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UNIVERSITY OF THE
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JOHANNESBURG

"Toxic Thoughts" – Impact of Chronic Kidney Disease on cognitive functioning and psychological well-being

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A research project submitted in fulfilment of the requirements for the degree of Master of Arts in Psychology through the Faculty of Humanities, University of the Witwatersrand, Johannesburg

Declaration

I declare that this research project is my own, unaided work. It has not been submitted before for any other degree or examination at this or any other university

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Glen Ansell

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Chapter 1 - Introduction

There is an abundance of research on pathophysiological factors associated with End Stage Kidney Disease (ESKD) (Akman, Haberal, Sezer, & Micozkadioglu, 2004; Barsoum, 2006; Eddy, 2006). There is however less research that directly addresses the cognitive impacts associated with ESKD, due to reasons such as uremia or psychological disorders that are commonly found comorbid with the condition.

Issues of cognitive functioning, depression and anxiety are all areas that can have a profound impact on sufferers of the disease. These issues have the capacity to impact on quality of life and compliancy to treatment or medication. Research findings are inconclusive as to whether there is a significant difference in rates of depression pre and post kidney transplant (Brouhard et al., 2000; Gelb, Hill, & Thornton, 2008; Griva, Jayasena, Davenport, Harrison, & Newman, 2006). Further to this, albeit that there is some research to suggest that there is an improvement in cognitive functioning after kidney transplant, the numerous variables associated with a process such as renal transplant make much of the evidence inconclusive as to the source of such improvement. Although research associated with the issues mentioned above have received attention of the academics to some degree, many of the results have been inconsistent. It is the aim of this paper to contribute to the knowledge already gained, while helping gain valuable data that diminishes the inconsistent findings found to date.

Chronic Kidney Disease (CKD) is a progressive deterioration of kidney function characterised by multiple symptoms including increased need to urinate, itchy skin, muscle cramps, high blood pressure, erectile dysfunction, weight loss, poor appetite, shortness of breath, and blood or protein in the urine (Griva, Jayasena, Davenport, Harrison, & Newman, 2006). The disease has shown increasing prevalence in recent years, with particular concern growing, relative to the prevalence of the disease in the elderly (Madero & Sarnak, 2008). There has also been increased awareness of, and attention given to, chronic kidney disease globally (Adam, Robbins, Seliger, Gregory, & Dore, 2012; Coresh & Stevens, 2008; Eddy, 2006; Kasiske et al., 2005; Naicker, 2003;).

This increased awareness of the disease can be attributed to five factors. The first factor being the dramatic and growing increase of prevalence of the disease (Levey, et al., 2010). The second would be that the cost of treatment of patients, is a high and ever increasing cost

(Cukor, Jindal, Brown, & Kimmel, 2009; Eddy, 2006; Russ & Kaufman, 2005). The next factor pertains to issues surrounding that the overt disease merely shadows the covert disease challenges found in sufferers (Russ & Kaufman, 2005). A further factor is that there is evidence pointing towards the role chronic kidney disease plays in comorbid diseases. These include diseases such as cardiovascular disease, which with the importance placed on the disease in today's society, has further highlighted it's potential comorbidity with CKD (Hedayati & Finkelstein, 2012). The fifth and final factor is the recent technological advancements that have been made in improving the combatant and prevention of the overall progression of the disease in sufferers. The development of these technological advancements have also played a role in highlighting the importance of combatting such a disease (Pascazio et al., 2010).

The progression of CKD is measured in stages, as proposed by the K/DOQI Clinical Practice Guidelines for Managing Dyslipidemias in Chronic Kidney Disease (Kasiske et al., 2003). One of the criteria used to establish the stage that a CKD sufferer is in, is based on a combination of two properties. Firstly, the extent of the damage suffered by the kidney, which is evaluated against the albuminuria levels in a patient. Secondly, against the decreased ability of the kidney to function as an organ of filtration, quantified against the serum creatinine concentration in the blood stream (Coresh & Stevens, 2008). This is established by measuring a value known as the Glomerular Filtration Rate (GFR), an indicator of kidney function (Griva, Jayasena, Davenport, Harrison, & Newman, 2006). A GFR which remains consistently lower than 15 ml/min per 1.73m^2, is an indication that the patient is in End Stage Kidney Disease. At this stage, for the patient to successfully remove waste and fluid, there would be a need for an therapeutic intervention, be that transplant or dialysis (Griva, Jayasena, Davenport, Harrison, & Newman, 2006). The stages range from 1 to 5 with stage one being kidney damage with normal GFR, end stage CKD or stage 5, showing signs of kidney failure (Kasiske, et al., 2003). Although these measurements serve to document the degree of kidney dysfunction in a patient, the patients' circumstances concerning other comorbid diseases or circumstances of that patient are also carefully considered when establishing the stage of the disease in patients.

Chapter 2 - Literature Review

This section describes the condition of Kidney Disease coupled with that of the associated psychological impairments comorbid with the physiological occurrence of the disease.

2.1 Kidney Disease

2.1.1 Healthy Kidneys: The kidneys are two bean-shaped organs, both approximately the size of a fist. They are situated just below the rib cage, one on each side of the spinal column. The kidneys filter between 113 and 141 liters of blood per day to produce about 1 to 2 liters of urine. This is made up of various wastes the body needs to expel coupled with unwanted fluid (Department of Health and Human Services - USA, 2014).

The kidneys are an important component in the human body, as they ensure that the makeup of the blood is stable for optimal body functioning by maintaining the required levels of electrolytes, sodium, potassium and phosphates, while additionally producing hormones that play a critical role in blood pressure, making red blood cells and maintaining bone strength (Greger, 1996).

2.1.2 Unhealthy Kidneys: Chronic Kidney Disease (CKD) is a condition characterised by damage to both kidneys resulting in a long-term condition. This damage is usually irreversible and coupled with comorbid dysfunction in other areas of the body (NHS Quality Improvement Scotland , 2008). This damage has effects on the functions of the kidney causing various complications. Firstly, sufferers of the disease experience increased levels of potassium. They also experience increased levels of sodium and electrolytes. There is also excess retention of fluid, which effects issues such as increased swelling in their limbs, increased blood pressure, or excess fluid in their lungs known as pulmonary edema. Further to these complications sufferers have been known to develop pericarditis, which is an inflammation of the membrane surrounding the heart.

Bones also become weak and brittle, and more likely to break than would be the case in the absence of the disease. Red blood cell count can reduce, causing fatigue and weakness

(anemia), but should be noted that it can have severe adverse psychological effects in sufferers of this disease. Lastly, their immune system can become weakened making them more susceptible to various infectious diseases (National Center for Chronic Disease Prevention and Health Promotion, 2014).

2.1.3 Causes of Kidney Disease:

There are various elements that can contribute to the development of Chronic Kidney Disease. These include the likes of diabetes, prolonged periods of high blood pressure, glomerulonephritis, kidney problems that develop in the womb, inherited diseases (for example Polycystic kidney disease), autoimmune disease, and extended exposure to toxic substances (BMJ Group, 2015).

a) Diabetes

Nearly 45% of all CKD is attributed to the effects of diabetes (Weiner, 2007). Diabetic kidney disease may take many years to develop post the onset of diabetes. Due to the high levels of blood sugar caused by diabetes, the kidneys filter too much blood, causing strain on the filtration system. After a prolonged period of having to do this, the filtration system can leak, causing small amounts of protein in the urine called microalbuminuria, leading to CKD and eventually ESKD. Not all individuals with diabetes will develop CKD however, as genetics, blood pressure and blood sugar control can serve as a protective role against diseases comorbid with diabetes. (National Kidney and Urologic Diseases Information Clearinghouse, 2014)

b) High Blood Pressure

Nearly 20% of all CKD is attributed to hypertension or, as it is more commonly known, high blood pressure (Weiner, 2007). As time goes by, high blood pressure damages blood vessels throughout one's body, causing reduced blood flow to important organs like the kidneys (Morgado & Neves, 2012). This reduced blood flow in turn reduces the amount of waste and fluid removed from the body, while at the same time increasing blood pressure compounding the problem (National Kidney Foundation, 2010).

c) Glomerulonephritis

Glomerulonephritis is a group of diseases that cause inflammation and hence damage to the filtering units of the kidneys. This damage to the kidneys is attributed to issues with the body's immune system. The occurrence of Glomerulonephritis is considered to be the third most common cause for CKD (National Kidney Foundation, 2010).

d) Autoimmune Diseases causing CKD

Auto immune diseases arise when an over active immune system erroneously attacks healthy body tissue rather than protecting the body from disease and infection, so as to consider the body tissue or part, as a pathogen. The kidneys are often a candidate for such an attack, hence many autoimmune diseases such as Lupus often catalyse the onset of CKD post attack on the kidneys (Page, du Toit, & Page, 2012).

e) Toxic Substance Exposure causing CKD

Prolonged exposure to toxic substance may result in impaired kidney function. This may instigate further damage in a cyclical self-exacerbating fashion as the compromised kidney is less able to dispel these substances efficiently from the body (Page, du Toit, & Page, 2012).

Nephrotoxicity of drugs and chemicals is variable and is influenced by the following factors: the direct effects on a specific type of nephron cell; level of metabolic activity and specifically in particular sections of the nephron; the pharmacological effect of a certain drug on renal function; high intratubular concentrations of the drug potentially causing crystallisation and / or precipitation of certain types of drugs (De Broe, 1999).

f) Kidney Problems developed in Utero

During development stages within the mother's womb, malformations can occur, such as narrowing of the urinal tracts, which prevents normal excretion of urine, causing urine to flow back up the tracts, and into the kidney (National Kidney Foundation, 2010).

2.1.4 Sequela of Chronic Kidney Disease

There are numerous sequela associated with that of chronic kidney disease that should also be understood when establishing neuropsychological / psychological profiles of CKD, as these are often comorbid diseases that could be contributing factors to the neuropsychological / psychological profiles on patients. Some of the more common sequela of CKD are:

a) Cardiovascular disease

Much of the increased burden associated with CKD is often contributed by the increased prevalence of cardiovascular disease risk factors. This plays a role in increasing the stage of CKD for patients, having a direct positive correlation on each other in increasing the prevalence of both diseases in individuals. An example of one these interplays would be the effects of anemia on CKD patients, which may predispose individuals to left ventricular hypertrophy or cardiac remodeling, and therefore an increased stage of cardiovascular disease. According to one source (Weiner, 2007), far more patients suffering from CKD, die from cardiovascular disease rather than from renal failure.

b) Anemia

There are numerous effects that anemia can have on individuals suffering from CKD. Firstly, those with the condition experience reduced hemoglobin levels which have been found to have a strong negative correlation with overall quality of life. Secondly, reduced hematocrit levels have been found to have a negative correlation to neurocognitive functioning. Anemia is also a known non-traditional risk factor for the onset of cardiovascular disease causing further issues in a patient's life as discussed in the cardiovascular section above (Weiner, 2007).

2.2 Treatments for ESKD

2.2.1 Hemodialysis

One effective way of treating patients with ESKD, is through the use of dialysis (Brouhard et al., 2000; Karaminia et al., 2007; Kimmel, 2005; Russ & Kaufman, 2005; Dirks, 2006). There are two forms of dialysis available, hemodialysis and peritoneal dialysis (Dirks, 2006; Kasiske et al., 2003; Russ & Kaufman, 2005). The primary type of treatment of greatest importance in this study is that of hemodialysis.

Hemodialysis is the most common form of treatment, and the most accessible sample to collect data from. This study's specific cohort was that of participants that have undergone hemodialysis or are currently undergoing hemodialysis. Renal hemodialysis is a therapy introduced in the 1940's as a short term intermittent procedure for patients suffering from ESKD. Through this process, blood is cycled out of the patient's body and into a machine that removes waste such as urea and ammonium, as well as excess fluid, essentially acting as an artificial kidney (Russ & Kaufman, 2005).

With many countries suffering from limited medical resources, the ratio between ESKD sufferers and dialysis machines is significantly disproportionate. Driven by the limited availability of resources, controlling bodies have been forced to introduce inclusion criteria established health boards controlling the access to dialysis (Dirks, 2006; Levey et al., 2010; Naicker, 2003; Russ & Kaufman, 2005). In South Africa an exclusion rather than and inclusion principle applies. This policy incorporates stringent guidelines as to those exclusion criteria, due to the abovementioned lack of resources to facilitate renal dialysis in our government medical institutions. This disproportionate number of available machines to patients have in turn brought about many ethical considerations for health organisations looking to deliver dialysis to patients(Russ & Kaufman, 2005).

One of the exclusion criteria for such treatment is financial costs. This inevitably limits access of lower income sectors who cannot afford private healthcare (Dirks, 2006). South African policy contains the following exclusion criteria: Medical exclusion; Psychological exclusion; and Adherence exclusion (Department of Health - Republic of South Africa, 2009). Exclusion criteria make it challenging for many ESKD patients seeking treatment under public health.

Access to facilities is also often limited from a geographic perspective as can be seen in Table 2.1 below representing the available facilities in 2012, both private and public. Note : Provincial Acronyms represent Eastern Cape (EC), Free State (FS), Gauteng(GT), Kwa-Zulu Natal(KZ), Limpopo(LP), Mpumalanga(MP), North-West(NW), Northern Cape(NC) and the Western Cape(WC).

Table 2.1
Private and public healthcare facilities available for ESKD treatment as of 2012 adapted from (Davids, Marais, & Jacobs, 2012)

	EC	FS	GT	KZ	LP	MP	NW	NC	WC	ALL
Public	3	6	6	4	0	0	3	1	5	28
Private	12	9	50	43	6	6	7	4	26	163
Total	15	15	56	47	6	6	10	5	31	191

A further concern is the lack of resources from government embarking on the development of new facilities in our country as can be seen in Table 2.1. The private sector has consequently taken on the challenge to establish these centers. This still leaves financial means as a major exclusion criterion for those that cannot afford private healthcare. The disparity in facility growth over the last 18 years up until 2012, between government and private facilities is immense as can be seen by Table 2.2 below:

Table 2.2
Private and public healthcare facilities increase between 1994 and 2012 in South Africa adapted from (Davids, Marais, & Jacobs, 2012)

	1994	**2012**
Public Sector	26	5
Private Sector	28	163
Total	**54**	**168**

2.2.2 Renal Transplant

In cases where patients are in advanced or permanent kidney failure, another treatment method that can be implemented is that of renal transplant. This allows for a less invasive level of

treatment post-transplant, in comparison to that of hemodialysis. This is due to the required intervention post-transplant, only being immunosuppressant adherence and avoidance of potential pathogenic environments that could put the patients at risk (Olbrisch, Benedict, Ashe, & Levenson, 2002).

The initial kidney transplants were performed in the 1950's. Since then, major advancements in the science of renal transplant have been gained, including organ rejection prevention treatments, as well as side effect minimisation of immunosuppressants on patients having undergone such surgery (National Institute of Diabetes and Digestive and Kidney Diseases, 2006).

Although transplant is one of the most effective treatments for ESKD, access to donor organs are incredibly scarce on a global scale and this issue is heighted in context of South Africa. Over and above the issues around donor scarcity there are also a myriad of ethical considerations to take into account with regards to donor selection as well as patient selection due to the scarcity of the abovementioned organ donations (Department of Health - Republic of South Africa, 2009). We also have cultural and religious issues surrounding organ transplant to consider in South Africa.

Problems arising from the scarcity of deceased donor kidneys can be addressed via the living donor option. This has the advantage of increased success rates (Chilcot, Walter, Spencer, Maple, & Mamode, 2014) but does not come without its own ethical considerations. Ensuring that there is an appropriate balance between the benefits gained and potential harm associated with transplant for both donor and recipients of the utmost importance in conducting clinical judgment.

Although Living-Donor transplantation is considered to be a regrettable necessity in practice, it is due to the scarcity of deceased donor organs, as well as the increased success rate of living-donor transplantations, that have made this a favorable means of treatment (Castro, Soledad, Vigueras, & Thomas, 2012; Kälble et al., 2014). The physical and psychosocial well-being of these donors are of the utmost importance. It is recommended that the donor has their own team of psychological and nephrological evaluation teams, so as to advise on the process. It is imperative that the donor be given an unbiased psychological evaluation by a mental health professional. This is in the effort of understanding the donor's mental capacity to make

such a decision. The donor decision can be incredibly difficult, and is filled with psychological constructs of self and the relationship with that of the recipient of the organ. Even though the motivation behind donation is altruistic in nature, there still elements of concepts such as self-mutilation, potential fears concerning death or not being of full function post-surgery (Jordan et al., 2004; Kälble et al., 2014).

Deceased donor donation is naturally less fraught with psychological considerations for the donor compared with that of a living-donor, but still has many ethical considerations when considering recipient selection with the scarcity of donors in South Africa (Department of Health - Republic of South Africa, 2009).

2.3 Cognitive impact of CKD

Cognitive impairment can be directly related to poor kidney filtration, or can result from the treatment mechanisms for sufferers of CKD. Treatment for such kidney filtration challenges as experienced in CKD may take the form of either chronic dialysis or kidney transplant, the latter requiring the use of immunosuppressant medication (Adam, Robbins, Seliger, Gregory, & Dore, 2012; Brouhard et al., 2000; Fennell, Fennell, & Morris, 1984; Griva, Jayasena, Davenport, Harrison, & Newman, 2006; Lawryl & Cunningham, 1994; Madan, Agarwal, & Tandon, 2007; Madero & Sarnak, 2008; Weisberg & Strub, 1989)

In evaluating the impacts of the disease and the effects of the treatment on cognitive functioning, this section will evaluate the two above-mentioned types of CKD treatment individually and the cognitive effects identified within sufferers of the disease.

There is an abundance of research into cognitive deficits associated with CKD (Adam, Robbins, Seliger, Gregory, & Dore, 2012; Brouhard et al., 2000; Elias, Seliger, Narsipur, Dore, & Robbins, 2009). One study evaluating cognitive deficits in CKD sufferers, broke down the cognitive functioning areas into general cognitive functioning, verbal learning correlates, flexibility in mental functioning, visual attention correlates, and executive functioning, evaluating the state of those cognitive functions against sufferers of CKD (Elias, Seliger, Narsipur, Dore, & Robbins, 2009). Evidence suggests that neither the transplant nor the demographic factors affect the level of cognitive functioning in any of the abovementioned domains of cognitive functioning. Rather it was that individuals are in ESKD, which

influences lower cognitive functioning due to the physiological impacts on overall cognitive functioning.

The concept of kidney transplant negatively affecting cognitive functioning however contradicts much of the literature (Brouhard et al., 2000; Gelb, Hill, & Thornton, 2008; Griva, Jayasena, Davenport, Harrison, & Newman, 2006; Kasiske et al., 2003). The literature rather postulates that kidney transplant has a significant impact in improving cognitive functioning of individuals, should they have been suffering from CKD in its end stage form.

Research has also shown a progressive gradual decline in cognitive functioning due to CKD, pointing at two interesting observations (Adam, Robbins, Seliger, Gregory, & Dore, 2012; Elias, Seliger, Narsipur, Dore, & Robbins, 2009). The first observation being that the rate of cognitive decline increases the longer a patient undergoes dialysis (Madero & Sarnak, 2008). The second being that elevated dementia seemed prevalent in ESKD patients. The abovementioned study was longitudinal in nature and established that there is a temporal consideration when understanding the correlation between ESKD and cognitive functioning, being that the effects are long term and not short lived between dialysis sessions. To further establish some of the impacts dialysis could have on sufferers, it would be important to understand how dialysis works and what benefits are derived therefrom. This will be outlined in the subsequent section.

2.3.1 Cognitive impact specific to Hemodialysis Patients

Research has shown that is common to find cognitive impairment in hemodialysis patients. Cognitive dysfunction, in areas such as attention (Mendley et al., 2015; Williams, Owolabi, Ogunniyi, & Ezunu, 2013), memory impairment (Khatri et al., 2009), reduced perceptual-motor coordination, intellectual impairment (Brouhard et al., 2000; Elias, Seliger, Narsipur, Dore, & Robbins, 2009; Gelb, Hill, & Thornton, 2008) and overall mental alertness (Khatri et al., 2009), have been reported in much of the literature. Further to this, it has also been found that while cognitive dysfunction exists in ESKD patients, those that are on dialysis do perform better on tests of cognitive functioning than those that are not in any form of dialysis treatment program, but that cognitive dysfunction still prevails while on dialysis (Pliskjn, Yurk, Ho, & Umans, 1996; Williams, Owolabi, Ogunniyi, & Ezunu, 2013).

To illustrate the abovementioned cognitive findings, a study was done with 338 subjects all of whom at the time of study were undergoing hemodialysis. They were evaluated against 3 domains of cognition. Domains were identified as memory, executive function, and language. The results found that 36.1% of participants fell into the category of mild cognitive impairment, 37.3% of participants fell in the category of moderate cognitive impairment, while only 12.7% fell into the category of severe cognitive impairment (Murray et al., 2006). This finding represented 86.1% of all participants having some form of cognitive impairment.

In a further study done with 383 participants (Tamura et al., 2010) undergoing hemodialysis, the researchers did tests using a global cognitive function score as a measurement tool. A variety of neuropsychological tests were used. In the study they also looked at 5 specific explanatory variables for the cognitive impairment. These variables were urea clearance, nutritional markers, hemodynamic measures, anemia, and central nervous system (CNS)-active medications. The researchers found that 16% of the participants had global cognitive impairment, while a further 29% had impaired executive functioning. They also found that the utilization of H1-receptor antagonists as well as opioids had an association to impaired executive functioning in the participants. The only major dialysis factor that showed associations with executive impairment or overall global cognitive impairment was that of CNS-active medications, but that urea clearance, nutritional markers, hemodynamic measures, anemia, had no major impact on the participants' cognitive functioning (Tamura et al., 2010). The above findings lay groundwork for this paper as, as there seems to be conflicting findings with regards to cognitive decline as it pertains to patients suffering from CKD while undergoing hemodialysis treatment. Furthermore, the physiological interventions other than that of dialysis or transplant, don't seem to show significant differences in these patients when evaluating them against improved cognitive functioning in these patients. That said, the evidence does show a stronger bias towards the fact that cognitive functioning is a diminished capacity within these sufferers, but more so while on hemodialysis as opposed to having had renal transplant.

2.3.2 Cognitive impact specific to Renal Transplant patients

As mentioned earlier, another alternative and preferred treatment to dialysis for ESKD sufferers, is renal transplant. Traditionally studies of renal transplant have placed focus on the post-surgery mortality or complication rates seen in sufferers of ESKD (Baines & Jindal, 2002; De Broe, 1999; de Bruijne et al., 2003). While more recent studies have looked into the psychological and psychosocial (Siegel, Calsyn, & Cijddihee, 1987; Tavallaii, Einollahi, Farahani, & Namdari, 2009; Tossani & Fava, 2005) impact on ESKD sufferers and their caregivers, less emphasis has been placed on the cognitive impacts of ESKD of those undergoing dialysis or renal transplant. This is an incredibly important aspect to be given attention to when considering the role it plays on an individual's social and vocational ability, which have in studies, both been found to be independent predictors of mortality in ESKD sufferers (Griva et al., 2006).

These cognitive improvements were associated with kidney transplant in ESKD sufferers, and also specifically demonstrated improvement in areas of visual planning, abstract thinking, and psychomotor speed (Brouhard et al., 2000; Fennell, Fennell, & Morris, 1984; Gelb, Hill, & Thornton, 2008; Griva, Jayasena, Davenport, Harrison, & Newman, 2006; Harciarek, Biedunkiewicz, Lichodziejewska-Niemierko, Debska-Slizień, & Rutkowski, 2009; Madero & Sarnak, 2008; Mendley, 1999). It is the aim of this study, to ascertain whether the abovementioned significant improvements in cognitive functioning in areas of general cognitive functioning, verbal learning correlates, flexibility in mental functioning, visual attention correlates, and executive functioning post renal transplant can be found within a similar cohort within the South African context.

There are further studies contradicting some of these findings, that attribute cognitive decline in kidney transplant patients to the effects of immunosuppressants (Weisberg & Strub, 1989). Some of the common side effects of the immunosuppressants include symptoms such as insomnia, irritability, impaired concentration, mood changes, mania, psychosis, depression, and delirium/confusion (Butters et al., 2000; Cricco, Simonsick, & Foley, 2002). Although extraneous variables in context of cognitive functioning, they can have an impact on one's cognitive functioning indirectly. These symptoms would all considerably impact on overall cognitive abilities.

Immunosuppressants are an essential medication for kidney transplant patients that act as a defense against the body's defense mechanisms rejecting the kidney been transplanted into the patient. By suppressing immunity, immunosuppressants prevents the rejection of the graft by the patient. This medication is a necessity for the balance of the patient's life, and therefore should the findings be accurate, would have considerable implications on cognitive performance and decline for these patients into the future (Kasiske et al., 2003).

In a further study, utilising 28 medically-stable patients having undergone renal transplant surgery, a pre and post-test evaluation was done to evaluate cognitive functioning of these patients. These tests were coupled with the incremental effects that transplant may have had on their overall cognitive function. The tests performed on these participants evaluated concentration, psychomotor abilities, attention and memory functions. Transplant function was evaluated to be positive post-surgery on stable dosage of immunosuppressants in the participants, without any inclination of potential organ rejection at the time of participant testing. The results of this research showed a significant improvement in memory function in the participants, but no major improvement in attention, psychomotor functioning or concentration (Griva et al., 2006). The importance of research such as this, is that it shows the ability to reverse much of the negative effects on cognition that dialysis can have on patients suffering from ESKD, which in turn can have positive impacts on their overall life satisfaction and other potential psychological complications brought on by ESKD.

A further study evaluating pre and post cognitive function in renal transplant patients, evaluated other aspects of cognitive function, namely psychomotor speed, visual planning, retrieval of learned material and abstract thinking, while also testing for associated variables such as length of CKD, age and organ function post-surgery. While the study found similar positive improvement in cognitive function as with the supporting studies, the importance of this study illustrated the varying degrees of improvement. These improvements had a high association to the variables tested in the study such as length of CKD (which in turn would indicate length of dialysis) (Harciarek, Biedunkiewicz, Lichodziejewska-Niemierko, Debska-Ślizien, & Rutowski, 2009).

2.4 Chronic Kidney Disease and Psychological Impact

Psychological disorders are often comorbid with ESKD patients. Anxiety and depression specifically, is often found to be associated with ESKD. ESKD associated estimates of depression have been found to be prevalent in around 25-30% of all patients (Alavi & Sharifi, 2009). Understanding and the treatment of these psychological disorders in ESKD patients are of paramount importance when considering the ramifications these disorders have on the patients' physiological well-being. Psychological disorders have an influence on elements of treatment such as immunosuppressant compliance, or hemodialysis compliance. Issues such as noncompliance inevitably leads to increased mortality rates, and the root psychological causes should therefore be identified and addressed accordingly
(Kimmel, 2005).

With psychological disorder having been attributed as a leading cause of morbidity in ESKD sufferers, one of the specific disorders that has been given less focus is that of anxiety and its effects on morbidity. Few studies have been conducted in this area, but those that have tried to evaluate this association have found inconsistent results supporting such an association (Alavi & Sharifi, 2009; Baines & Jindal, 2002; Gelb, Hill, & Thornton, 2008; Griva, Jayasena, Davenport, Harrison, & Newman, 2006; Karaminia et al., 2007; Kimmel, 2005; Noohi et al., 2007; Pascazio et al., 2010).

From the existing research, it is unclear as to whether the levels of anxiety between hemodialysis patients and kidney transplant patients differ significantly. The natural thought process would have one believe that kidney dialysis patients would have lower levels of anxiety from not waiting on the donor selection list (Karaminia et al., 2007). It could also be argued that these patients have a different trigger to anxiety, being that of organ rejection (DiMartini, Crone, Fireman, & Dew, 2008). One of the key drivers behind this paper's analysis would be that psychological disorders have been found to be negatively correlated with cognitive functioning (Akman, Sezer, Micozkadioglu, & Haberal, 2004; Department of Health - Republic of South Africa, 2009; Noohi et al., 2007; Overbeck et al., 2005; Pascazio et al., 2010; Rocha, de Figueiredo, d'Avila, & Saitovitch, 2001; Tossani & Fava, 2005; Weisberg & Strub, 1989).

Another psychological disorder that has far reaching consequences for ESKD sufferers is that of depression. Negative emotional states of patients are considered to be a very distinctive determining quality of life after transplant, as well as compliance to treatment medication or procedures (Baines & Jindal, 2002). In previous research it has been demonstrated that patients on dialysis may present with moderate to severe depression, while their counterparts who have undergone kidney transplant suffer milder to no symptoms of depression (Rocha, de Figueiredo, d'Avila, & Saitovitch, 2001).These studies have further shown that the assessed level of depression in these patients is proportionate to longevity of the disease. One study found Becks Depression Index (BDI) scores of 14 and greater having died within two years and those having displayed scores of 10 and under having survived much longer (Rocha, de Figueiredo, d'Avila, & Saitovitch, 2001).

There are important cognitive associations known to be comorbid with such psychological disorders such as anxiety and depression. This could have a compounding effect on the fact that cognitive functioning is already compromised by the uremia earlier discussed (Tossani & Fava, 2005; Weisberg & Strub, 1989).

Much of the existing research has found a correlation between anxiety / depression and that of cognitive functioning levels. Further to these findings, it has been found that the areas most affected by these disorders are that of episodic memory and executive functioning (Adam, Robbins, Seliger, Gregory, & Dore, 2012; Elias, Seliger, Narsipur, Dore, & Robbins, 2009; Weisberg & Strub, 1989;).

The existing body of knowledge seems to be primarily focused on looking at the cognitive deficits created by ESKD, rather than the cognitive improvement created by kidney transplant, nor that of the correlates between cognitive functioning and the association between that and psychological disorder. Previous studies have found no significant correlates of cognitive functioning with other transplant dependent variables such as, lack of instrument sensitivity and also not having been done in SA where social support structures and living conditions may contribute to deficits in cognitive functioning.

2.4.1 Psychological impact specific to Hemodialysis Patients

It is important to note that other than the financial implications of dialysis, there are significant quality of life issues associated with the treatment, as the treatment can be lengthy and heavily impact on one's living conditions (Alavi & Sharifi, 2009; Kaltsouda et al., 2011; Odden & Shlipak, 2006). With hemodialysis, one typically undergoes treatment approximately three times per week for three to four hours at a time. This amount of time spent on dialysis and travelling to and fro from dialysis has the power to render this life threatening medical condition, rather than work or family, central to the sufferer's life (Kaltsouda et al., 2011; Ogutmen et al., 2006).

In one research study, it was found that emotional challenges faced by dialysis patients was approximately 50% of all participants (Siegel, Calsyn, & Cijddihee, 1987). This figure represents between three and five times the rate of psychological maladjustment of the general population. Further to this statistic, it was also found that ESKD patients where 100 times more likely to commit suicide, due to the elevated levels of depression experienced by them (Siegel, Calsyn, & Cijddihee, 1987).

Depression and anxiety are very common in ESKD patients undergoing hemodialysis, with research showing the prevalence of these comorbid disorders of depression and anxiety varying between 20% and 70% (depression), and 30% and 60% (anxiety) respectively. The implications underlying the association between anxiety and depression associated with ESKD patients on dialysis include factors such as adherence to treatment, its overall efficacy as well as various other effects it has on patients undergoing the treatment (Bossola, Ciciarelli, Conte, Luciani, & Tazza, 2010).

Besides the physiological impact of dialysis on patients, there is also the psychosocial aspects that play an important role on the patients well-being, considering the incredible amounts of time absorbed by the process of dialysis. These include times that might have been spent on their vocation or socialising, which they can no longer partake in due to the time pressures added by dialysis.

2.4.1.1 Depression in Hemodialysis Patients

Depression has been associated as the most significant psychological challenges facing hemodialysis patients suffering for ESKD from the research studies done, while also having been associated with death rates of those patients. A challenge however in dissociating depression or uremia as a predictor in these cases, makes the true predictors of mortality in hemodialysis patients very difficult to assess (Kimmel, Weihs, & Peterson, 1993). It is difficult to effectively quantify the somatic effects of hemodialysis from that of the physiological effects that depression can have on patients undergoing therapy. This is by virtue of the effects that depression can have on aspects such as: therapy compliance; nutrition, immunological functions; which all in turn play a role in the effectiveness of the treatment. Further compounding the problem is that depression could even play a direct role in influencing mortality as an independent variable. While few studies having been done on the positive effects treating depression in hemodialysis patients could have, it would be reasonable to believe that treatment of such disorders could yield favorable results in these patients with regards to mortality (Kimmel, 2005).

In 2002, a study was done on 5256 participants from both the United States and Europe, evaluating mortality and hospitalisation, against depression in hemodialysis patients. The study found a high correlation between the two variables (mortality / hospitalization) and depression in patients undergoing hemodialysis treatment (Lopes et al., 2002).

In a similar study to the one above, where similar results were found, the researchers found the following model in Figure 1. to hold true as to the influencing factors of depression on hemodialysis patients, illustrating further the complexities around identifying independent variables associated with depression in these patients (Kimmel, Weihs, & Peterson, 1993).

Influencing factors of depression on hemodialysis patients adapted from End-Stage Renal Disease Patients Treated with Hemodialysis (Kimmel, P, 2005, 91)

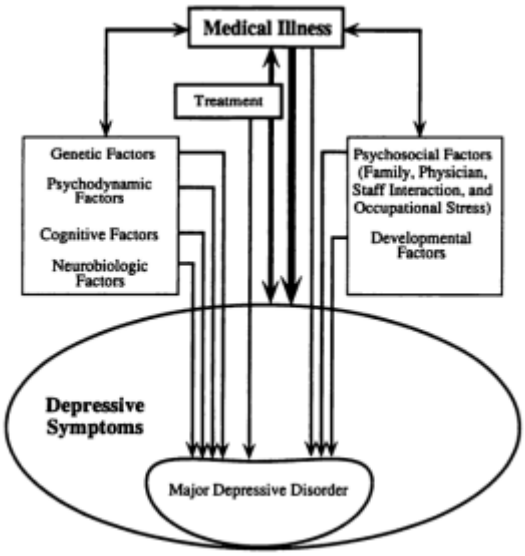


Figure 2.1

2.4.1.2 Anxiety in Hemodialysis Patients

Anxiety and anxiety somatic symptoms have been associated with renal failure and patients undergoing dialysis. The entire treatment of dialysis and process thereof, can cause extreme anxiety due to the many complications associated to dialysis (De Sousa, 2008). Often in patients with End-Stage Kidney Disease, the symptoms of anxiety are perceived to represent symptoms of depression instead, and have for this reason not had that much attention in research in this domain (Cukor et al., 2008).

One of the major causes of anxiety in patients undergoing hemodialysis is due to a lack of social and professional activities, stemming from the amounts of time spent on hemodialysis and ancillary effects of having to undergo the treatment, such as fatigue. This found patients having lower levels of self-esteem and a poor image of themselves while in turn decreasing social support, naturally lending itself to higher levels of anxiety in sufferers of the disease (Bayat et al., 2012). Issues such as these should be taken very seriously by caregivers and medical practitioners alike, as they can have significant knock on effect on patients undergoing hemodialysis.

2.4.2 Psychological impact specific to Renal Transplant patients

Psychological health issues post-transplant has been identified since the earliest transplants conducted on human beings. When observations of post-transplant psychological distress and affective disorders arising in patients pre-transplant began to bring into question what was considered to be positive outcomes of renal transplant in physiological terms (Olbrisch, Benedict, Ashe, & Levenson, 2002). Issues of psychological distress in renal transplant patients is one of critical concern, as it has been shown that psychological distress has direct correlations with that of drug adherence, which in turn is essential in the success of kidney graft procedures (Penkowera et al., 2003).

2.4.2.1 Depression in Renal Transplant Patients

Depression is a major factor in ESKD patients. Although renal transplant offers significant advantages to sufferers of ESKD over those undergoing dialysis, depression is still a factor in over 25% of patients having undergone a renal transplant. Significant correlations between depression in patients having undergone renal transplant surgery include: inflammation; affective illness; kidney function status; malnutrition; income; and marital status. It is an important psychological construct to deal with in these patients if one is to ensure positive outcomes of the overall treatment and holistic improvements of physiological and psychological well-being in these patients (Chilcot, Walter, Spencer, Maple, & Mamode, 2014).

Depression is one of the key correlates of noncompliance. In one study it was found that the relationship between depression and noncompliance of treatment, was very significant with an odds ratio of 3.03 (95% confidence interval, 1.96-4.89). This effectively tells us that the odds are 3 times larger that patients who are suffering from depression, will be more likely to be non-compliant on their medical treatment (DiMatteo, Lepper, & Croghan, 2000).

Added to these findings, a study on 58 adult renal transplant patients, measured elements relating to health beliefs, depression and functional status using questionnaires. This study however found that the reduced belief in the medication's (immunosuppressants) efficacy in treatment, was a strong factor associated with non-compliance in medication taking in those patients. Although depression was common in post-transplant patients, there was no significant

correlation found between depression and that of medical adherence to the required medication (Butler, et al. 2004).

With reference to the two studies discussed, the current research seems to point to distinct elevated levels of depression in renal transplant patients but that it is still inconclusive as to the validity that depression is a major contributing factor to non-compliance on required medication within these patients. What is however evident from the existing research, is that reduced depression is a strong correlate to that of overall transplant outcome and survival rates of patients (Akman, Ozdemir, Sezer, Micozkadioglu, & Haberal, 2004).

2.4.2.2 Anxiety in Renal Transplant Patients

A further well documented and researched psychological maladaptive correlate of ESKD, and in this section specifically post renal transplant surgery, is that of anxiety. One study even suggests that the prevalence of abnormal levels of anxiety exists in more than 50% of renal transplant patients, post-surgery (Noohi et al., 2007). There is however much debate around whether hemodialysis patients, versus renal transplant patients have equal or differential amounts of anxiety (Karaminia et al., 2007).

In a study by Pascazio et al. (2010) 42 renal transplant patients and 42 control subjects were assessed for various psychological symptoms including that of anxiety. The outcome of the study showed that there were no significant differences in levels of anxiety between the experimental or control group, questioning whether transplant does increase/reduce anxiety relative to patients undergoing hemodialysis (Pascazio et al., 2010).

The above study is in conflict with much of the existing bodies of research, whereby anxiety levels in renal transplant patients are still higher than normal, but the reasons behind that anxiety are naturally varied depending on the treatment path taken by those patients. There were however other factors found to be contributors to the level of anxiety experienced by post renal transplant patients, with income level being a significant one (Tavallaii, Einollahi, Farahani, & Namdari, 2009).

2.4.2.3 Quality of Life in Renal Transplant Patients

One of the most critical indicators of psychological well-being in renal transplant patients, is that of perceived quality of life. Quality of life (QoL) has been shown to have anxiety and depression as correlates of perceived QoL levels (Pascazio et al., 2010). Most studies have shown that there is an improved subjective view of quality of life in ESKD patients after having undergone renal transplant surgery. In one study, the perceived quality of life in 76 renal transplant patients was compared to that of 65 non transplant ESKD sufferers. The groups were required to answer questions pertaining to their: socio-demographic information; personality; employment history; assessment of anxiety and depression; quality of life; and questions on the ESKD symptom checklist. The results of this study found that there were significantly higher degrees of quality of life in patients that had undergone renal transplant in contrast to those ESKD sufferers that were still undergoing other forms of treatment such as dialysis. The following specific results were found: Physical functioning ($P <= 0.01$); General Health Perceptions ($P<= 0.01$); Social Functioning ($P <= 0.01$); Physical Summary ($P <= 0.001$) (Overbeck, et al., Changes in Quality of Life After Renal Transplantation, 2005).

In a further study conducted comparing renal transplant patients and ESKD dialysis patients, less favorable results were found in the post-transplant patients than that of the dialysis treatment patients. Psychological measures were assessed in 59 patients treated for ESKD. Although patients having been treated with renal transplantation showed more evidence of physical and vocational rehabilitation than that of their dialysis counterparts, measures of perceived quality of life showed very little difference between the two groups. What was however noticed was the reduced perceived quality of life in patients having undergone renal transplant, but where the graft procedure failed (Johnson, McCauley, & Copley, 1982).

2.5 Conclusion

There seems to be little research focusing on the cognitive effects hemodialysis has on patients, in contrast to that of renal transplant. Such research could shed light on the effects renal transplant can have on cognitive functioning in ESKD sufferers, but also the potential role cognitive decline plays in patients' psychological well-being, while also having an influence indirectly on depression levels in these patients compounding these issues further.

Further to the issues surrounding cognitive decline in ESKD sufferers, are the psychosocial and psychological effects of ESKD, namely depression, anxiety and quality of life of which depression specifically has shown associations with that of mortality rates in sufferers of the disease. Understanding these psychological facets of the disease and its treatment better, would be very beneficial in treating the disease not only from a somatic perspective but also from a psychological perspective. This could potentially reduce some of the associated outcomes such as mortality rates in the disease, compliance of treatment, as well as overall education to patients, easing some of the issues surrounding the evident lack of knowledge of the psychological impacts of the disease on patients.

There is also a serious lack of knowledge of the abovementioned issues in context of South Africa, and our understanding of ESKD from a cognitive impairment and psychological perspective. Considering South Africa's socioeconomic variables, unique dynamics of our private and public healthcare system, and overall cultural nuances, understanding some of the psychological and cognitive correlates of ESKD can be beneficial in both understanding the non-somatic impacts of the disease further. This could potentially provide a platform to further research that might support therapeutic interventions supporting improved outcomes and reduced mortality rates in sufferers of ESKD. This research therefore intends to contribute to the understanding of prevalence in cognitive decline / improvement in ESKD sufferers, the prevalence in depression in ESKD sufferers depending on treatment type, the prevalence in anxiety in ESKD sufferers depending on treatment type and lastly the differential in cognitive functioning between patients who have undergone kidney transplant and their level of functioning before transplant.

2.6 Research Questions

Based on the above discussion of the literature relevant to the present study, the four questions guiding the study are as follows:

1. Is there a significant difference in cognitive functioning in chronic kidney disease patients post-transplant, versus chronic kidney patients not having undergone transplant surgery?

2. Is there a significant difference in anxiety levels between chronic kidney disease patients on dialysis and those that have undergone kidney transplant?

3. Is there a significant difference in depression levels between chronic kidney disease patients on dialysis and those that have undergone kidney transplant?

4. Is there a significant difference in cognitive functioning between the kidney transplant patients before transplant to after they have undergone the transplant?

Chapter 3 - Method

3.1 Research Aims:

This paper is directed at gaining a better understanding pertaining to cognitive and psychological impacts associated with end-stage kidney disease (ESKD). The explicit aims of this paper are to:

1. Understand if there is a significant difference in cognitive functioning between sufferers who have undergone kidney transplant surgery, and those who have not, and are still undergoing dialysis. This aim is in the effort of understanding the impact of the kidney transplant on the brain through improved blood quality supply, harmful toxin removal, and other medical improvements gained through such surgery that are outside of the scope of this paper but contribute to the decline in cognitive functioning in individuals.

2. Evaluate the difference in anxiety levels of sufferers of the CKD, between those who have undergone kidney transplant surgery and those sufferers that are still undergoing dialysis treatment. To answer the question, the research will not be delving into the underlying issues causing anxiety, as these are amorphous in nature with numerous factors involved, but rather look at the level of change in anxiety between the two participants' states.

3. Establish whether there is a significant difference in depression levels of ESKD sufferers, between those who have undergone kidney transplant surgery and those sufferers that are still undergoing dialysis treatment. This is a very important question in context of ESKD, as depression in sufferers is strongly linked to issues such as compliancy and indirectly impacts on their overall level of functioning post-transplant, as well as pre transplant with dialysis.

3.2 Research Design

The overall research design used was quantitative in nature, and was quasi experimental.

For the first, second and third research question evaluating whether there are significant differences in cognitive functioning / depression / anxiety in chronic kidney disease patients post-transplant versus patients suffering from chronic kidney disease not having undergone a transplant, the study had a control group being patients that were still on hemodialysis and an experimental group of patients having undergone a renal transplant. The control group is however inherently more of a comparison group, but due to using the information from the RBANS in the initial assessment to provide equivalence, this group functioned as a control group for statistical purposes. Due to the participants already having been part of a study that collected the initial baseline cognitive functioning levels, randomisation could not be achieved. Secondly, due to the nature of the participants, random assignment could also not be achieved.

For the fourth research question evaluating whether there were significant differences in cognitive functioning between the kidney transplant patients before transplant to after they had undergone the transplant, the study had a control group being the data from the patients before they underwent transplant surgery and an experimental group of the data on the same patients after having undergone a renal transplant, essentially having a pre post evaluation. Due to the participants already having been part of a study that collected the initial baseline cognitive functioning levels, randomisation could not be achieved. Secondly, due to the nature of the participants, random assignment could also not be achieved.

3.3 Sampling strategy

There were two groups of participants in this sample. The first group in the sample (N=8) consisted of participants, all of whom had been diagnosed with chronic kidney disease, and are currently undergoing dialysis at various dialysis center facilities situated around the Gauteng region.

The second group in the sample (N=8) consisted of participants who have been diagnosed with ESKD, received chronic hemodialysis, and have undergone a kidney transplant. These participants underwent organ transplant, and were successful in so far as their surgery established good renal filtration occurring post-surgery.

All participants in this study were referred by the Wits Donald Gordon Medical Centre Transplant Clinic.

Although the characteristics of the population all include the participants having been diagnosed with ESKD, the progression of the disease was not used as a sampling characteristic, other than the fact that the progression of the disease is at end-stage.

An important inclusion criterion was that the participants all have had their initial cognitive functioning data collection been done, more than 6 months prior to this studies data collection, as this is a criterion of the instrument (RBANS) used for that specific data collection. For the patients that underwent kidney transplant surgery, inclusion criteria would be that they have also had their transplant at least 6 months prior to the research, so as to establish results that have allowed for stabilisation post-surgery.

Demographic information was also collected from the sample for post hoc analysis, but none of the demographic data was used in exclusion criteria for sample formation.

3.4 Instruments:

3.4.1 Demographic Questionnaire

The first step in the research was to administer a questionnaire to the individual to capture demographical information such as, Age, Population Group, and Highest Level of Schooling. The full demographic questionnaire can be found in Appendix A. Much of this information was utilized as a prerequisite in the RBANS instrument as Age for example was associated to the norms that existed within the RBANS scoring tools.

The demographic questionnaire was delivered in English, and any questions regarding comprehension or language constraints identified, were dealt with by the administrator of the questionnaire. The language barrier was never insurmountable throughout the data collection that a translator was ever required, as the level of English comprehension was relatively high throughout.

3.4.2 Cognitive Battery

The next step in the data collection was to conduct the same cognitive battery that was conducted in the initial data collection of the participants that established baselines for the individuals' level of cognitive functioning, which was the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

The entire battery took less than 60 minutes to administer, and the results of the battery yielded normalised scores for five cognitive domains, being Immediate Memory, Visuospatial / Constructional, Language, Attention and Delayed Attention. There are numerous reliability and validity scores available from existing research utilising the RBANS instrument, having shown the use thereof in various domains such as schizophrenia, traumatic brain injury and so forth (Groth-Marnat, 2009).

Regarding validity, the RBANS was found to be sensitive when used to detect the associated neurocognitive impairments when compared to matched normal controls. It also shows excellent divergent and convergent validity showing correlations to tests like the WAIS-R Full

Scale IQ of 0.78. The RBANS showed a split-half reliability of 0.98 for the overall cognitive sore, and had a range between 0.82 for the Language component, and 0.88 for the Immediate memory component of the test (Groth-Marnat, 2009). A unique characteristic of the RBANS is that it has four equivalent alternate forms, which allows for retesting patients without the confound of significant content-related practice effects, whereby the new tests to be done on the patients would be done with an alternative form of the test. Test-Retest reliability has shown that the time interval ranged from 1 to 134 days, and that there was no apparent effect of time on retest performance over this interval range (Randolph, 1998).

3.4.3 Brief Symptom Inventory 18 (BSI)

The brief symptom inventory was then administered during this the data collection in this research, but the results of the BSI that were collected in the baseline data collection were not utilised. The post-transplant data was gathered in a more comprehensive manner than was done on initial testing. Although this data is rich, it did to a large extent preclude comparison with the intake data.

The BSI 18 is an18-item self-report inventory whereby participants have to rate the extent to which they had been bothered recently by various psychological symptoms in three domains, namely somatic, depression and anxiety. It is a shortened version of the full BSI that has nine subscales that has be constructed to assess individual symptom groups, being somatisation, obsessive-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism.

The BSI 18 scale then also captures global psychological distress levels in participants. Convergent validity and concurrent validity was examined for the BSI, with both showing high levels of association with the clinical diagnosis of depression and anxiety.
These studies include validity tests against kidney disease patients. Reliability scores are relatively high ranging between 0.82 and 0.87 (Khalil, Hall, Moser, Lennie, & Frazier, 2011).

3.5 Procedure

3.5.1 Participant Identification

The participants in the study were all part of a pool that underwent psychological testing that included a cognitive battery assessment and a brief symptom inventory at WDGMC, at least 6 months prior to the study. These made up the potential participants that were used as a base for recruitment into the study. There were other tests run on these participants such as the Stroop and Trailmaking, but the use of that data did not form part of this study.

3.5.2 Kidney Specialist Consent

Upon evaluation of the available pool of participants, the researcher also contacted the kidney specialists in charge of each case to gain permission to conduct the research on their patients. An agreement between the primary researcher on this study and the kidney specialist responsible for each of the participants was discussed and concluded.

3.5.3 Participant Recruitment

The abovementioned pool of participants were contacted telephonically to request their participation in the study. The participants received a research pack containing:

- Description and the full details of the study
- Consent Form

All participants who agreed to participate in the study, completed the abovementioned form allowing the study to meet the standards imposed by the medical ethics committee of the University of the Witwatersrand.

3.5.4 Location where research was conducted

Patients undergoing hemodialysis were assed at the Sunninghill hospital for data collection purposes, as it was the most convenient time for these patients to participate in the study. The renal transplant patient data collection happened at the places of work or alternatively at their homes or at a site elected by the participant for convenience purposes.

3.5.5 Ethical Considerations

This study was evaluated by and considered to meet the ethical requirements of the Human Research Ethics Committee, Wits University. This was approved with the following protocol number: M141024.

Participants were informed about their right to withdraw from the interviews at any time should they wish to, without their being any recourse or negative impact on them whatsoever.

In an effort to ensure confidentiality, all of the participant names were removed from the data before analyses were done, and the interviews were identified only by an appropriate code. Due to the nature of the data collection, it was however not possible to ensure anonymity from the researcher, but with the data being coded, participant anonymity was however maintained post coding within the research results.

The study did not put any of the participants at risk of any emotional or physical harm. Should there have been a requirement for any further intervention with any of the participants, Dr. Tina Sideris, the resident Clinical Psychologist at WGDMC, as well as their respective kidney specialists treating them, would have been duly notified. This never transpired and hence there was never a requirement or escalation to the abovementioned parties.

3.6 Data analysis

With regard to data analysis in the research, the research predominantly used Mann-Whitney U tests, and a Signed-rank Wilcoxon matched-pairs test to analyse significant differences between the 2 groups (renal transplant and hemodialysis) as well as within group in the case of the kidney transplant group testing pre and post functioning. A Mann-Whitney U was also utilised to assess the equivalence of the two groups (renal transplant and hemodialysis) pre transplant. This was to ensure the research was in a position in the study to compare the two groups fairly.

The study calculated descriptive statistics about the sample, including descriptive information on age, gender, level of schooling, as well as the means, modes, range, and standard deviations for the psychological, and RBANS tests. This was in the aim of understanding baseline values before explicitly running statistical tools such as the Mann-Whitney U's or Signed-rank Wilcoxon matched pairs tests. The Signed-rank Wilcoxon matched-pairs test was used to analyse the difference in cognitive functioning levels in the group that had undergone kidney transplant.

Regarding distribution of the samples, the first, second and third research questions' data could not be assumed normally distributed. They were therefore tested for normality of the samples, through the use of Kolmogorov–Smirnov, as well as analyses of the distribution of the data in a histogram format to meet the requirement of a normal distribution. It was found that more than 90% of the dependent variables were normally distributed, but with that said, receiving false positives as to distribution in small sample sizes is a regular occurrence and hence the research selected non-parametric tools to account for assumed non normality.

For the fourth research question, a non-parametric test was utilized and hence normality of the sample distribution was not required. Normality in distribution of the sample was however tested in the sample through the use of Kolmogorov–Smirnov, as well as an analysis distribution of the data in a histogram format to at least see if we do meet the requirement of a normal distribution. The sample was found to be normally distributed.

A breakdown of the specific hypotheses to be tested per research question are shown below in null form:

Research Question 1 – Is there a significant difference in cognitive functioning in chronic kidney disease patients post-transplant, versus chronic kidney patients not having undergone transplant surgery?

- Statistical tool – Mann-Whitney U
- Tool Description – This statistical tool is a non-parametric tool that is used to determine if two sets of data are significantly different from one another, and is utilised when the sample for the dependent variable does not meet all of the required assumptions for a parametric test of this type. In this case, we were unable to assume normality of the data due to the data's sample size.
- Appropriateness – A Mann-Whitney U will be an appropriate statistical method to use as the question being answered merely requires an answer as to whether there is a significant difference in the mean score ranks of the 2 groups in the study, while ensuring that there they were equivalent in the first place when the initial cognitive test was done. Both groups have participants that are independent from each other, have originally been in the same physical condition creating a baseline, with the experimental group having undergone transplant surgery.
- Assumptions:

• The scale of measure for the dependent variable in this case being cognitive functioning level, is interval data.

Research Question 2 – Is there a significant difference in anxiety levels between chronic kidney disease patients on dialysis and those that have undergone kidney transplant?

- Statistical tool – Mann-Whitney U
- Tool Description – This statistical tool is a non-parametric tool that is used to determine if two sets of data are significantly different from one another, and is utilised when the sample for the dependent variable does not meet all of the required assumptions for a parametric test of this type. In this case, we were unable to assume normality of the data due to the data's sample size.
- Appropriateness – A Mann-Whitney U will be an appropriate statistical method to use as the question being answered merely requires and answer as to whether there

is a significant difference between the mean score ranks of the 2 groups in the study, while ensuring that there they were equivalent in the first place when the initial cognitive test was done. Both groups have participants that are independent from each other, having originally been in the same physical condition creating a baseline, with the experimental group having undergone transplant surgery.

- Assumptions:

• The scale of measure for the dependent variable in this case being anxiety level, is interval data after having been normalised meeting the requirement.

Research Question 3 – Is there a significant difference in depression levels between chronic kidney disease patients on dialysis and those that have undergone kidney transplant?

- Statistical tool – Mann-Whitney U

- Tool Description – This statistical tool is a non-parametric tool that is used to determine if two sets of data are significantly different from one another, and is utilised when the sample for the dependent variable does not meet all of the required assumptions for a parametric test of this type. In this case, we were unable to assume normality of the data due to the data's sample size.

- Appropriateness – A Mann-Whitney U will be an appropriate statistical method to use as the question being answered merely requires and answer as to whether there is a significant difference between the mean score ranks of the 2 groups in the study, while ensuring that there they were equivalent in the first place when the initial cognitive test was done. Both groups have participants that are independent from each other, have originally been in the same physical condition creating a baseline, with the experimental group having undergone transplant surgery.

- Assumptions:

• The scale of measure for the dependent variable in this case being depression level, is interval data after having been normalised meeting the requirement.

Research Question 4 – Is there a significant difference in cognitive functioning between the kidney transplant patients before transplant to after they have undergone the transplant?

- Statistical tool – Signed-rank Wilcoxon matched-pairs test
- Tool Description – This statistical tool is used to determine if two dependent sets of data are significantly different from one another, and is utilised when parametric requirements are not met to conduct parametric statistical analyses. In this case because the group is
- Appropriateness – Because the data is derived from a pre and post-test of cognitive functioning in the kidney transplant group, they are not independent and hence require a matched pairs test. The size of the group is only 15 participants and therefore does not meet the requirements for a parametric test, whereby the Signed-rank Wilcoxon matched-pairs test would be an appropriate non-parametric alternative to a Matched pairs t-test.
- Assumptions:
  - The scale of measure for the dependent variable in this case being cognitive functioning level, is nominal meeting the requirement.

Chapter 4 - Results

Descriptive Statistics

The means of the two groups combined represented by (M) and their associated Standard Deviations represented by (S) were calculated for the demographic information on this sample (summarized in Table 4.1)

Table 4.1
Descriptive statistics of the demographics of the total sample of patients at WDGMC (n=16)

	N	Range	Minimum	Maximum	Mean (*M*)	Std. Deviation (*S*)	Variance	Skewness
Age	16	40.0	20.0	60.0	40.563	12.5271	156.929	.030
Years of Education	16	4.0	12.0	16.0	13.125	1.5000	2.250	.978
Perception of Responsibilities	16	2.0	1.0	3.0	-	-	-	-
Perception of Support	16	1.0	2.0	3.0	-	-	-	-
Employment Status	16	7.0	1.0	8.0	-	-	-	-
Pre CKD Employment Status	16	5.0	1.0	6.0	-	-	-	-

As can be seen in Table 4.1, the average age of all participants in the study is 40.563 with a minimum age of 20 and a maximum age of 60. It should be noted that any patients under the age of 18 were excluded from the study as some of the psychometric tools utilised in the study were unable to cater for patients younger than 18, namely the BDI 18. The average years of education is 13.125, with the minimum years of education being 12 and the maximum being 16. Consideration of the fact that the sample was taken from a population of individuals

receiving treatment and diagnosis from the private healthcare sector, whereby financial ability to study may have been a factor in the mean levels of education should be noted. This will be discussed further in the limitations section of the study.

Testing for pre transplant equivalence of the 2 groups of participants

Before delving into the specific research questions and their associated statistics, it was also important to understand whether there were any significant differences in the participants from both groups before the one group underwent renal surgery, so as to ensure that the individuals were equivalent. To achieve this, a Mann-Whitney U test was run on the cognitive functioning scores overall and in the sub domains of functioning, on the participants in the study pre renal transplant.

The following results were found:

Table 4.2
Test Statistic results on Pre Transplant for both Groups (*n=16*)

	Pre Overall Cognitive Functioning	Pre Immediate Memory Functioning	Pre Visuospatial / Constructional Functioning	Pre Language Functioning	Pre Attention Functioning	Pre Delayed Memory Functioning
Mann-Whitney U	26.5	31.5	27.5	21	21.5	22
Wilcoxon W	62.5	67.5	63.5	57	57.5	58
Z	-0.578	-0.053	-0.474	-1.161	-1.116	-1.054
Asymp. Sig. (2-tailed)	0.563	0.958	0.636	0.246	0.264	0.292

In considering the results in Table 4.2, the research achieved no significant results across global cognitive functioning nor in any of the sub domains of cognitive functioning. This leads one to believe that there was equivalence between the two groups before half of the participants underwent renal transplant surgery, and further to that allowing the research to make comparisons between the two groups.

Research Question 1

For the first research question, it was hypothesised that there is a significant difference between the level of cognitive functioning in chronic kidney disease patients post-transplant compared to those not having undergone transplant who are still undergoing hemodialysis treatment. This was tested using a variety sub tests within the RBANS. These tests looked at overall (1) Cognitive functioning levels, (2) Immediate memory function, (3) VisuoSpatial / Constructional function, (4) Language function, (5) Attention, and (6) Delayed Memory functioning.

1. Overall Cognitive Functioning Difference between Transplant and Dialysis patients

Table 4.3
Mean Ranks and Sum of Ranks between Dialysis and Transplant Patients relating to overall cognitive functioning (n=16)

	Treatment	N	Mean	Mean Rank	Sum of Ranks
Overall Cognitive Functioning	Dialysis	8	87.75	5.75	46
	Transplant	8	104.38	11.25	90
	Total	16			

Table 4.4
Test Statistics between Dialysis and Transplant Patients relating to overall cognitive functioning (n=16)

	Overall Cognitive Functioning
Mann-Whitney U	10
Wilcoxon W	46
Z	-2.31
Asymp. Sig. (2-tailed)	0.021

As can be seen by Table 4.3 whereby the Sum of Ranks differ significantly and in Table 4.4 where the Mann-Whitney U yields a significance of (U = 0.021) which is less than 0.05 (our confidence level), there is quite a significant statistical difference in overall Cognitive Functioning between CKD sufferers in the two groups. Furthermore, the transplant group's

mean overall cognitive function is (M = 104.38) while the dialysis group is only (M = 87.75) showing the transplant group having a greater overall cognitive function. With the above results we reject the Null Hypotheses (H_0) in favor of the alternative Hypothesis (H_1), allowing us to conclude that renal transplant may have a positive impact on overall cognitive functioning compared to people undergoing hemodialysis.

2. Immediate Memory Functioning difference between Transplant and Dialysis patients

Table 4.5
Mean Ranks and Sum of Ranks between Dialysis and Transplant Patients relating to immediate memory functioning (n=16)

	Treatment	N	Mean	Mean Rank	Sum of Ranks
Immediate Memory Functioning	Dialysis	8	88.98	6.38	51
	Transplant	8	103.5	0.63	85
	Total	16			

Table 4.6
Test Statistics between Dialysis and Transplant Patients relating to Immediate Memory functioning (n=16)

	Immediate Memory Functioning
Mann-Whitney U	15
Wilcoxon W	51
Z	-1.796
Asymp. Sig. (2-tailed)	0.073

As can be seen by Table 4.5 whereby the Sum of Ranks do not differ significantly and in Table 4.6 where the Mann-Whitney U yields a non-significant result of (U = 0.073) which is greater than 0.05 (our confidence level), there is not a significant statistical difference in Immediate Memory functioning between CKD sufferers in the two groups. With the above results we accept the Null Hypotheses (H_0) allowing us to conclude that renal transplant may

not have an impact on Immediate Memory functioning compared to people undergoing hemodialysis.

3. Visuospatial / Constructional Functioning difference between Transplant and Dialysis patients

Table 4.7
Mean Ranks and Sum of Ranks between Dialysis and Transplant Patients relating to Visuospatial / Constructional functioning (n=16)

	Treatment	N	Mean	Mean Rank	Sum of Ranks
Visuospatial / Constructional functioning	Dialysis	8	86.63	5.81	46.5
	Transplant	8	105.38	11.19	89.5
	Total	16			

Table 4.8
Test Statistics between Dialysis and Transplant Patients relating to Visuospatial / Constructional functioning (n=16)

	Visuospatial / Constructional functioning
Mann-Whitney U	10.5
Wilcoxon W	46.5
Z	-2.295
Asymp. Sig. (2-tailed)	0.022

As can be seen by Table 4.7 whereby the Sum of Ranks differ significantly and in Table 4.8 where the Mann-Whitney U yields a significance of (U = 0.022) which is less than 0.05 (our confidence level), there is quite a significant statistical difference in Visuospatial / Constructional Functioning between CKD sufferers in the two groups. Furthermore, the transplant group's mean overall cognitive function is (M = 105.38) while the dialysis group is only (M = 86.63) showing the transplant group having a greater overall cognitive function. With the above results we reject the Null Hypotheses (H_0) in favor of the alternative

Hypothesis (H_1), allowing us to conclude that renal transplant may have a positive impact on visuospatial / constructional functioning compared to people undergoing hemodialysis.

4. Language Functioning difference between Transplant and Dialysis patients

Table 4.9
Mean Ranks and Sum of Ranks between Dialysis and Transplant Patients relating to Language functioning (n=16)

	Treatment	N	Mean	Mean Rank	Sum of Ranks
Language Functioning	Dialysis	8	93	6.19	49.5
	Transplant	8	100	10.81	86.5
	Total	16			

Table 4.10
Test Statistics between Dialysis and Transplant Patients relating to Language functioning (n=16)

	Language Functioning
Mann-Whitney U	13.5
Wilcoxon W	49.5
Z	-1.952
Asymp. Sig. (2-tailed)	0.049

As can be seen by both Table 4.9 whereby the Sum of Ranks differ significantly and in Table 4.10 where the Mann-Whitney U yields a significance of (U = 0.049) which is less than 0.05 (our confidence level), there is a significant statistical difference in Language Functioning between CKD sufferers in the two groups. Furthermore, the transplant group's mean overall cognitive function is (M = 100) while the dialysis group is only (M = 93) showing the transplant group having a greater language function. With the above results we reject the Null Hypotheses (H_0) in favor of the alternative Hypothesis (H_1), allowing us to conclude that renal transplant may have a positive impact on language functioning compared to people undergoing hemodialysis.

5. Attention Functioning difference between Transplant and Dialysis patients

Table 4.11
Mean Ranks and Sum of Ranks between Dialysis and Transplant Patients relating to Attention functioning (n=16)

	Treatment	N	Mean	Mean Rank	Sum of Ranks
Attention Functioning	Dialysis	8	88	5.94	47.5
	Transplant	8	100.88	11.06	88.5
	Total	16			

Table 4.12
Test Statistics between Dialysis and Transplant Patients relating to Attention functioning (n=16)

	Attention Functioning
Mann-Whitney U	11.5
Wilcoxon W	47.5
Z	-2.162
Asymp. Sig. (2-tailed)	0.031

As can be seen by both Table 4.11 whereby the Sum of Ranks differ significantly and in Table 4.12 where the Mann-Whitney U yields a significance of (U = 0.031) which is less than 0.05 (our confidence level), there is a significant statistical difference in Attention Functioning between CKD sufferers in the two groups. Furthermore, the transplant group's mean overall cognitive function is (M = 100.88) while the dialysis group is only (M = 88) showing the transplant group having a greater attention. With the above results we reject the Null Hypotheses (H_0) in favor of the alternative Hypothesis (H_1), allowing us to conclude that renal transplant may have a positive impact on attention functioning compared to people undergoing hemodialysis.

6. Delayed Memory Functioning difference between Transplant and Dialysis patients

Table 4.13
Mean Ranks and Sum of Ranks between Dialysis and Transplant Patients relating to Delayed Memory functioning (n=16)

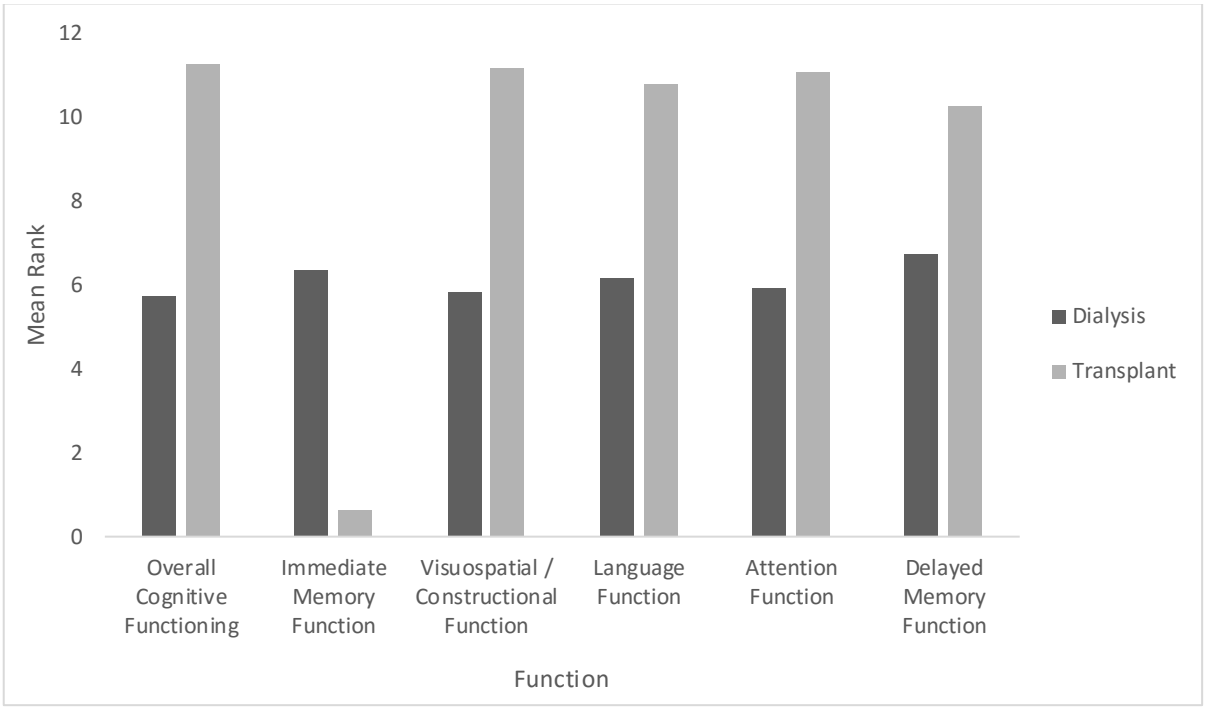
	Treatment	N	Mean	Mean Rank	Sum of Ranks
Delayed Memory Functioning	Dialysis	8	98.38	6.75	54
	Transplant	8	103.5	10.25	82
	Total	16			

Table 4.14
Test Statistics between Dialysis and Transplant Patients relating to Delayed Memory functioning (n=16)

	Delayed Memory Functioning
Mann-Whitney U	18
Wilcoxon W	54
Z	-1.474
Asymp. Sig. (2-tailed)	0.141

As can be seen by both Table 4.13 whereby the Sum of Ranks do not differ significantly and in Table 4.14 where the Mann-Whitney U yields a non-significant result of (U = 0.141) which is greater than 0.05 (our confidence level), there is not a significant statistical difference in Delayed Memory functioning between CKD sufferers in the two groups. With the above results we accept the Null Hypotheses (H_0) allowing us to conclude that renal transplant may not have an impact on Delayed Memory functioning compared to people undergoing hemodialysis.

Figure 4.1
Mean Rank comparison of Dialysis versus Transplant Patients relating to Delayed Memory functioning (n=16)



A summary of the results for Cognitive Functioning between CKD patients undergoing hemodialysis compared to those having undergone renal transplant surgery can be seen in table 4.14.1 below:

Table 4.14.1
Summary of Results of Cognitive Functioning between hemodialysis patients and renal transplant patients

	Result
Overall Cognitive Functioning	Significant
Immediate Memory	Not Significant
Visuo Spatial / Constructional	Significant
Language	Significant
Attention	Significant
Delayed Memory	Not Significant

In summary of the results from Figure 4.1 and Table 4.14.1 we can see that overall cognitive functioning and all sub domains thereof, excepting for either immediate or delayed memory differ significantly between the two groups. Looking at the means of the various results, the improvements are all also in favor of the renal transplant group.

Research Question 2

For the second research question, it was hypothesised that there is a significant difference between the level of anxiety distress in chronic kidney disease patients post-transplant compared to those not having undergone transplant. This was tested utilising normalised scores from the BSI 18, but specifically the Anxiety domain of the test.

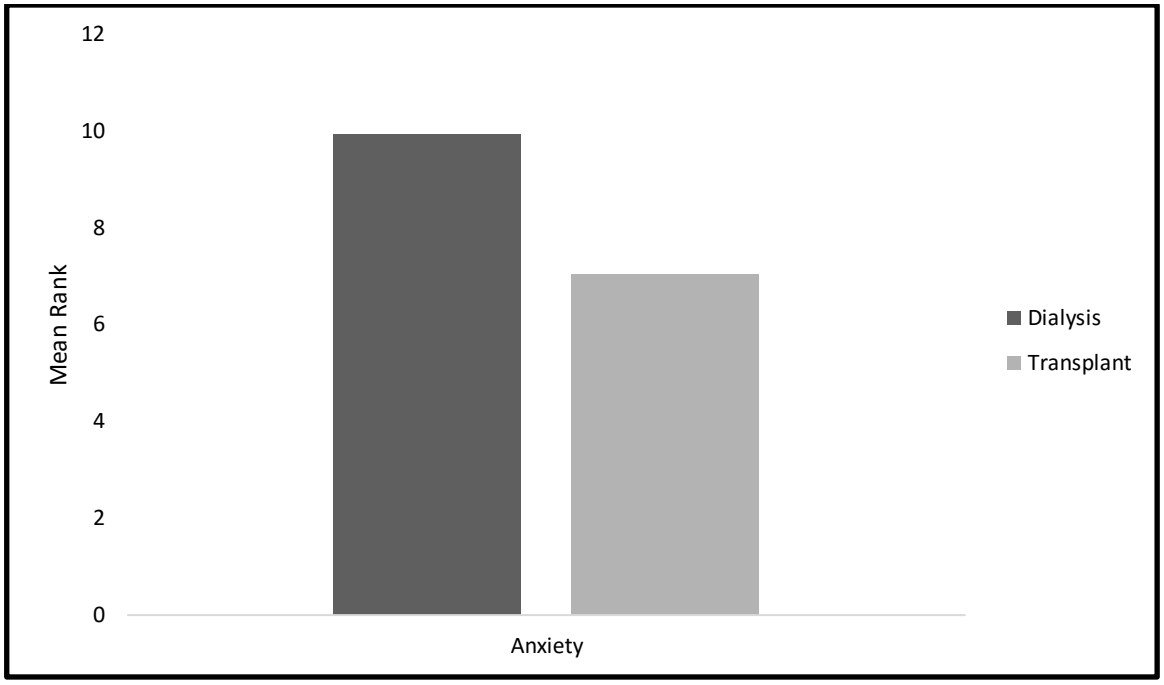
Table 4.15
Mean Ranks and Sum of Ranks between Dialysis and Transplant Patients relating to Anxiety Distress(n=16)

	Treatment	N	Mean	Mean Rank	Sum of Ranks
Anxiety Distress	Dialysis	8	52.5	9.94	79.5
	Transplant	8	47.5	7.06	56.5
	Total	16			

Table 4.16
Test Statistics between Dialysis and Transplant Patients relating to Anxiety Distress (n=16)

	Anxiety Distress
Mann-Whitney U	20.5
Wilcoxon W	56.5
Z	-1.241
Asymp. Sig. (2-tailed)	0.215

Figure 4.2
Mean Rank Comparison of Dialysis versus Transplant Patients relating to Anxiety (n=16)



As can be seen by both Figure 4.2 and Table 4.15 whereby the Sum of Ranks do not differ significantly and in Table 4.16 where the Mann-Whitney U yields a non-significant result of (U = 0.215) which is greater than 0.05 (our confidence level), there is not a significant statistical difference in Anxiety Distress functioning between CKD sufferers in the two groups. With the above results we accept the Null Hypotheses (H_0) allowing us to conclude that renal transplant may not have an impact on Anxiety Distress functioning compared to people undergoing hemodialysis.

Research Question 3

For the third research question, it was hypothesised that there is a significant difference between the level of depression experienced in chronic kidney disease patients post-transplant compared to those not having undergone transplant. This was tested utilising normalised scores from the BSI 18, but specifically the Depression domain of the test.

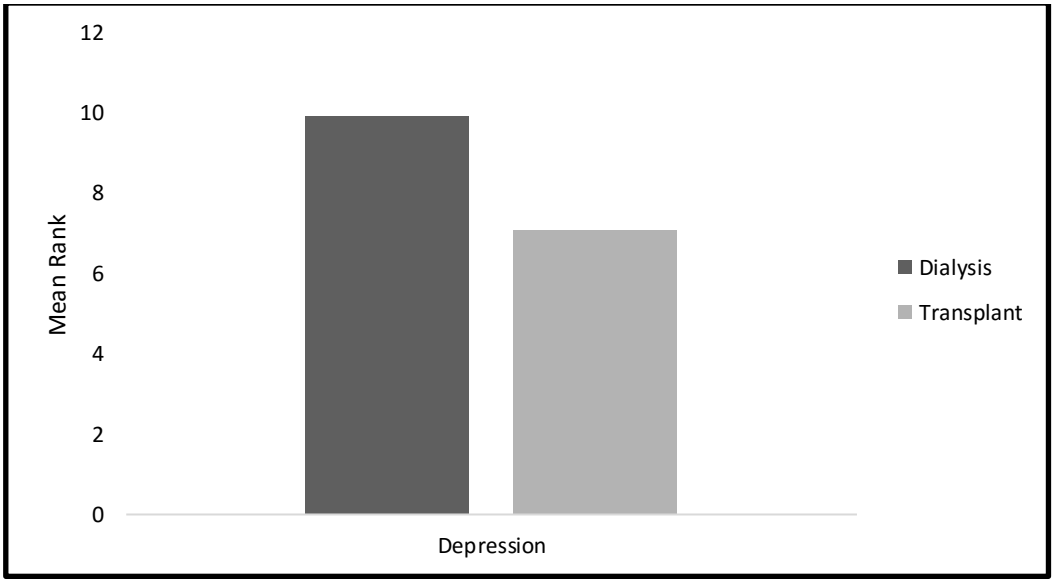
Table 4.17
Mean Ranks and Sum of Ranks between Dialysis and Transplant Patients relating to Depression Distress(n=16)

	Treatment	N	Mean	Mean Rank	Sum of Ranks
Depression Distress	Dialysis	8	52.13	9.94	79.5
	Transplant	8	48	7.06	56.5
	Total	16			

Table 4.18
Test Statistics between Dialysis and Transplant Patients relating to Depression Distress (n=16)

	Depression Distress
Mann-Whitney U	20.5
Wilcoxon W	56.5
Z	-1.234
Asymp. Sig. (2-tailed)	0.217

Figure 4.3
Mean Rank Comparison of Dialysis versus Transplant Patients relating to Depression (n=16)



As can be seen by both Figure 4.3 and Table 4.17 whereby the Sum of Ranks do not differ significantly and in Table 4.18 where the Mann-Whitney U yields a non-significant result of (U = 0.217) which is greater than 0.05 (our confidence level), there is not a significant

statistical difference in Depression Distress functioning between CKD sufferers in the two groups. With the above results we accept the Null Hypotheses (H_0) allowing us to conclude that renal transplant may not have an impact on Depression Distress functioning compared to people undergoing hemodialysis.

Research Question 4

For the fourth and final research question, it was hypothesised that there is a significant difference between the level of cognitive functioning in chronic kidney disease patients post-transplant compared to pre-transplant. This was tested using multiple sub tests within the RBANS. These tests looked at overall (1) Cognitive functioning levels, (2) Immediate memory function, (3) VisuoSpatial / Constructional function, (4) Language function, (5) Attention, and (6) Delayed Memory functioning.

1. Overall Cognitive Functioning Difference between Pre Transplant and Post-Transplant Patients

Table 4.19

Means, Std. Dev.'s, Maximum's and Minimum's between transplant Patients before and after the transplant relating to their overall cognitive functioning(n=16)

						Percentiles		
	N	Mean	Std. Deviation	Minimum	Maximum	25th	50th (Median)	75th
Pre Transplant RBANS Total Index Score	16	93.437	16.9508	73	144	84.25	89.5	100
Post-Transplant RBANS Total Index Score	16	96.063	15.2555	78	139	85.25	94	103.5

Table 4.20

Mean Ranks and Sum of Ranks between transplant Patients before and after the transplant relating to Overall Cognitive Functioning(n=16)

		N	Mean Rank	Sum Of Ranks
Post-Transplant RBANS Total Index - Pre Transplant RBANS Total Index	Negative Ranks	4[a]	9.5	38
	Positive	11[b]	7.45	82

Ranks		
	Ties	1[c]
	Total	16

Notes: a. Post-Transplant RBANS Total Index < Pre Transplant RBANS Total Index

b. Post-Transplant RBANS Total Index > Pre Transplant RBANS Total Index

c. Post-Transplant RBANS Total Index = Pre Transplant RBANS Total Index

Table 4.21
Test Statistics between transplant Patients before and after the transplant relating to Overall Cognitive Functioning(n=16)

	Post-Transplant RBANS Total Index - Pre Transplant RBANS Total Index
Z	-1.255
Asymp. Sig. (2-Tailed)	0.210

As can be seen by Table 4.21 where the Wilcoxon's Signed Rank Test yields a non-significant result of 0.210 which is greater than 0.05 (our confidence level), there is not a significant statistical difference in Overall Cognitive functioning between renal transplant patients before and after their transplant. With the above results we accept the Null Hypotheses (H_0) allowing us to conclude that renal transplant may not have an impact on Overall Cognitive functioning compared.

2. Immediate Memory Functioning difference between Pre Transplant and Post-Transplant Patients

Table 4.22
Means, Std. Dev.'s, Maximum's and Minimum's between transplant Patients before and after the transplant relating to their Immediate Memory functioning(n=16)

						Percentiles		
	N	Mean	Std. Deviation	Minimum	Maximum	25th	50th (Median)	75th
Pre Transplant Immediate Memory Score	16	94.563	18.7864	69	140	81	95.5	108.25
Post-Transplant RBANS Immediate Memory Score	16	96.687	13.6905	78	114	82.5	100	109

Table 4.23
Mean Ranks and Sum of Ranks between transplant Patients before and after the transplant relating to Immediate Memory Functioning(n=16)

		N	Mean Rank	Sum Of Ranks
Post-Transplant RBANS Immediate Memory - Pre Transplant RBANS Immediate Memory	Negative Ranks	5[a]	9.1	45.5
	Positive Ranks	10[b]	7.45	74.5
	Ties	1[c]		
	Total	16		

Notes : a. Post-Transplant Immediate Memory < Pre Transplant Immediate Memory

b. Post-Transplant Immediate Memory > Pre Transplant Immediate Memory

c. Post-Transplant Immediate Memory = Pre Transplant Immediate Memory

Table 4.2
Test Statistics between transplant Patients before and after the transplant relating to Immediate Memory Functioning(n=16)

	Post-Transplant RBANS Immediate Memory- Pre Transplant RBANS Immediate Memory
Z	0.825
Asymp. Sig. (2-Tailed)	0.409

As can be seen by Table 4.24 where the Wilcoxon's Signed Rank Test yields a non-significant result of 0.490 which is greater than 0.05 (our confidence level), there is not a significant statistical difference in Immediate Memory functioning between renal transplant patients before and after their transplant. With the above results we accept the Null Hypotheses (H_0) allowing us to conclude that renal transplant may not have an impact on Immediate Memory functioning compared.

3. VisuoSpatial/Contructional functioning difference between Pre-Transplant and Post-Transplant Patients

Table 4.25
Means, Std. Dev.'s, Maximum's and Minimum's between transplant Patients before and after the transplant relating to their Immediate Visuospatial / Constructional Functioning(n=16)

						Percentiles		
	N	Mean	Std. Deviation	Minimum	Maximum	25th	50th (Median)	75th
Pre Transplant Visuospatial / Contructional Score	16	94.625	19.4006	64	131	81	94	102
Post-Transplant Visuospatial / Contructional Score	16	96	16.1823	62	131	85.25	98	102

Table 4.26
Mean Ranks and Sum of Ranks between transplant Patients before and after the transplant relating to Visuospatial / Constructional Functioning(n=16)

		N	Mean Rank	Sum Of Ranks
Post-Transplant Visuospatial / Constructional – Pre-Transplant Visuospatial / Constructional	Negative Ranks	7[a]	7.57	53
	Positive Ranks	8[b]	8.38	67
	Ties	1[c]		
	Total	16		

a. Post-Transplant Visuospatial / Constructional < Pre Transplant Visuospatial / Constructional

b. Post-Transplant Visuospatial / Constructional > Pre Transplant Visuospatial / Constructional

c. Post-Transplant Visuospatial / Constructional = Pre Transplant Visuospatial / Constructional

Table 4.27
Test Statistics between transplant Patients before and after the transplant relating to Visuospatial / Constructional Functioning(n=16)

	Post-Transplant Visuospatial / Constructional - Pre Transplant Visuospatial / Constructional
Z	-0.398[b]
Asymp. Sig. (2-Tailed)	0.691

As can be seen by Table 4.27 where the Wilcoxon's Signed Rank Test yields a non-significant result of 0.691 which is greater than 0.05 (our confidence level), there is not a significant statistical difference in Visuospatial / Constructional functioning between renal transplant patients before and after their transplant. With the above results we accept the Null Hypotheses (H_0) allowing us to conclude that renal transplant may not have an impact on Visuospatial / Constructional functioning compared.

4. Language Functioning difference between Pre Transplant and Post-Transplant Patients

Table 4.28
Means, Std. Dev.'s, Maximum's and Minimum's between transplant Patients before and after the transplant relating to their Language Functioning(n=16)

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles 25th	50th (Median)	75th
Pre-Transplant Language Score	16	97.688	13.5288	71	127	89	97	104.75
Post-Transplant Language Score	16	96.5	12.5433	85	131	89	91	100.50

Table 4.29 showing Mean Ranks and Sum of Ranks between transplant Patients before and after the transplant relating to Language Functioning(n=16)

		N	Mean Rank	Sum Of Ranks
Post-Transplant Language Functioning - Pre Transplant Language Functioning	Negative Ranks	8[a]	7.69	61.5
	Positive Ranks	6[b]	7.25	43.5
	Ties	2[c]		
	Total	16		

Notes: a. Post-Transplant Language Functioning < Pre Transplant Language Functioning
b. Post-Transplant Language Functioning > Pre Transplant Language Functioning
c. Post-Transplant Language Functioning = Pre Transplant Language Functioning

Table 4.30
Test Statistics between transplant Patients before and after the transplant relating to Language Functioning(n=16)

	Post-Transplant Language Functioning - Pre Transplant Language Functioning
Z	-0.565
Asymp. Sig. (2-Tailed)	0.572

As can be seen in Table 4.30 where the Wilcoxon's Signed Rank Test yields a non-significant result of 0.572 which is greater than 0.05 (our confidence level), there is not a significant statistical difference in Constructional Functioning functioning between renal transplant patients before and after their transplant. With the above results we accept the Null Hypotheses (H_0) allowing us to conclude that renal transplant may not have an impact on Language Functioning.

5. Attention Functioning difference between Pre Transplant and Post-Transplant Patients

Table 4.31
Means, Std. Dev.'s, Maximum's and Minimum's between transplant Patients before and after the transplant relating to their Immediate Attention Functioning(n=16)

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles 25th	50th (Median)	75th
Pre Transplant Attention Functioning	16	91	12.3342	75	128	82.75	88	96.25
Post-Transplant Attention Functioning	16	94.437	15.5947	72	125	82.75	89.5	102.25

Table 4.32 showing Mean Ranks and Sum of Ranks between transplant Patients before and after the transplant relating to Attention Functioning(*n=16*)

		N	Mean Rank	Sum Of Ranks
Post-Transplant Attention functioning - Pre Transplant Attention functioning	Negative Ranks	7[a]	6.5	45.5
	Positive Ranks	8[b]	9.31	74.5
	Ties	1[c]		
	Total	16		

Notes: a. Post-Transplant Attention functioning < Pre Transplant Attention functioning
b. Post-Transplant Attention functioning > Pre Transplant Attention functioning
c. Post-Transplant Attention functioning = Pre Transplant Attention functioning

Table 4.33

Test Statistics between transplant Patients before and after the transplant relating to Attention Functioning(n=16)

	Post-Transplant Attention Functioning - Pre Transplant Attention Functioning
Z	-0.828[b]
Asymp. Sig. (2-Tailed)	0.408

As can be seen in Table 4.33 where the Wilcoxon's Signed Rank Test yields a non-significant result of 0.408 which is greater than 0.05 (our confidence level), there is not a significant statistical difference in Attention functioning between renal transplant patients before and after their transplant. With the above results we accept the Null Hypotheses (H_0) allowing us to conclude that renal transplant may not have an impact on Attention Functioning.

6. Delayed Memory Functioning difference between Pre-Transplant and Post-Transplant Patients

Table 4.34

Means, Std. Dev.'s, Maximum's and Minimum's between transplant Patients before and after the transplant relating to their Delayed Memory Functioning(n=16)

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles 25th	50th (Median)	75th
Pre-Transplant Delayed Memory Functioning	16	96.812	12.9111	60	121	90.5	97.5	102.5
Post-Transplant Delayed Memory Functioning	16	100.938	15.5112	56	121	94.25	101	111.75

Table 4.35 showing Mean Ranks and Sum of Ranks between transplant Patients before and after the transplant relating to Delayed Memory Functioning(*n=16*)

		N	Mean Rank	Sum Of Ranks
Post-Transplant Delayed Memory - Pre Transplant Delayed Memory	Negative Ranks	4[a]	3.13	12.5
	Positive Ranks	8[b]	8.19	65.5
	Ties	4[c]		
	Total	16		

Notes: a. Post-Transplant Delayed Memory < Pre Transplant Delayed Memory
b. Post-Transplant RBANS Total Index > Pre Transplant Delayed Memory
c. Post-Transplant Delayed Memory = Pre Transplant Delayed Memory

Table 4.36
Test Statistics between transplant Patients before and after the transplant relating to Attention Functioning(n=16)

	Post-Transplant Delayed Memory - Pre Transplant Delayed Memory
Z	-2.087
Asymp. Sig. (2-Tailed)	0.037

As can be seen in Table 4.36 where the Wilcoxon's Signed Rank Test yields a significant result of ($Z = 0.037$, $p < .05$) which is less than our confidence level, and hence there is a statistically significant difference in Delayed Memory functioning between renal transplant patients before and after their transplant. With the above results we reject the Null Hypotheses (H_0) in favor of the alternate hypothesis allowing us to deduce that there may be a difference in renal transplant patients post-transplant regarding Delayed Memory Functioning. This was expected when considering the previous result when comparing pre cognitive functioning in dialysis patients and renal transplant patients.

Figure 4.4 below shows a summary of all statistical findings from the pre / post tests done on transplant patients relative to cognitive functioning.

Figure 4.4
Mean Rank Comparison of Pre-Transplant Patients versus Post-Transplant Patients relating to Cognitive Functioning (n=16)

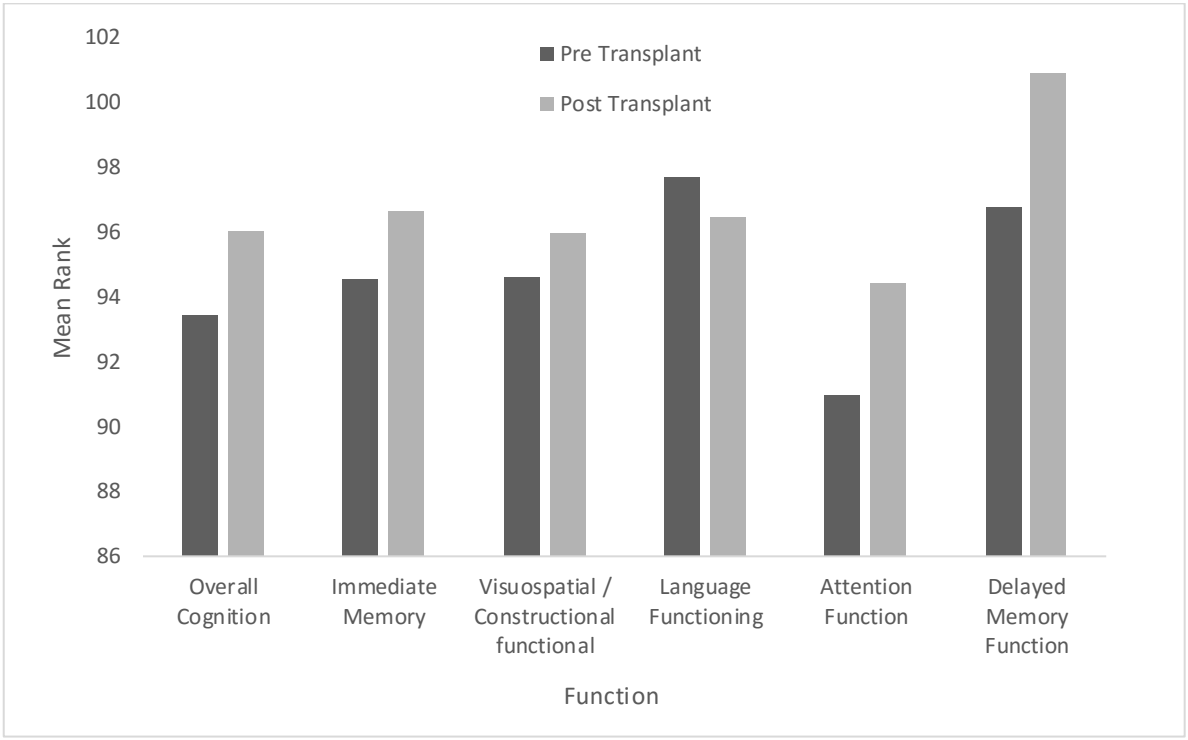


Figure 4.4 above clearly supports the findings that there is a significant difference in delayed memory post-transplant for CKD sufferers, while non-significant differences in other areas of cognition.

Chapter 5 – Discussion

Historical literature in the field of cognitive functioning as it pertains to sufferers of ESKD has focused on physiological outcomes only. With complex interactions and associations that exist between physiology and psychological constructs that can be seen in some of the results of this paper, medical practitioners could potentially yield better overall results with patients to combat issues such as non-conformance to immunosuppressant requirements, or dialysis compliance.

This study revealed that there are differences in cognitive functioning between renal transplant patients and those patients undergoing dialysis treatment, on a global cognitive functioning level. Further to that, when evaluating the various sub domains of cognitive functioning it was further revealed that although there is a global cognitive functioning difference between the two groups, there were specifically significant differences in the visuospatial / constructional, language and the attention domain of cognitive functioning in the two groups. The sub domain of memory did not result in significance differences in either the immediate or delayed memory areas. As mentioned in the limitations section however, it is the authors' belief that a larger sample size would yield even further significant results in other domains of cognitive functioning potentially.

From these findings, it is this researcher's belief that further investigations with larger sample sizes that are more representative of the South African population on a whole could deliver crucial results in helping better understand CKD. Furthermore, these results could have a significant impact in educating both CKD sufferers and their caregivers about the cognitive impacts resulting from the disease. Such research could also play a pivotal role in defining intervention programs that help limit the level of decline by either ascertaining both physiological and psychological interactions that exist with cognitive functioning and CKD. Such interventions may yield positive overall life satisfaction for sufferers of the disease so that these cognitive complications don't further compound already very challenging physiological and psychological issues faced by these sufferers.

Over and above the positive impact that could be derived by sufferers and caregivers from such further research, results could possibly even support medical practitioners in this space to better understand the disease holistically.

As it pertained to the differences in anxiety and depression levels between the two groups in the study, it was found that there were no significant differences. This result does not however allow one to assume that they are not feeling any levels of anxiety or depression, but rather that their levels of depression or anxiety do not necessarily significantly change post-transplant. This is an important result and should be understood in context of the psychological intervention requirements for patients who are either undergoing hemodialysis or have undergone renal transplant. Even more so in lieu of the fact that the literature has also shown that psychological distress has been shown to have an association with that of mortality rates in both dialysis treatment patients and that of renal transplant. Intervention in this area, could potentially reduce mortality rates indirectly, through potential outcomes like improved immunosuppressant adherence, improved physical activity due to improved physiological status, and overall improved quality of life. A larger sample size with a more representative sample of South Africans who suffer from CKD would in the opinion of the researcher yield more conclusive results in this space.

The test results for cognitive functioning differences between pre transplant surgery CKD sufferers and their cognitive functioning post-surgery, showed no significant differences in overall cognitive functioning levels, except for one of the sub domains of cognitive functioning being delayed memory functioning. This was an unexpected result, and it is the authors belief that again a larger sample size would yield further significant results in cognitive improvement, when able to utilise parametric statistical testing tools, as was performed ad hoc tests in this study, yielding exactly that. These results are not published due to inadherence to the assumptions of parametric testing. That said, there could also be a time factor associated to the results found, being that 6 months post-surgery does not give a significant enough time for transplant patients to fully recover to optimal cognitive functioning.

CKD is a disease that has a tremendous psychological and physiological impact on sufferers and their families. Understanding all aspects of the disease is critical to further the levels of treatment and support given to these individuals. With the high and increasing rates of prevalence of the disease, continued research in this space is incredibly important and should be continued to deliver the best available treatment to individuals afflicted with the disease.

Representation of Sample

The study selected participants from a population of CKD sufferers that underwent psychological and neurocognitive evaluation at the WGDC. Both groups of patients, were either undergoing hemodialysis treatment or underwent renal transplant surgery, but still came from the same population, allowing for the ability of this research to make generalisations and claims based on the statistical outcomes of the analyses of the data collected. The renal transplant patients that were selected for transplant, came from the same pool of dialysis patients, as they were also undergoing dialysis pre transplant. The selection process for transplant includes a multidisciplinary panel that determine viability of transplant based on numerous factors associated to both the disease, coupled with that of the potential outcomes of such surgery.

Psychosocial and psychological functioning and distress are one of these important factors, hence the sample being selected from those individuals who underwent psychological evaluation at WGDC by Dr. Tina Sideris.

Limitations and recommendations for future study

There are a couple of limitations to the research that could dramatically improve significance of the tests done, coupled with eliminating certain variables that could be creating certain confounding outcomes in the results, including:

Larger sample size – Due to the difficulty of data collection in the cohort utilised for this research, a sample size of only 16 was possible in the timeframes allowed, and hence the use of non-parametric statistical methods so as to not disobey required assumptions for parametric testing. In this case specifically whereby not knowing if the distribution of the sample is normal, the assumption for normal distribution could not be adhered to as is required for a parametric test. Further tests were done utilising, a 2 sample t-test as well as ANCOVA's on the data, which yielded results closer to the expected results, and as such, it is the belief of this research that should the sample size be large enough to assume normal distribution, more supporting outcomes of cognitive improvement post renal transplant would be found.

Duration on dialysis – Duration on dialysis is not a variable that was collected during the data collection for this research, but is however one that could play an important role of understanding the actual effects of dialysis on CKD patient's cognitive functioning, anxiety and depression levels. The duration on which they undergo Dialysis could have relationships to the abovementioned levels, and should therefore be analysed in future research of this kind.

Cross Section – In line with the abovementioned limitation, utilising a longitudinal study as opposed to a cross sectional study as this one has done, would support much richer data and potentially better statistical outcomes for research of this kind.

Immunosuppressant adherence – Within the Renal Transplant group, immunosuppressant effects were not considered in this research when evaluating cognitive functioning, anxiety distress or depression distress levels. By understanding the effects of immunosuppressants, it might be able to shed some light on the potential reasons for the abovementioned challenges faced by CKD sufferers. Such research would be challenging however due to the need for immunosuppressant's with renal transplant patients, but could potentially be tested by evaluating the effects of non-adherence to immunosuppressant's, as has been highlighted in the literature review as an issue with certain patients. That said, it was also mentioned that depression, can play a role in non-compliance of the use of immunosuppressant's which could create confounding results. This is an area of research in this field that could prove to be incredibly challenging and would require a lot of thought, as to how to achieve meaningful results, and would also require large sample sizes.

Private Care Sample – The sample utilised in this study, both in the renal transplant and dialysis patients, were all from the private care sector of healthcare. There are numerous factors such as income levels, education levels, access to support from caregivers to name a few which might play an important role in the psychological functioning and cognitive functioning of these individuals. Patients receiving healthcare in the public healthcare arena, may be under very different pressures compared to those used in this study, and should be considered in future studies.

Non-Probability Convenience sampling strategy – This study made use of a non-probability convenience sampling strategy. This approach was a necessity in this study due to the

difficulty of access to such participants. This approach is however prone to causing systematic sampling errors, with one of the important elements in such a strategy being that volunteers often perform differently, and could create confounding results for the study.

Peritoneal Dialysis – The study only looked at the difference between sufferers of CKD that were undergoing hemodialysis treatment for their condition or had renal transplant surgery as a form of treatment for the disease. As mentioned in the literature review, there is however a further form of treatment being peritoneal dialysis, which could be accounted for in further studies as the level of toxicity and hence the effects thereof in patients could show further results as it pertains to psychological and neurocognitive functioning in these patients.

Conclusion

In summary, this exploratory study evaluated the psychological stress and cognitive functioning differences between dialysis patients and patients who have undergone renal surgery, coupled with the cognitive functioning differences between pre surgery and post-surgery for those patients that underwent renal transplant. Renal surgery as a treatment option for sufferers of ESKD shows a marked improvement in delayed memory post treatment, while also illustrating that there is continued overall cognitive decline in patients continuing with hemodialysis treatment. The results indicate that attention should be given by practitioners to not only support the physiological requirements of sufferers of the disease but also the compounding psychological issues they face when considering the marked differences in cognitive functioning experienced through the varying treatment methods available today.

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Appendix A – Demographic Questionnaire

Age

Q. What is your current age?

Psychological and Physiological Responsibilities

Q. Support: Perception of current responsibilities?

• Low

• Medium

• High

Psychological and Physiological Support Received

Q. Support: Perception of current support received against responsibilities?

• Low

• Medium

• High

Present Professional or Employment Status

Q. Employment Status: Are you currently…?

• Employed for wages

• Self-employed

• Out of work and looking for work

• Out of work but not currently looking for work

• A homemaker

• A student

• Military

• Retired

• Unable to work

Pre CKD Diagnosis Professional or Employment Status

Q. Employment Status: Pre Diagnosis, were you…?

• Employed for wages

• Self-employed

• Out of work and looking for work

• Out of work but not currently looking for work

• A homemaker

• A student

- Military
- Retired
- Unable to work

Education

Q. Education: What is the highest degree or level of school you have completed? If currently enrolled, highest degree received.

- No schooling completed
- Nursery school to standard 8
- Some high school, no diploma
- High school graduate, diploma or the equivalent
- Some university credit, no degree
- Trade/technical/vocational training
- Bachelor's degree
- Master's degree
- Professional degree
- Doctorate degree

Population Group

Q. Ethnicity origin (or Race): Please specify your ethnicity.

- Black
- White
- Coloured
- Asiatic
- Other

Gender

Q. Ethnicity origin (or Race): Please specify your ethnicity.

- Female
- Male