Facial Affect version undated
    - Example of Baron-Cohen's Eyes Test version undated
    - Auditory Verbal Learning Test (AVLT) version undated
    - Screen shot of Virtual Week (Computer Test) version undated

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Members of Eastern Health									
Argliss Hospital Tel (03) 9764 6111	Box Hill Hospital Tel (03) 9895 3333	Healesville & District Hospital Tel (03) 5962 4300	Marcondah Hospital Tel (03) 9671 3333	Peter James Centre Tel (03) 9881 1888	Wantima Health Tel (03) 9955 1200	Yarra Ranges Health Tel (03) 9091 8888	Yarra Valley Community Health Service Tel 1300 130 381		



5 Arnold Street, Box Hill Victoria 3128 Australia PO Box 94, Box Hill 3128 Tel (03) 9895 3281 Fax (03) 9895 4896 info@easternhealth.org.au ABN 68 223 819 017

www.easternhealth.org.au

- Judgment belief version undated
- Email from Dr Jan Cameron dated 10 January 2012

Confidentiality Agreement – Tina Hobota signed dated 03 January 2012.

The committee also commends the presentation of this submission.

**IMPORTANT**: A final progress report should be submitted on project completion. If the project continues beyond 12 months an annual progress report should be submitted in **December 2012**. Continuing approval is subject to the submission of satisfactory progress reports. Progress report template can be downloaded from our web-page: <a href="http://www.easternhealth.org.au/research/ethics/progressreports.aspx">http://www.easternhealth.org.au/research/ethics/progressreports.aspx</a>

Yours sincerely

Gavin Davies Administrative Assistant Eastern Health Research and Ethics

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	Members of Eastern Health									
Angliss Hospital Tel (03) 9764 6111	Box Hill Hospital Tel (03) 9895 3333	Healesville & District Heepital Tel (03) 5962 4300	Marcondah Hospital Tel (03) 9871 3333	Peter James Centre Tel (03) 9881 1888	Wantima Health Tel (03) 9955 1200	Yarra Ranges Health Tel (03) 9091 8888	Yarra Valley Community Health Service Tel 1300 130 381			

# Appendix B.3 ACU – Modification (Control group)

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Ms Kylie Pashle	у									
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#### Appendix C Participant Recruitment

# Appendix C.4 Eastern Health Information Letter and Consent (CHF group)





#### PATIENT PARTICIPANT INFORMATION AND CONSENT FORM

VERSION: 5

PROTOCOL NUMBER: LR39/1112

NAME OF PARTICIPANT:

UR NUMBER:

#### FULL PROJECT TITLE: Evaluation of an assessment tool to guide heart failure support NAME/S OF INVESTIGATOR/S:

Principal Researcher: Dr Jan Cameron, CVRC/ACU Melbourne

Associate Researchers: A/Prof Chantal Ski, Prof David Thompson, Dr Gary Gordon, Prof Peter Rendell, Ms Tina Habota, Ms Mollie Flood

#### 1. Introduction

You have been invited to take part in a research involving Chronic Heart Failure (CHF) patients. We have obtained your name from the ward-list at Eastern Health or from your heart failure nurse. The aim of the research is to evaluate a clinical screening tool that assesses patient self-care ability to guide the level of heart failure support required by each patient. The assessment tool will be used by the CHF nurses in guiding their level of involvement and educational strategies directed at promoting self-care in CHF patients. Three months into the study, we shall invite participants to complete an assessment of their mental processes (cognition) to determine if this aspect is related to the health outcomes to be measured.

This Participant Information and Consent Form provide details of the research project and explain what is involved to help you decide if you want to take part.

Please read this information carefully.

Participation in this research is voluntary. If you don't wish to take part, you don't have to.

If you decide you want to take part in the research project, you may be asked to sign the consent section. By signing it you are telling us that you:

- understand what you have read;
- consent to take part in the research project;
- consent to be involved in the procedures described;
- consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

#### 2. What is the purpose of this research project?

#### Background:

When living with a chronic health condition, self-care behaviours are considered an essential aspect of promoting and maintaining good health. Nonetheless, it has been identified that many individuals with CHF do not carry out effective patient self-care and this has significant individual, clinical, and economic consequences. To support patients and their families learn and adopt patient self-care skills and behaviours two key strategies are recommended: 1) provision of comprehensive patient education and 2) patient monitoring in the form of home visits or telephone follow-up. Despite this support, it remains difficult for many patients with CHF to develop sufficient knowledge and skills to adequately undertake patient self-care. Previous research by Dr Cameron has identified three factors essential for patients to learn CHF self-care skills and behaviours: physical, emotional and cognitive functioning. It has been recognised that patients with CHF often have subtle impairments in mental processing ability that are unrecognised by health professionals. These impairments do not impact on an individual's ability to care for themselves on a daily basis but can cause memory problems, such as following medication regimens. Ultimately, impairments in mental processing or cognitive functioning increase the risk for unfavourable health outcomes that can increase the risk of being readmitted to hospital.

This study will expand upon Dr. Cameron's previous findings by: 1) evaluating a CHF selfcare screening tool that will provide clinicians with a measure (low, medium, high) of self-care ability for each of the three factors and 2) further examining the relationship between mental processing (cognitive functioning) and patient self-care. The screening tool will also provide guidance for the level of nursing involvement and educational strategies to promote CHF patient self-care. The current research has been funded by a Nurse's Board of Victoria Legacy Limited grant.

#### Aims:

The aim of this study is to: 1) evaluate the clinical application of the CHF self-care assessment tool and 2) examine the relationship between cognitive functioning and health outcomes, including patient self-care. The research will be conducted at the Eastern Health sites that conduct a CHF management program (Box Hill, Maroondah and Angliss hospitals). Recruitment to the study will be conducted over a 16 month period. A research associate from Eastern Health's Cardiology Research Department will recruit approximately 240 patients from the three CHF management programs within Eastern HARP.

#### 3. What does participation in this research project involve? Procedures

A research associate will collect information about you from your medical records and in person. Data collected will include demographic characteristics, medications, current diagnosis, medical history, your use of mobile information technology (i-phone or similar) and how independently you perform activities such as shopping. At this time, you may also be asked to complete some questionnaires that assess; 1) your knowledge of CHF self-care skills, 2) medication adherence, 3) your quality of life, and 4) your confidence in managing this chronic condition. It is anticipated that this will take 30-40 minutes of your time.

Participants from all three groups will be asked to complete the self-care screening tool. However, only two out of the three CHF management programs will be randomly allocated to follow the nursing guidelines recommended on the self-care screening tool. Accordingly, you may or may not be in the CHF management program allocated to implement changes to the nursing care you would normally receive. You will not be able to choose your group allocation. Those in the study group, who are not allocated to receive the new approach to developing a nursing care plan, will receive the standard care given by CHF nurses in this program. No individual's care will be compromised by being in one study group or another.

The self-care screening tool will be administered by the CHF nurse or research associate, during their visit with you and will take about 10 minutes of your time to complete. If there are any questions that make you feel uncomfortable, you do not need to answer them. Information gathered from this assessment will be used in planning your follow-up care within the CHF management program over the following three months.

All participants will have a number of questionnaires posted to them at three and six months following recruitment into this study. The questionnaires will assess; 1) your knowledge of CHF self-care skills, 2) medication adherence, 3) your quality of life, 4) your confidence in managing this chronic condition and 5) unscheduled contacts with your doctors or hospital admissions. It is anticipated that completing these questionnaires will take 30-40 minutes of your time. A self-addressed reply paid envelope will be supplied so that you can return the questionnaires. In the event the questionnaires have not been received within a two week time-frame, the research associate will contact you to ask if you want to continue in the study. If you agree to continue in the study, the research associate will discuss an appropriate time in which to complete the questionnaires.

Participants may be invited to take part in an interview with the psychologist, Ms Habota (PhD student). If you agree, we will ask you and a person you nominate (i.e., family member or close friend) to complete a questionnaire telling us about your ability to remember to perform skills related to daily functioning. The nominee will not be informed of any of your responses, and you will not be informed of any of their responses. Additionally, we will ask you about your ability to remember to perform tasks specific to heart failure self-care; this information will be obtained through a discussion with the psychologist. It is anticipated that this interview will take approximately 60 minutes to complete. Participants may also be invited to undergo an assessment of their mental processing abilities at the three month time point. If you agree to this assessment it will be conducted at a mutually convenient location and time by the psychologist or Psychology Honours student, Ms Mollie Flood. The assessment will take 60-90 minutes to complete and will include a number of short tasks that assess cognitive and emotion processing abilities. These measures have been used successfully and without problems and undue stress in previous research. Some of the assessments conducted by Ms. Habota and Ms. Flood will need to be audio taped.

Data about any hospitalisations you encounter during the period of the study and for 6 months after will be sourced from a database belonging to the Victorian Department of Health. This data will be returned to the researcher in such a manner that personal identifying information has been removed. This is done to ensure the research conforms to the protection of your privacy and only information related to the study is sourced.

All information collected will be entered into an electronic database for the purposes of this study and possibly in future, related research directed at enhancing CHF self-care and improving health outcomes. Consent is being sought for storing information in an electronic database that may be used for any future, related research. Appropriate ethics approval will be obtained for any future, related research projects.

If you have particular cultural considerations you wish to have taken into consideration please inform the researcher of the study.

You will not be paid for your participation in this research.

#### 4. What are the possible benefits?

We cannot guarantee or promise that you will receive any direct benefits from this project; however possible benefits may include improvements in your understanding of patient self-care behaviours that are relevant to CHF. The screening tool may benefit nurse clinicians enabling them to establish the level of support and education you require in learn CHF self-care skills. The assessment of mental processing will assist in establishing whether or not memory problems are apparent in patients with CHF and if they exist, whether or not they predict health outcomes, including patient self-care. Information gathered from this study will be used to inform future studies directed at assisting heart failure patients in performing specific heart failure self-care behaviours.

#### 5. What are the possible risks?

There are no expected risks from participation in this research.

The only difference between groups is the use of the screening tool to guide the level of nursing involvement in assisting you to learn CHF self-care skills. Each group will receive nursing care that is considered standard within the Eastern HARP program. Therefore there is no benefit or disadvantage for being in one group or another.

If you become upset or distressed as a result of your participation in the research, the researcher will contact your heart failure nurse who can arrange counselling or other appropriate support for you. Any counselling or support will be provided by <u>staff who</u> are not members of the research team.

#### 6. Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and change your mind later, you are free to withdraw from the project at a later stage. If you decide to withdraw, please notify a member of the research team.

If you decide to withdraw from the project, the researchers would like to keep the personal and/or health information about you that has been collected. This is to help them make sure that the results of the research can be measured properly. If you do not want them to do this, you must tell them before you withdraw from the research project.

Your decision whether to take part or not, or to take part and then withdraw, will not affect your relationship with those treating you.

#### 7. How will I be informed of the final results of this research project?

The results of this work will be disseminated internally to Eastern Health's Research Network and to the wider health professional and research community via reports, articles and conference presentations. Only aggregate data will be presented, no information that identifies individuals will be produced. Upon written request, results of the completed study can be made available to you. Please address correspondence to Dr Jan Cameron, CXRC, Locked Bag 4115, <u>Fitzrox</u> MDC 2065.

#### 8. What will happen to information about me?

Any information obtained in connection with this research project that can identify you will be treated as confidential and securely stored. The information may be used in future, related research as described in Section 3 above. Your information will only be disclosed with your permission, except as required by law. The research team and those employed in the position of research associates for the purposes of the conduct of this research, are the only personnel who will have access to the information. The nature of the access will be in the form of data collection, data analyses and interpretation of findings.

All information will be stored either within the Cardiology Research Department or at the Cardiovascular Research Centre (CARC) in a locked cupboard in a security protected office which is accessed only by research team members. In any publication or presentation, information will be provided in such a way that you cannot be identified, except with your expressed permission.

As per Eastern Health research policy, all participant data will be kept for a minimum of 5 – 7 years from publication or completion of the project. As data may be used for future research all data will be kept indefinitely.

#### 9. Can I access research information kept about me?

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to access the information collected and stored by the researchers about you. Please contact one of the researchers named at the end of this document if you would like to access your information. In addition, in accordance with regulatory guidelines, once data collection has finished, identifying information will be removed and data stored in a databank.

You must be aware that the information collected about you may at some point not be able to be identified once the identifying information has been removed. Access to information about you after this point will not be possible.

#### 10. Is this research project approved?

The ethical aspects of this research project have been approved by the Human Research Ethics Committee of Eastern Health and the Australian Catholic University.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

#### 11. Who can I contact?

The person you may need to contact will depend on the nature of your query. Therefore, please not the following:

If you want further information concerning this project or if you have any problems which may be related to your involvement in the project (for example feeling distressed), you can contact the principal researcher Dr Jan Cameron on 9953 3698.

#### 12. Complaints

If you have any complaints about any aspect of the study or the way in which it is being conducted you may forward the complaint to the Chairperson of the Human Research Ethics Committee through the Eastern Health Research and Ethics Office Telephone: 9895 3398. You will need to state the name of the person who is noted above as principal investigator.

Participant Information & Consent Form (clean copy) – Version 5 06/04/2013 Page 5 of 6

#### 13. Consent

I have read, or have had this document read to me in a language that I understand, and I understand the purposes, procedures and risks of this research project as described within it.

 ${\rm I}$  have had an opportunity to ask questions and  ${\rm I}$  am satisfied with the answers  ${\rm I}$  have received.

I freely agree to participate in this research project as described, realising that I can withdraw my consent at any time without adverse consequences.

I agree that research data collected for the study may be published or may be provided to other researchers in a form that does not identify me in any way.

I understand that I will be given a signed copy of this document to keep.

Participant's name (printed) .....

Signature

Date

Declaration by researcher\*: I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Researcher's name (printed) .....

#### Signature

Date

Note: All parties signing the consent section must date their own signature.

Participant Information & Consent Form (clean copy) – Version 5 06/04/2013 Page 6 of 6

# Appendix C.5ACU Information Letter (Control group)





TITLE OF PROJECT: Everyday Cognition in Older Adulthood PRINCIPAL SUPERVISOR: Prof Peter Rendell CO-SUPERVISOR: Dr Skye McLennan STUDENT RESEARCHER: Tina Habota CO-INVESTIGATORS: Assoc Prof Julie Henry (University of Queensland), Prof Matthias Kliegel (University of Geneva), Dr Mareike Altgassen (Radboud University), & Prof Louise Phillips (Aberdeen University), Dr Jan Cameron (Australian Catholic University) COURSE: Master of Clinical Psychology / Doctor of Philosophy

#### INFORMATION LETTER TO PARTICIPANTS

Dear Participant,

You are invited to take part in a research project investigating prospective memory, which refers to remembering to do things in the future. This type of memory is important for everyday tasks such as keeping appointments and remembering to take medication or returning library books.

The project is part of ongoing research by Professor Peter Rendell (School of Psychology, Australian Catholic University), with <u>Assoc Prof.</u> Julie Henry, <u>Prof.</u> Matthias <u>Kliegel</u>, Dr <u>Mareike</u> <u>Altgassen</u>, and Prof Louise Phillips, funded by an Australian Research Council (ARC) discovery grant. This ongoing research is investigating prospective memory. This specific project is being conducted by Ms Tina Habota for her Doctor of Philosophy thesis at the Australian Catholic University, in collaboration with Dr Jan Cameron.

This project involves adults (55+ years) who have no history of neurological disorders, no history of Chronic Heart Failure, and who have not had recent treatment (past 3 months) for cardiovascular problems. Participants will be asked to complete an individual testing session of approximately 2-3 hours. The testing session will be at a mutually convenient time and place which can include the participant's own home. During the session, there will be a variety of tasks and opportunities for breaks. Participants will be reimbursed up to \$30 for their involvement in this study.

We will ask you to complete several short tasks, such as word solving puzzles and memory tests, in addition to a longer computerised task. Some of the shorter tasks require verbal responses which may be audio taped to ensure accuracy of scoring. Participants will be asked to complete one of two longer computer tasks. The first is a board game version of going through the day with decisions to make and things to remember to do. As you move around the board, you will be given options for daily activities, and you will be required to indicate your choice of one activity. In addition, you are given things to remember to do as you move around the board.

Australian Catholic University Limited, ABN 15 050 192 660 Melbourne Campus,115 Victoria Parade Pitroy Vic 3065, Australia Locked Bag 4115 Pitroy MCD VIC 3065 Australia CRICOS registered provider: 000046, 00112C, 00873F, 00885B





We are also interested in learning more about how you personally have been feeling lately, so we will ask you to complete a short measure that ask you to rate your mood and feelings over the last week. There will be a few background questions about age, gender, years of education, general health, and health related to cardiovascular disorders and risk. Finally, we will ask a few questions about your ability to perform daily self-care activities within the home (i.e., laundry, handling finances), and in outdoor environments (i.e., shopping, transportation).

Participation in this research project is voluntary. You are free to withdraw from the study at any stage without giving any reason. Confidentiality will be maintained during the study and in any report. All participants will be given a code and names will not be retained with the data. The students will be reporting the findings in a thesis and we plan to also report the findings at a conference and/or in a scientific journal. It is emphasized that individual participants will not be able to be identified in any report of the study, as only aggregate data will be reported.

Any questions regarding this project can be directed to the staff supervisor: Professor Peter Rendell in the School of Psychology, St. Patrick's Campus (Australian Catholic University, 115 Victoria Parade, Fitzroy 3065, phone 03 9953 3126).

The Human Research Ethics Committee at Australian Catholic University has approved this study. In the event that you have any complaint or concern about the way you have been treated during the study, or if you have any query that the Student Researcher and Staff Supervisor have not been able to satisfy, you may write to:

Chair, Human Research Ethics Committee C/o Research Services, Australian Catholic University, Locked Bag 4115, FITZROY, VIC. 3065 Tel: 03 9953 3157 Fax: 03 9953 3315

Any complaint will be treated in confidence and investigated fully and any participant lodging such a complaint will be informed of the outcome.

If you are willing to participate please sign the attached informed consent forms. You should sign both copies of the consent form and keep one copy for your records and return the other copy to the staff supervisor. Your support for the research project will be most appreciated.

Yours Sincerely

Principal Supervisor	Co-Supervisor		Student Researcher			
Prof. Peter Rendell	Dr Skye McLer		Tina Habota			
Co Investigators: Assoc Prof Julie Henry Dr Jan Cameron	Prof Matthias Kliegel	Dr Mareike Altgasse	Q Prof Louise Phillips			

Professor Peter Rendell School of Psychology Tel: 03 9953 3126 Fax: 03 9953 3205 Email: pstgr.rendell@acu.edu.gu...Web: https://apps.acu.edu.gu/stattbl/rectory/?pstervendell

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# Appendix C.6 ACU Consent Form (Control group)





TITLE OF PROJECT: Everyday Cognition in Older Adulthood PRINCIPAL SUPERVISOR: Prof Peter Rendell CO-SUPERVISOR: Dr Skye McLennan STUDENT RESEARCHER: Tina Habota CO-INVESTIGATORS: Assoc Prof Julie Henry (University of Queensland), Prof Matthias Kliegel (University of Geneva), Dr Mateike Altgassen (Dresden University), & Prof Louise Phillips (Aberdeen University), Dr Jan Cameron (Australian Catholic University) COURSE: Master of Clinical Psychology / Doctor of Philosophy

#### INFORMED CONSENT FORM

Copy for Participant to Keep

I agree to participate in this activity, realising that I can withdraw at any time. If I am an ACU student, I understand that withdrawal will in no way affect my ACU studies. I agree that research data collected for the study may be published or provided to other researchers in a form that does not identify me in any way. I am over 18 years of age.

Name of participant		block letters)
---------------------	--	----------------

Signature: ..... Date: .....

Student Researcher: Tina Habota Signature

Date .....

Principal Supervisor: Prof. Peter Rendell
Signature
Date

Australian Catholic University Limited, ABN 15 050 192 660 Melbourne Campus, 115 Victoria Parade Fittroy Vic 3065, Australia Locked Bag 4115 Fittroy MCD VIC 3065 Australia CRICOS registered provider: 000046, 00112C, 00873F, 00885B

#### **Recruitment Poster (Control group)** Appendix C.7

#### PARTICIPANTS Would you like to be part of a WANTED memory? Core testing (1.5 hours) CONTACT Activities include: Ms Tina Habota Computerised board game

Psychologist Master of Clinical Psychology | PhD student Phone: <u>9953 3243</u> or Mob: <u>0411 487 074</u>

Professor Peter Rendell Primary Research Supervisor

Dr Skye McLennan Secondary Research Supervisor

This project has been g raw at any time.



# study examining everyday

#### The testing involves a single session!

- Additional testing (decide on the day if you would like to complete additional activities).
- Question-answer tasks
- Picture based activities

You will receive a small payment to compensate you for your time.

# ELIGIBILITY

- 55<sup>+</sup> years old
- Male and Female participants needed
- No history of Chronic Heart Failure
- No recent treatment for cardiovascular problems



Appendix D.1 Demographic and Clinical Questionnaire (CHF group)

1965263901
AUSTRALIAN CATHOLIC UNIVERSITY
Clinical and Demographics Details Collected
ScreeningDate: / / / EnrolmentNumber:
To fill out this form, use crosses where applicable. Do not use ticks.
Demographics
Q1. Gender Male Female
Q2. Age:
Q3. Date of Birth: / / / /
Q4. Country of birth:
Q5. Is English the 1st language? Yes No if no how many years speaking English yrs
Q6. Marital Single Married/Defacto Divorced/Separated Widowed
Social Situation
Q7. Do you currently live with anyone?
Q8. Do you have someone you can confide in?
Q9. How would you rate the quality of the support you receive? Poor Satisfactory Good Very good
Q10. Years of education yrs
Q11. Highest level of education achieved (please select one)         No Formal Schooling       Completed Primary School         Completed High School       University/Tertiary (Undergraduate)         University/Tertiary (Post-graduate)
Q12. Occupation
Q13. Before this cardiac event, what was your employment status?
Employed Full-time     Employed Part-Time     Employed Casually     Retired     On sickness Benefits     Unemployed     Home Duties     Student
••

Cardiac Related         Q14. Cardiac risk factors	
Alased cholesterol       Hypertension       Smoking       Diabetes         Perression       Family history       Obesity         O15. Diabetes Mellitus:       Never       type 1       type 2 det       type 2 OHA       type 2 Insulin         O16. Smoking history:       Current smoker       Recent (stopped between 1 month and 1 year encounter)       type 2 month       type 2 insulin         O17. On average, how often do you drink alcoholic beverages?       Never       Offer than 7 drinks per week       More than 7 drinks per week         O18. Previously history of depression and/or anxiety?       Yes       No         O19. Previous or current treatment for depression or anxiety?       Yes       No         Please specify	Cardiac Related
Q16. Smoking history:	Raised cholesterol Hypertension Smoking Diabetes
□ Current smoker       □ Recent (stopped between 1 month and 1 year encounter)         □ Former (Stopped more than 1 year before encounter)       □ Never smoked         Q17. On average, how often do you drink alcoholic beverages?       □         □ Never       □ of never alcoholic drinks per week       □ 2-7 drinks per week       □ More than 7 drinks per week         □ S or more drinks on occasion       Q18. Previously history of depression and/or anxiety?       □ Yes       □ No         Q19. Previous or current treatment for depression or anxiety?       □ Yes       □ No         Please specify       □       □       □         Q20. Admission Diagnosis:	Q15. Diabetes Mellitus: Never type 1 type 2 diet type 2 OHA type 2 Insulin
□       Former (Stopped more than 1 year before encounter)       Never smoked         Q17. On average, how often do you drink alcoholic beverages?	Q16. Smoking history:
Q17. On average, how often do you drink alcoholic beverages?	Current smoker Recent (stopped between 1 month and 1 year encounter)
Never               1 or fewer alcoholic drinks per week             2-7 drinks per week             3 or more drinks on occasion               More than 7 drinks per week          Q18. Previously history of depression and/or anxiety?       Ves       No         Q19. Previous or current treatment for depression or anxiety?       Ves       No         Please specify	Former (Stopped more than 1 year before encounter)
□ 5 or more drinks on occasion         Q18. Previously history of depression and/or anxiety?       □ Yes       □ No         Q19. Previous or current treatment for depression or anxiety?       □ Yes       □ No         Please specify       □       □	Q17. On average, how often do you drink alcoholic beverages?
Q19. Previous or current treatment for depression or anxiety?       Yes       No         Please specify	
Please specify         Q20. Admission Diagnosis:         Q21. Length of time living with heart failure         Date CHF first diagnosed (month and year if known):         Length of time with CHF:         Q22. Diagnosis for CHF >2month?         Q23. Heart failure type as noted in medical records         Q24. Heart failure aetiology as noted in medical records         Q25. Echocardiogram results (if available):         Q26. Date of Echocardiogram:         Q27. Ejection fraction:         Q28. Heart failure treatments (beyond medical therapy)         Surgical therapy (CABG, valve replacement)         Date:       /         Q28. Heart failure treatments (beyond medical therapy)         Burgical therapy (CABG, valve replacement)         Date:       /         Q29. Type of implanted cardiac rhythm device (please select all that apply)         Implantable cardio-defibrillator	Q18. Previously history of depression and/or anxiety?
Q21. Length of time living with heart failure         Date CHF first diagnosed (month and year if known):	
Date CHF first diagnosed (month and year if known):	-
Q23. Heart failure type as noted in medical records       Systolic       Diastolic       Mixed       Unspecified         Q24. Heart failure aetiology as noted in medical records       Ischeamic       Nonischemic       Idoiopathic       Other:         Q25. Echocardiogram results (if available):	Date CHF first diagnosed (month and year if known):
Q24. Heart failure aetiology as noted in medical records       Ischeamic       Nonischemic       Idoiopathic       Other:         Q25. Echocardiogram results (if available):	Q22. Diagnosis for CHF >2month?
Q25. Echocardiogram results (if available):	Q23. Heart failure type as noted in medical records
Q26. Date of Echocardiogram:      /      /         Q27. Ejection fraction:	Q24. Heart failure aetiology as noted in medical records Scheamic Nonischemic Idoiopathic Other:
Q27. Ejection fraction:         Q28. Heart failure treatments (beyond medical therapy)         Surgical therapy (CABG, valve replacement)       Date:         Percutaneous Coronary Intervention       Date:         L-VAD or other assistant device       Date:         Implanted Cardiac Rhythm Device       Date:         Other device or therapy       Date:         None       V         Q29. Type of implanted cardiac rhythm device (please select all that apply)         Implantable cardio-defibrillator	Q25. Echocardiogram results (if available):
Q28. Heart failure treatments (beyond medical therapy)         Surgical therapy (CABG, valve replacement)       Date:       /       /         Percutaneous Coronary Intervention       Date:       /       /       /         L-VAD or other assistant device       Date:       /       /       /       /         Implanted Cardiac Rhythm Device       Date:       /       /       /       /       /         Other device or therapy       Date:       /       /       /       /       /       /         Q29. Type of implanted cardiac rhythm device (please select all that apply)       _       _       _       _       _	Q26. Date of Echocardiogram:
Surgical therapy (CABG, valve replacement)       Date:       /       /         Percutaneous Coronary Intervention       Date:       /       /         L-VAD or other assistant device       Date:       /       /         Implanted Cardiac Rhythm Device       Date:       /       /         Other device or therapy       Date:       /       /         None       Vone       /       /         Q29. Type of implanted cardiac rhythm device (please select all that apply)       Bi-Ventricular pacemaker for HF	Q27. Ejection fraction:
Percutaneous Coronary Intervention       Date:       /       /         L-VAD or other assistant device       Date:       /       /         Implanted Cardiac Rhythm Device       Date:       /       /         Other device or therapy       Date:       /       /         None       Other device or therapy       Date:       /       /         Implanted cardiac rhythm device (please select all that apply)       Bi-Ventricular pacemaker for HF	Q28. Heart failure treatments (beyond medical therapy)
Implantable cardio-defibrillator Bi-Ventricular pacemaker for HF	Percutaneous Coronary Intervention     Date:     /     /       L-VAD or other assistant device     Date:     /     /       Implanted Cardiac Rhythm Device     Date:     /     /       Other device or therapy     Date:     /     /

2

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						_
30.	Charlson Comorbidity Questionnaire					
1.	Myocardial Infarction: One or more instances of definite or probable MI (enzyme changes):	No	Yes	score	1	
2.	Congestive Heart Failure: History of exertional or paroxysmal nocturnal dyspnea with symptomatic response to dig, diuretics or after load reducers:	No	Yes	score	1	
3.	Peripheral Vascular Disease: Current: intermittent claudication, gangrene, acute arterial insufficiency, or untreated thoracic or abdominal aneurysm (8cm or more) or history of arterial bypass:	No	Yes	score	1	
4.	Cerebrovascular Accident: CVA with minor or no residual or transient ischemic attack (TIA):	No	Yes	score	1	
5.	Chronic Obstructive Pulmonary Disease: Asthma, emphysema, chronic bronchitis, or chronic obstructive lung disease (dyspenic at rest or with activity)	No	Yes	score	1	
6.	Ulcer Disease: Peptic ulcer disease requiring treatment (including hx of bleed):	No	Yes	score	1	
7.	Diabetes requiring medication (oral or insulin), not treated by diet alone	No	Yes	score	1	
8.	Connective tissue disease: Systemic lupus erythematosus, polymyositis, mixed connective tissue disease, Polymyalgia rheumatica, or moderate to severe Rheumatoid Arthritis:	No	Yes	score	1	
9.	Alzheimer's Disease, or another form of dementia:	No	Yes	score	1	
10.	Chronic hepatitis or Cirrhosis without history of portal HTN or variceal bleeding	No	Yes	score	1	
11.	Hemiplegia: Hemiplegia or paraplegia as a result of CVA or other condition:	№	Yes	score	2	
12.	Diabetes with end-organ damage: retinopathy, neuropathy or nephropathy:	No	Yes	score	2	
13.	Moderate or severe renal disease (serum creatinine>3 mg%, with uremia, on dialysis, or history of transplant:	_ No	Yes	score	2	
14.	Leukemia or polycythemia vera	No	Yes	score	2	
15.	Lymphoma	No	Yes	score	2	
16.	Cancer, other than skin cancer, leukemia, or lymphoma (Solid Tumor) Without metastasis but first treated less than 5 years ago	No	Yes	score	2	
17.	Cirrhosis with history of portal HTN or variceal bleeding	No	Yes	score	3	
18.	AIDS	No	Yes	score	6	
19.	Cancer (Solid Tumour) with metastasis	No	Yes	score	6	

Q30.

Charlston Total Score Comorbidity CATEGORY (Score of 1-2=1; 3-4=3; 5 or more = 5) List all other co-morbidities not identified by the Charlson Co-morbid index: (please print)

Q31. NYHA classification: Q32. Observations Systolic BP \_\_\_\_\_ Diastolic BP \_\_\_\_\_ HR \_\_\_\_ BNP \_\_\_\_\_ Hb \_\_\_\_\_ Sodium level \_\_\_\_\_ Creatinine level \_
Q33. Medication Assessment Date

	Aspirin	Name and dose					
	Antiplatelet	Name and dose					
	Anti-coagulation	Name and dose					
	Nitrate 1	Name and dose					
	Nitrate 2	Name and dose					
	Calcium Antagonist	Name and dose					
	ACE-1	Name and dose					
	ARB2	Name and dose					
	Beta-blocker	Name and dose					
	Diuretic	Name and dose					
	Aldosterone Antagonist	Name and dose					
	Digoxin	Name and dose					
	Anti-arrthythmic	Name and dose					
	Antidepressant	Name and dose					
	Antianxiolytic	Name and dose					
	Hypnotics	Name and dose					
	Lipid lowering 1	Name and dose					
	Lipid lowering 2	Name and dose					
	Hypoglyceamic 1	Name and dose					
	Hypoglyceamic 2	Name and dose					
	Other medications (please	e print)					
		• •					
-							
_							
Q34. In	general, would you say you	ır health is: 🛛 🗌 I	Excellent Ve	ery good	Good	E Fair	Poor
Q35. Co	ompared to 1 year ago, how	would you rate your	general health i	now?			
	Much better than 1 year ago	Somewhat better the	an 1 year ago	About	the same as 1	year ago	
	Somewhat worse than 1 year ag	o Much worse than 1	year ago				

Thank you for your time

4.

Participant	: ID Number:					Date							
	Demographics Questionnaire												
1. Age:	years		Da	ite of birth:									
<b>2. Gender:</b>	1ale emale												
3. Is English your first language:													
4. Country	of birth:												
	<b>ship status:</b> Single Partnered		Defacto Married		Separat Widowe	ed/Divorce ed	d						
6. Occupat	ion:												
7. Occupat	ion prior to retireme	nt (if	retired):										
8. Total ye	ars of education (equ	iivale	ent years of	full-time stu	dy):								
(a) Second	ary school (year leve	l con	pleted):										
(b) Post-se	condary education (r	numt	per of years)	:									
9. How wo	uld you describe you	r sta	te of <u>health</u>	:									
a. Today	<b>/?</b> excellent		very good		good		not very good		poor				
	the last month? excellent		very good		good		not very good		poor				
10. Do you	suffer from any of the Hypertension or cur Diabetes Mellitus (Tr Current smoker Previous smoker Obesity	rent	antihyperter										

### Appendix D.2Demographic Questionnaire (Control group)

□ High cholesterol or current cholesterol lowering medication

11. Do yo	u suffer from a	ny of the below	cardiovascula	ar disease, (tick i	if yes):		
	Chronic Hear						
	Ischaemic He	art Disease (incl	uding angina d	or heart attack)			
	Peripheral Va	scular Disease					
	Atrial Fibrillat	ion or Irregular	Heartbeat				
	Prior stroke						
	Prior transier	it ischaemic atta	ick (TIA or min	ii-stroke)			
12. Have	you received ar	ny treatments fo	or cardiovascu	ılar problems in	the past 3 n	nonths? If yes, o	lescribe below:
	No						
	Yes, described	below:					
13. Are yo	no any curre	nt medications?	r if yes, please	e list delow:			
	Yes, describe	helow:					
	res, describe	DEIOW.					
Me	edication name						
<u></u>							
14. Do yo	=	iculties with yoι	ur <u>vision</u> ? If ye	es, please descril	be:		
	No						
	Yes						
15 De	u have are diff		ur hoorin -2 if	voc places da	riha		
15. Do yo	u have any diff No	iculties with you	ur <u>nearing</u> ? If '	yes, please desc	ribe:		
	185						
16. How <b>\</b>	would you desc	ribe how vou ha	ave been sleer	oing over the las	st few week	s?	
	excellent	-	y good	good		not very good	poor

# Appendix D.3.1 ACE-R (first page only)

ADDEN						TION - A					
Name : Date of birth : Hospital no. :				Tester's na Age at leav Occupation	ving full-time e n:	ducation:					
Addressograph Handedness:											
ORIENTATION											
> Ask: What is the	Day	Date	м	lonth	Year	Season	[Score 0-5]	N O			
> Ask: Which	Building	Floor	Т	own	State	Country	[Score 0-5]	АТІ			
								⊢ N			
REGISTRATIO	N							ш			
<ul> <li>Tell: 'I'm going to gi After subject repea the first trial (repea Register number of tria</li> </ul>	ts, say 'Try to re t 3 times if neces	member them b					[Score 0-3]	N&ORI			
ATTENTION &	CONCENT	RATION						0			
Ask the subject: ' c to take away anoth	ATTENTION & CONCENTRATION  Ask the subject: 'could you take 7 away from a 100? After the subject responds, ask him or her to take away another 7 to a total of 5 subtractions. If subject make a mistake, carry on and check the subsequent answer (i.e. 93, 84, 77, 70, 63 -score 4)  [Score 0-5] [Core										
Stop after five subtract > Ask: 'could you ple		.D for me? Ther	n as	sk him/her to	spell it backwa	rds:		АТТ			
MEMORY - Recal			•	••••••		******		-			
Ask: 'Which 3 word		o repeat and re	me	mber?'			[Score 0-3]	۲			
MEMORY - Antero Tell: 'I'm going to g doing that 3 times,	give you a name	and address an				e. We'll be	[Score 0-7]	œ			
Score only the third tria	al 1 <sup>st</sup> Trial	2 <sup>nd</sup> Tr	ial		: 3 <sup>ro</sup> Trial			0			
Linda Clark		;		••••••••••••••••••••••••••••••••••••••							
59 Meadow Street								×			
Milton											
M E M O R Y - Retrog	rime Minister						[Score 0 -4]	ш			
<ul> <li>Name of the Premi</li> <li>Name of the USA p</li> <li>Name of the USA p</li> </ul>	president							×			

#### Appendix D.3.2 Verbal Fluency

Verbal Fluency Task

You will be told a letter and you must tell me as many words as you can that begin with that letter, excluding proper nouns (e.g. people' names, countries, towns etc), numbers, and the same word with a different suffix (e.g. big, bigger, biggest). You can also include swear words. You have one minute for each letter. You should try not to repeat words. For example, if the letter is 'N', you could say 'Nasty', 'Natural' and 'Night'. Any Questions? Okay let's begin.

#### Please tell me as many words as you can that begin with the letter R

#### Please tell me as many words as you can that begin with the letter W

### Appendix D.3.3 NART

This test is protected by copyright and could not be presented. For a copy of this test see:

Nelson, H. E. (1982). National Adult Reading Test (NART): Test Manual. Windsor: NFER.

### Appendix D.3.4 TMT

This test is protected by copyright and could not be presented. For a copy of this test see:

Reitan, R. M. (1992). Trail Making Test: Manual for administration and scoring. Tucson,

AZ: Reitan Neuropsychology Laboratory.

#### Appendix D.3.5 Digit Span

This test is protected by copyright and could not be presented. For a copy of this test see:

Wechsler, D. (2008). Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV). San

Antonio: Pearson.

### Appendix D.3.6 Hayling Sentence Completion

This test is protected by copyright and could not be presented. For a copy of this test see:

Burgess, P. W., & Shallice, T. (1997). *The Hayling and Brixton Tests*. Thurston: Thames Valley Test Co. Ltd.

### Appendix D.3.7 RAVLT

This test is protected by copyright and could not be presented. For a copy of this test see:

Rey, A. (1958). L'examen clinique en psychologie. Oxford: Presses Universitaries De

France.

INSTRUMENTAL ACTIVITIES OF	DAILY LIVING SCALE (IADL)
M.P Lawton & E.M. Brody	
To fill out this form, use crosses where applicable. Do not use	ticks.
ScreeningDate: / / /	EnrolmentNumber:
A. Ability to use telephone     Operates telephone on own initiative:     looks up dials number, etc     Dials a few well-known numbers	B. Shopping 1 Takes care of all shopping needs independently 2 Shops independently for small purchases
<ul> <li>3 Answers telephone but does not dial</li> <li>4 Does not use telephone at all</li> </ul>	<ul> <li>3 Needs to be accompanied on any shopping trip</li> <li>4 Completely unable to shop</li> </ul>
<ul> <li>C. Food Preparation</li> <li>1 Plans, prepares and serves adequate meals independently</li> <li>2 Prepares adequate meals if supplied with ingredients</li> <li>3 Heats, serves and prepares meals or prepares meals or prepares meals or prepares meals but does not maintain adequate diet</li> <li>4 Needs to have meals prepared and served</li> </ul>	<ul> <li>D. Housekeeping</li> <li>1 Maintains house alone or with occasional assistant (e.g. "heavy work domestic help")</li> <li>2 Performs light daily tasks such as dishwashing, bed making</li> <li>3 Performs light daily tasks but cannot maintain acceptable level of cleanliness</li> <li>4 Needs help with all home maintenance tasks</li> <li>5 Does not participate in any housekeeping tasks</li> </ul>
E. Laundry  1  Does personal laundry completely  2  Launders small items; rinses stocking, etc  3  All laundry must be done by others	<ul> <li>F. Mode of Transportation <ol> <li>Travels independently on public transportation</li> <li>or drives own car</li> <li>Arranges own travel via taxi, but does not otherwise use public transportation</li> <li>Travels on public transportation when accompanied by another</li> <li>Travel limited to taxi or automobile with assistance of another</li> <li>Does not travel at all</li> </ol></li></ul>
G. Responsibility for own medications          1       Is responsible for taking medication in correct dosages at correct time         2       Takes responsibility if medication is prepared in advance in separate dosage         3       Is not capable of dispensing own medication	H. Ability to Handle Finances  I Manages financial matters independently (budgets, writes checks, pay rent, bills goes to bank, collects and keeps track of income  Q Manages day-to-day purchases, but needs help wit banking, major purchases etc  3 Incapable if handling money

Please read each item below and tick next to the reply which comes closest to how you have been feeling in the past week. Don't take too long over your replies, your immediate reaction will probably be more accurate than a long thought-out response.

Name:	Date:
I feel tense or 'wound up'	I feel as if I am slowed down
Most of the time	Nearly all the time
A lot of the time	Very often
From time to time, occasionally	Sometimes
Not at all	Not at all
I still enjoy the things I used to enjoy Definitely as much Not quite so much Only a little Hardly at all	I get a sort of frightened feeling like 'butterfli in the stomach Not at all Occasionally Quite often Very often
I get a sort of frightened feeling as if something awful is about to happen Very definitely and quite badly Yes, but not too badly A little, but it doesn't worry me Not at all	I have lost interest in my appearance Definitely I don't take as much care as I should I may not take quite as much care I take just as much care as ever
I can laugh and see the funny side of things	I feel restless as if I have to be on the move
As much as I always could	Very much indeed
Not quite so much now	Quite a lot
Definitely not so much now	Not very much
Not at all	Not at all
Worrying thoughts go through my mind	I look forward with enjoyment to things
A great deal of the time	As much as I ever did
A lot of the time	Rather less than I used to
Not too often	Definitely less than I used to
Very little	Hardly at all
I feel cheerful	I get sudden feelings of panic
Never	Very often indeed
Not often	Quite often
Sometimes	Not very often
Most of the time	Not at all
I can sit at ease and feel relaxed	I can enjoy a good book or radio or television
Definitely	programme
Usually	Offen
Not often	Sometimes
Not at all	Not offen

Very seldom

HADS

'butterflies'

### Appendix D.3.10 Ekman 60 Faces (example)

For each of the following slides please select the **emotion** that you feel best describes

what each person is feeling

HappinessSurpriseAnger

Fear

Disgust

Sadness

#### Appendix D.3.11 Mind in the Eyes (example)

For each set of eyes, choose which word **best describes** what the person in the picture is **thinking or feeling**. You may feel that more than one word is applicable but please choose just one word, the word which you consider to be most suitable. Before making your choice, make sure that you have read all 4 words. You should try to do the task as quickly as possible but you will not be timed. If you don't know what a word means you can look it up in the definition handout.

# jealous

# panicked



arrogant

hateful

# Appendix D.4.1 SCHFI

Dateco	ompleted:			Enrolm		nber:						
To fill (	SELF-CARE OF HEART FAILURE INDEX           To fill out this form, use crosses where applicable. Do not use ticks.											
Think	about how you have been feeling in the last	t month or sinc	e we les	at en ok	e ee vou	comple	ata tha	ee item				
	ION A:	cmonutor sinc	e we las	Never		Sometimes		quently		vays or		
Q1.	Weigh yourself?			rarely			_		dai	-		
Q2.	Check your ankles for swelling?					2	_	]3 ]3	_	_4 _4		
Q3.	Try to avoid getting sick (e.g., flu shot,	avoid ill peop	le)?			]2 ]2	_	 3		 74		
Q4.	Do some physical activity?					]2 ]2	_	 3	_	 74		
Q5.	Keep doctor or nurse appointments?					 2	_	 3	_	 ]4		
Q6.	Eat a low salt diet?					 2	_	 ]3	_	 4		
Q7.	Exercise for 30 minutes?					]2	_	 3	_	 74		
Q8.	Forget to take one of your medicines?					2	_	 3		 74		
Q9.	Ask for low salt items when eating out		hers?			2		3		 4		
Q10.	Use a system (pill box, reminders) to he remember your medicines?		1		2	C	3	٢	4			
SECTI	ON B:											
Many heart f	patients have symptoms due to their heart fai ailure.	ilure. Trouble b	reathing	and a	nkle swel	ing are	comm	ion syn	ptoms	s of		
Q11.	In the past month, have you had troubl	e breathing or	r ankle :	swellir	ng?	No No		Yes				
Q12.	If you had trouble breathing or ankle s	welling in the	past mo	onth								
		Have not had these	l did no recogni		Not quickly	Some quickl		Quick		Very quickly		
	How quickly did you recognise it as a symptom of heart failure?	□ N/A								4		
Listed	below are remedies that people with heart fai	ilure use. If you	i have tr	ouble I	breathing	orank	de swe	lling, h	ow like	ely are		
you to	try one of these remedies?		Not	t	Somew	hat L	ikely	Ve	ery			
Q13.	Reduce the salt in your diet		like		likelv		3		ely 4			
Q14.	Reduce your fluid intake			]1					4			
Q15.	Take an extra water pill			] 1	2		3		4			
Q16.	Call your doctor or nurse for guidance			] 1	2		3		4			
Q17.	Think of a remedy you tried the last tim	e you had tro	uble bre	eathing	g or ankl	e swel	lling.					
		I did not anything		Not sure	Some	what	Sure	•	Very sure			
	How sure were you that the remedy helped or did not help?			1		2		3		4		
SECTI	ON C:		Not	fident	Somewhat confident		Very confiden		xtremel			
Q18.	Keep yourself free of heart failure symp	ptoms?	- Con						4			
Q19.	Follow the treatment advice you have b	een given?							4			
Q20.	Evaluate the importance of your sympt	oms		] 1	2		3		4			
Q21.	Recognise changes in your health if the	ey occur?		]1	2		3		4			
Q22.	Do something that will relieve your sym	ptoms?		1	2		3		4			
Q23.	Evaluate how well a remedy works?	1.		] 1	2		3		4			

### Appendix D.4.2 Medication Adherence Scale

	SELF-EFFICACY TO MANAGE HEART FAILURE										
Pleas	se indicate	e your lev	el of confid	dence from	1 'not con	nfident' to 1	0 'very co	nfidenť, or	the follo	wing 5 questions	
Q1.		nce to ta	ke action:	s to mana	ge your he	eart failure	e on a reg	ular basis			
	Not confident									Very Confident	
	1	2	3	4	5	6	7	8	9	10	
Q2.	Confide Not	nce to ju	dge when	changes	indicate a	need to v	isit your (	GP or Car	diologist		
	confident									Very Confident	
	1	2	3	4	5	6	7	8	9	10	
Q3.	Confide or Card		mplete ta	sks neede	ed to mana	age heart i	failure so	as to red	uce the r	leed to see your	GP
	Not confident									Very Confident	
	1	2	3	4	5	6	7	8	0	10	
Q4.	Confide	nce to re	duce the	emotional	distress of	of heat fail	ure so it o	loes not a	affect eve	eryday life	
	Not confident									Very Confident	
	1	2	3	4	5	6	7	8	9	<b>10</b>	
Q5.	Confide everyda		o things, o	ther than	taking me	edications	, to reduc	e the imp	act of he	art failure on	
	Not confident									Very	
		□2	□3	□4	□5	6		□8	0	Confident	
Sect	ion A: Ge	neral inf	ormation								
Q1.				for pills d	o you hav	e?		Numbe	rofprescr	iptions	
Q2.	How m	any pills	do you ne	eed to tak	e each dag	y?		 	umber of p	oills	
Q3.		-	s each da le schedu	y do you i les?	need to ta	ke pills		4	nes a day		
Q4.	How de	o you kee	p track of	f pill times	?						
	No spe	cific method	ls, just look a	t each medio	ation bottle						
	Use a v	written sche	dule								
	Use an	alarm clock									
	Use a p	oill box please spec	ify)								
Q5.	Do you	have any	ybody wh	o helps m	ake your	medicatio	n schedu	le?			
	<b>No</b> [	My famil	y members h	elp me organ	nise the sche	dule 🗌 Nur	ses help me	organise the	schedule		
	Pharma	acist helps r	ne organise t	the schedule	Other						-
Q6.	Is there	e any pill	that you o	lo not like	to take?						-
	Why	/									
Q7.	Which	pill is it tl	hat you co	ommonly	don't take	or skip?_					
	Why	/									

2.

5060053616

#### Section B: Knowledge

For each of the statements below, indicate how much you agree with the statement by crossing the appropriate number.												
	Stron; disagi										Strongly agree	
In general I believe it is important to take all of the pills my doctor prescribes	0 []	<b>□</b> 1	2	3	4	5	6	7	8	0	10	
In general I believe it is important to take all of the pills on time	0 []	<b>1</b>	2	3	4	5	6	7	8	9	10	
I believe that it is OK to skip my pills when I am feeling better	0 []	1	2	3	4	5	6	7	8	0	10	
I understand why I need to take pills prescribed for me	0	1	2	3	4	5	6	7	8	0	10	
I know all the names of pills that I take everyday		1	2	3	4	5	6	7	8	0	10	
I know the dose of each pill that I take every day	0	1	2	3	4	5	6	7	8	9	10	
I know the side effects of the pills that I take everyday, even if I do not have any side effects	0 []	<b>1</b>	2	3	4	5	6	7	8	0	10	
Section C: Barriers												
Q1. Do you ever skip taking some of your pills	? 🗆 N	lo	Ves									
If yes, how important is each of these causes of not tak 1 means not important cause, and 10 means the mo						kip you	r medio	ations,	cross (	) for ea	ach item.	
	Never skip	1. No impor	t rtant cau	ise							10. Very important cause	
Forgetting the time of medication		1	2	3	4	5	6	<b>7</b>	8	0	10	
Confusing the medication times		<u> </u>	2	3	4	5	6	7	8 🗌	0	10	
Not trusting the efficacy of medications in my disease	0	1	2	3	4	5	6	7	8	0	10	
Cost of medication	0	1	2	3	4	5	6	7	8	0	10	
Belief that I'll be fine even though I skip one dose of medication	0	1	2	3	4	5	6	7	8	0	10	
Belief that my symptoms are better	0	1	2	3	4	5	6	7	8	0	10	
Belief that my symptoms are the same even though I skip the medication	0	1	2	3	4	5	6	7	8	0	10	

Not carrying my medication when I am out	0	1	2	3	4	5	6	7	8	0	10
Amount of pills that I need to take a day	0	1	2	3	4	5	6	7	8	0	10
The frequency of my medication schedule	0	1	2	3	4	5	6	7	8	9	10
Having no support from my family or somebody for reminding me to take my medication	0 🗌	1	2	3	4	5	6	7	8 🗌	9	10
00 Publication Name											

Q2. Subjective Norm

Directions: For each of the statements below, indicate how much you agree with the statement by crossing the appropriate number using the following scale.

		Strongly	Disagree	Neutral	Agree	Strongly agree
My doctor thinks I should take all of my pills		1	2	3	4	5
My spouse or other family members think I should take all my pills		1	2	3	4	5
Generally, I want to do what my doctor thinks I should do		1	2	3	4	5
Generally, I want to do what my spouse or family members think I should do		ould do 1	2	3	4	5
Q3.	When you need to go out, how do you take your pills?					
	I usually take my pills in my purse or pill box when I go out	I usually skip pills				
	I usually take my pills earlier	I usually take my pills when I get home				

Q4. What do you do when you forget or skip the medication due to any reasons? Please specify the way you handle it.?

Q5. Do you have anybody who usually reminds you to take your medication? No Yes If yes, who reminds you? Spouse Children or other family member Friend Other