

FACTORS RELATED TO DEPRESSION IN END-STAGE RENAL DISEASE PATIENTS

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ABSTRACT

High prevalence rates of depression have been well documented in patients with chronic kidney disease (Egede, 2007; U.S. Renal Data System, 2013). Furthermore, depression seems to play a major role in the mortality and morbidity rates of this population (Kellerman, Christensen, Baldwin, & Lawton, 2010; U.S. Renal Data System, 2013). Therefore this study aimed to discover factors that may influence depression in this population. Ten end-stage renal disease (ESRD) patients' depression scores were examined in relation to various sociodemographic measures. High depression scores had a significantly negative relationship with social functioning, overall quality of life, and age. A combined model of social functioning, sleep quality, and age provides a stronger prediction than any variable alone. Results suggest that targeting social functioning, sleep quality, and age should be the focus of future studies examining interventions of these factors as augmentations to current pharmacological treatments of depression in ESRD populations.

Keywords: End-Stage Renal Disease, Depression

DEDICATION

To Mom and Dad.

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LIST OF ABBREVIATIONS

ESRD, End-Stage Renal Disease

CKD, Chronic Kidney Disease

CESD-R, Center for Epidemiologic Studies Depression Scale, Revised Version

SF-36, Short-Form 36 Health Related Quality of Life Questionnaire

PSQI, Pittsburgh Sleep Quality Index

SERRI, Southeastern Renal Research Institute

DSM-IV, American Psychiatric Association Diagnostic and Statistical Manual, Fourth Edition

SPSS, Statistical Package for the Social Sciences

HIPAA, Health Insurance Portability and Accountability Act

KDQoL-SF, Kidney Disease Quality of Life Questionnaire, Short Form

PAQoL, Patient-Assessed Quality of Life index

WHOQOL-BREF, World Health Organization Quality of Life assessment, abbreviated version

CHAPTER I

INTRODUCTION

Depression affects many people around the world regardless of age, health, gender, and ethnicity. However, research has shown that those with chronic diseases such as end-stage renal disease (ESRD) show higher rates of depression and are more prone to depressive symptoms compared to the general public (Egede, 2007; U.S. National Library of Medicine, 2014; U.S. Renal Data System, 2013). Furthermore, within the ESRD population, it has been shown that higher levels of depression may be predictive of higher mortality rates (Kellerman et al., 2010; U.S. Renal Data System, 2013). These two findings point to the increased need to reduce depression in those with chronic diseases. The current study aims to provide more information about the relationship of depression with other individual factors in kidney disease patients. The ultimate goal is to use this information to develop better intervention strategies that can lower the depression levels of those with chronic diseases, which may lead to lower mortality and improve the quality of life in this population.

Background

End-Stage Renal Disease (ESRD) is known as the fifth and final stage of Chronic Kidney Disease (CKD), and can be characterized by the individual requiring either a kidney transplant or some form of dialysis in order to live (U.S. National Library of Medicine, 2014). In 2011 it was estimated that nearly 400,000 people suffer from ESRD in the United States alone (U.S. Renal

Data System, 2013). Many times ESRD results from long-term kidney problems due to diabetes or hypertension, with diabetes accounting for one-third and hypertension accounting for one-fourth of the ESRD incidents in 2011 (U.S. Renal Data System, 2013). Additionally, ESRD patients often suffer from a variety of comorbidities, including cardiovascular disease, depression, and malnutrition, with depression being one of the most prevalent in the population. Multiple studies estimate the prevalence of depression to be between 20% and 25% in ESRD patients, as compared to a 2% to 4% prevalence in the United States population (Chiang, Livneh, Yen, Li, & Tsai, 2013; Egede, 2007; Kimmel, Cukor, Cohen, & Peterson, 2007). This high prevalence of depression within the ESRD population warrants even more attention due to the link between depression and increased mortality rates in those with ESRD. Several studies show significant positive correlations between depression and mortality in the ESRD population, including some results that indicate depression is associated with nearly a 22% increase in mortality for depressed patients compared to those who do not suffer from depressive symptoms (Kellerman et al., 2010; van Dijk et al., 2012; Ver Halen, Cukor, Constantiner, & Kimmel, 2012).

Objectives of the Study

The literature and statistics discussed in the previous section provide the rationale for setting the focus of the current study on depression and determining what factors play a role in the depression symptoms of this particular population. The main goal of the study is to provide more information on the roles of social functioning, quality of life, sleep quality, and length of time on dialysis in ESRD patients, to determine which factors may have the strongest relationship with depression in this population. With this information it is hoped that additional

treatments or care-taking strategies can be implemented that would promote the reduction of depression symptoms in ESRD patients, which may subsequently lower the mortality rate and increase quality of life. Furthermore, prolonging the lifespan of this population is crucial as it gives these patients more time to receive a transplant, which is well documented to have a tremendous effect on quality of life and life expectancy compared to dialysis patients (Álvares, Cesar, de Assis Acurcio, Andrade, & Cherchiglia, 2012; U.S. National Library of Medicine, 2014; U.S. Renal Data System, 2013).

The present study looks at perceived social functioning, quality of life, sleep quality, and age – factors studied previously in the literature. It adds to this literature by verifying previous findings, clarifying the literature on the effects of length of time on dialysis, while also contributing unique information by examining the effect of these factors combined. The following literature review examines each of the factors included in this study in detail, to understand what has previously been done and what is still missing from the literature.

CHAPTER II

LITERATURE REVIEW

Review of Related Studies

Social Functioning

Past research on factors that influence depression in ESRD patients has focused primarily on psychosocial factors such as perceived social support. It is important to notice the focus of perceived support, as the depression symptoms observed are often a result of how much support the patient perceives, rather than the amount of support an objective measure might suggest. Additionally, it is also important to note that social support is a broad term used to encompass a range of social constructs. Many have argued that the term social support is not specific enough to be a reliable research measure, because it is a measure that includes too many factors that should be studied individually (Barrera, 1986; Cohen & McKay, 1984; Cohen & Wills, 1985; Heller, 1979). The present study heeds to these suggestions by studying a specific aspect of support (social functioning) to determine how it may be related to depression symptoms in ESRD patients, compared to common literature studies focusing on social support as a generic term.

In one of the first studies examining social support as defined generically in ESRD patients, Christensen, Turner, Slaughter, and Holman (1989), grouped 57 ESRD patients into a high or low group based on their reported support levels. Christensen et al. (1989) found that those in the high social support group showed significantly lower depression and higher

psychological well-being levels compared to those in the low social support group. An additional study by Christensen and colleagues grouped subjects into a high support group and low support group, finding the group with low perceived support had a mortality rate of 58%, nearly three-times higher than those with high perceived support with a rate of 18% (Christensen, Wiebe, Smith, & Turner, 1994). Several others have also documented the impact of perceived social support on depression. Chan and colleagues (2011) conducted a meta-analysis of 57 studies to examine the role of the most commonly studied psychosocial factors, such as social support (subjective and objective), stress, and personality attributes, in chronic dialysis patients to assess which factors had the most significant impact on depression levels. Results of this meta-analysis showed perceived social support, along with stress, to have significantly higher effect sizes than all other factors, .33 and .37 respectively, in a pooled sample that included nearly 6,000 subjects (Chan et al., 2011).

In addition to the ESRD population, more recent research has shown the relation between social support and depression to hold steady in otherwise healthy populations as well. Wang and Zhao (2012) studied the relationship between depression and social support by comparing a group of older adults (ages 60-80) diagnosed with major depressive disorder to a group of non-depressed older adults in the same age group. Results showed that the depressed group showed significantly less perceived social support than the non-depressed group. Similar results were found in a study of depressed young adults (ages 16-21) with no comorbidities, where perceived social support was associated with lower levels of stress and depression (Raffaelli et al., 2013).

In summary, perceived social support plays an important role in depression levels of ESRD patients. It is not yet known whether specific subtypes of support, such as social functioning are equally important in depression. As Barrera (1986) suggests, the use of more

specific measures of social support should provide a more accurate view of the relation between support and depression.

Health Related Quality of Life

Health related quality of life refers to a combination of both physical and mental health factors (Ware & Sherbourne, 1992), and is another factor that is thoroughly discussed in the literature of ESRD patients. Health related quality of life is often measured by subjective report, similar to perceived social support, as it is often the perceived physical or mental health that is of interest when studying depression. While a great amount of literature focuses on perceived social support, a considerable amount of research has also explored the overall health related quality of life of ESRD patients. In addition, a recent study suggests that health related quality of life is becoming an even more important factor to consider for today's ESRD patients as medical advances have helped increase the life expectancy of patients on dialysis (Glover, Banks, Carson, Martin, & Duffy, 2011).

With an increase in life expectancy, the quality of life in the ESRD population must be monitored more closely. To better monitor health related quality of life, it is crucial to understand what factors influence it in the ESRD population. In their study of 49 ESRD patients, Steele et al. (1996) found that depression was strongly correlated to health related quality of life scores, as measured by the Patient-Assessed Quality of Life index (PAQoL), and advised that the link between the two should be considered carefully when devising caretaking plans for this population. More recent research has further accentuated the relationship between depression and health related quality of life. In 2005, a study of 194 dialysis patients showed depression was correlated more highly with health related quality of life than any other psychosocial factor

included in the study (Vázquez et al., 2005). Perales-Montilla, Garcia-Leon, and Reyes-del Paso (2012) also found depression to be a significant predictor of low health related quality of life in a sample of ESRD patients. These results reflect the need to consider health related quality of life as a factor that may influence depression in the current study, to determine if it should be a target for caretaking strategies of those suffering from both depression and ESRD.

Sleep Quality

Like poor health related quality of life, sleep disturbances are also frequently reported among ESRD patients (Brekke et al., 2013). Estimates from recent literature report between 65% and 75% of ESRD patients suffer from “poor sleep” as subjectively rated using the Pittsburgh Sleep Quality Index (PSQI), a commonly used measure of sleep quality in the ESRD literature (Brekke et al., 2013; Iliescu et al., 2003; Kusleikaite, Bumblyte, Razukeviciene, Sedlickaite, & Rinkunas, 2005). The high prevalence of sleep disturbances mark sleep quality as another target for inspection to determine if it has a role in predicting depression scores. An assortment of recent studies on ESRD patients’ sleep quality conclude that it does. Brekke et al. (2013) studied 301 dialysis patients to determine the association between sleep quality, as measured by the PSQI, and depression. The PSQI measure characterizes “poor sleep” as a score of greater than 5 out of 21 on a range of questions about patients’ sleep quality in the last month. The results showed “poor sleep” was significantly related to depression, and that “poor sleepers” scored significantly lower on mental components of health related quality of life measures than good sleepers. In another study, self-reported cases of insomnia were found to be associated with higher depression levels (Paparrigopoulos, Theleritis, Tzavara, & Papadaki, 2009). Additionally, poor sleep quality may lead to more problems and higher depression in otherwise healthy adults

as well. In a large sample of over 3,000, “poor sleepers” assessed by the PSQI showed an increase in comorbidities (60%) compared to “good sleepers” (38%), while the proportion of depression increased significantly as sleep quality worsened (Hayashino et al., 2010).

Collectively, this literature provides another possible link with depression that can be assessed through the present study, to determine if sleep quality should be another focus when considering ways to lower depression levels in the ESRD population.

Length of Time on Dialysis

Unlike some of the other factors discussed thus far, length of time on dialysis is an important demographic factor in this population that is not often examined or discussed in the literature regarding the ESRD population. Early research reported a significant relationship between length of time on dialysis and self-reported depression (Kutner, Fair, & Kutner, 1985), and more recently, a study found a significant difference in the perceived consequences of treatment in participants with varying lengths of time on dialysis (Jansen et al., 2013). In this study, perceived consequences of treatment were assessed by the Treatment Effects Questionnaire which asks the participant to answer questions about the impact of side-effects due to treatment, how much their life revolves around the treatment, and whether the treatment “keeps them from enjoying themselves.” Results of this study showed that the perceived treatment consequences were significantly more negative for patients who were on dialysis for longer lengths of time (Jansen et al., 2013). These studies provide some evidence that length of time on dialysis may play a role in depression levels of ESRD patients. However, despite these findings the topic is still greatly understudied and needs to be further established in the literature.

Although evidence of a direct association between time on dialysis and depression scores is substantially understudied in the ESRD population, some studies have shown associations between time on dialysis and other factors that may be indirectly related to depression levels, such as adherence to treatment (Hudson, Fielding, Jones, & McKendrick, 1987). In contrast to length of time on dialysis, the association between adherence to medical treatment and depression in ESRD and other chronic disease populations is well documented in the literature (Bolkan et al., 2013; Sacco et al., 2007; Theofilou, 2013; Zhang et al., 2013). Collectively these findings provide evidence that length of time on dialysis could play an indirect role in depression levels.

Age

Age, like gender, is a common demographic collected in research that it is included in nearly every study regardless of the topic. The same is true for ESRD and depression studies; however, the results of the literature in the particular area of depression in ESRD populations may not be as transparently logical compared to other studies examining age effects. Studies that include age effects in their studies on depression in ESRD populations have found some interesting results as to which age group is more depressed. A study by Laudanski, Nowak, and Niemczyk (2013) examined quality of life, depression, and coping strategies of ESRD patients to determine if there were any age related differences in the way younger (mean age = 47.1) and older adults (mean age = 68.3) cope with their disease. It was found that while both groups showed higher levels of depression than a healthy, age-matched control group, younger ESRD patients showed higher levels of depression, and more frequently used emotional preoccupation strategies to cope than the older patient group. Additionally, younger patients made significantly

more complaints about sleep disturbances, which correlate strongly with depression levels, as reviewed earlier.

Additional studies have found similar results in ESRD populations, in which age is negatively correlated with depression and other measures of mental health (Chilcot et al., 2011; Griva et al., 2014). With these studies in mind, it is of interest to look more closely at age and its relationship with depression.

The Present Study

Many of the factors included in the present study have been shown in the literature to have either a direct, or possibly indirect, relationship with depression, providing the logic for including each of them in exploring some of the factors that might help better predict experiences of depression in ESRD patients. However, in the same way each of the factors is connected, they also each provide a unique target for intervention when it comes to the care of this population because they each examine the issue of depression from a different aspect. Therefore, the present study was designed to determine which of the factors included (social functioning, health related quality of life, sleep quality, length of time on dialysis, and age) or which combinations of these factors best predict levels of depression in ESRD patients.

Hypotheses

Based on the previous review of the literature, the following hypotheses were explored in the present study. Depression scores in the present study were assessed using the Center for Epidemiologic Studies Depression Scale, Revised Version (CESD-R), which is detailed in the

following methodology section, as is the SF-36 Health Related Quality of Life questionnaire (SF-36) and Pittsburgh Sleep Quality Index (PSQI).

H1: Perceived social functioning, as measured by the SF-36 subscale, will have a significant negative relationship with depression scores.

H2: Overall health related quality of life, as measured by the SF-36, will have a significant negative relationship with depression scores.

H3: Quality of sleep, as measured by the PSQI, will have a significant positive relationship with depression scores, as in this measure, higher scores are equivalent to a poorer quality of sleep.

H4: Length of time on dialysis will have a significant positive relationship with depression scores.

H5: Age will have a significant negative relationship with depression scores.

H6: ESRD participants will score significantly differently from healthy controls on measures of depression, social functioning, health related quality of life, and sleep quality.

CHAPTER III

METHODOLOGY

Participants

A sample of ESRD participants was recruited between November, 2012, and February, 2014, as part of a larger study (Tumlin, Harris, & Whitson, 2012) by a local kidney research institute (Southeastern Renal Research Institute, SERRI) in Chattanooga, Tennessee. Recruited participants were tested based on their availability, willingness to participate, and various inclusion and exclusion criteria. The full list of inclusion and exclusion criteria is included in Appendix A. Fifteen participants were recruited and qualified for testing during the study period; ten participants (66.7%) gave informed consent and completed the study. Two participants were excluded from the analysis on any model that included length of time on dialysis due to missing data, therefore the simple regression and multiple regression models that included length of time on dialysis were analyzed with only 8 participants. Demographic and medical data were collected after participants consented to this study, while all other participant data was collected at a single visit at the SERRI clinic prior to further tests included in the larger study (Tumlin et al., 2012) to ensure testing fatigue did not play a role in participants' responses. Five healthy (non-kidney disease) controls, matched on age, gender, and race, were recruited from a community sample to compare the kidney disease sample to the healthy sample on depression, social functioning, health related quality of life, and sleep quality.

Measures

Demographics

Demographic and medical data for ESRD participants included age, gender, race, and length of time on dialysis. Of the ten kidney disease participants, eight were male and two were female, four were Caucasian and six were African American. The ESRD sample had a mean age of 56.6 (SD = 12.3) ranging from 36 to 73, and the mean time on dialysis was 75.5 months (SD = 97.8) with a range of 3.2 to 251.4. The median time on dialysis was 29.9 months, which may be a more informative measure of central tendency due to the small sample size in this study. Of the five healthy control participants, four were male and one was female, four were Caucasian and one was African American. The mean age of the group was 54.4 (+/- 11.8) ranging from 42 to 70.

Center for Epidemiologic Studies Depression Scale, Revised Version

The Center for Epidemiologic Studies Depression Scale, Revised Version (CESD-R) is used to measure depression as defined by the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-IV) (Eaton, Smith, Ybarra, Muntaner, & Tien, 2004). The scale consists of 20 questions and measures depression symptoms on a Likert scale of 0 to 3 responses for all 20 questions, where 0 corresponds to the lowest level of depressive symptoms and 3 to the highest level of depression symptoms. A patient's depression score is obtained by simply taking the sum of all responses for a possible score of 0 to 60. The diagnostic cut-off for exhibiting clinical depression symptoms is 16, with varying levels of diagnosis (mild, moderate, severe) for those scoring above the cutoff. For the purposes of this study, the overall score from 0 to 60 for each participant was used in the analyses to represent depression level. Reliability and validity

analyses for this scale have demonstrated high reliability with a Chronbach's α of .928 and high convergent and divergent validity (Eaton et al., 2004; Van Dam & Earleywine, 2011).

Short Form – 36 Health Related Quality of Life Questionnaire

The Short Form-36 Health Related Quality of Life Questionnaire (SF-36) is a measure of quality of life relating to health issues, particularly measuring mental and physical components (Ware & Sherbourne, 1992). The scale consists of 36 questions that assess eight subscales, including social functioning, and two main components of mental and physical health. All questions use a Likert scale, with each question varying in the range of responses (0-3, 0-5, 0-6). Scoring of the SF-36 for each component and subscale is achieved by converting the raw score to a percentage score, where a score of 100 represents the highest possible level of functioning and 0 represents the lowest possible level of functioning. For the purposes of this study, the social functioning percentage score and the mean of all subscale percentage scores are used in analysis to represent perceived social functioning and overall quality of life, respectively. Reliability and validity estimates of the social functioning subscale and the questionnaire overall both show a Chronbach's α of .85, and high convergent and discriminant validity (McHorney, Ware, Lu, & Sherbourne, 1994).

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) is a self-report questionnaire used to assess sleep quality and disturbances over the month prior to the subject taking the questionnaire (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). The questionnaire consists of nine questions, some of which are free quantitative responses about sleep time and latency, and others

on a Likert Scale from 0 to 3. The scale can be separated into seven components, or used as an overall measure that is equal to the sum of each component score. Component scores are computed on a 0 to 3 scale, while the overall score has a range from 0 to 21, where an overall score of 5 or greater indicates “poor sleep.” For the purposes of this study, the overall score from 0 to 21 for each participant is used in the analyses to represent sleep quality. It is important, for interpretive purposes, to be mindful that a higher score indicates worse sleep quality for the PSQI. Reliability and validity analyses conducted by the creators of the questionnaire revealed strong reliability with an overall Chronbach’s α of .83, and significant convergent validity correlations (Buysse et al., 1989).

Procedure

Participants were recruited at the SERRI clinic during a routine visit. After consenting, kidney disease participants were scheduled for an appointment at SERRI at a later date for data collection. Upon arrival at SERRI on the day of the appointment, participants were given a questionnaire packet including the PSQI, SF-36, and CESD-R in that order. After completing the packet, the participant’s involvement in this particular study was complete and they were free to continue with the procedures of the larger study (Tumlin et al., 2012). If participants completed the larger study, they were given \$100 for their participation. Controls were recruited based on age, gender, and race match with a kidney disease participant and availability in the greater Chattanooga, Tennessee area. All healthy control data were collected in a single visit at The University of Tennessee at Chattanooga. Controls were not incentivized for their participation in the study. All data from ESRD participants and controls were entered into an encrypted

Statistical Package for Social Sciences file for analysis. All individuals involved in the collection or analysis of the data were HIPAA certified in the protection of human rights.

Statistical Analysis

IBM's SPSS version 21 for Macintosh (IBM Corporation, 2012) was used for all of the analyses in the study. First, an independent samples t-test was conducted to test for differences between the healthy and kidney disease samples on age and measures of social functioning, overall quality of life, sleep quality and depression. Age was tested here because not all ESRD participants were matched with a healthy control. The t-test was used to test for any significant difference in age between the control and kidney disease participants. Next, simple regressions for each variable included in the study were run for the kidney disease group. These regressions tested each factor's relationship to depression scores. Finally, multivariate regression models were used to determine if any combination of variables added significantly to the prediction of depression scores in this sample. These models were compared to simple regression models to assess the uniqueness of each predictor while the other variables were held constant.

CHAPTER IV

RESULTS

Findings

An independent samples t-test analysis was conducted first to determine if there was a difference between the kidney disease sample and the healthy sample on measures of social functioning, health related quality of life, sleep quality, and age. The results of analyses comparing the groups are shown in Table 4.1. It is important to note that there was no significant difference between the groups in age. These results indicate that age should not confound the other variables included in the analysis. Results of the analysis also showed that kidney disease participants differed significantly from the healthy control participants on measures of social functioning, overall quality of life, and sleep quality ($p < .05$). Depression levels between the two groups were marginally significant ($p = .075$).

Table 4.1

Independent Samples T-Test Results Between Kidney Disease and Control Group

Factor	Group	Mean	SD	<i>t</i>	<i>p-value</i>
Age	Healthy	54.4	11.8	-.331	.746
	Kidney Disease	56.6	12.3		
Depression	Healthy	5.2	4.0	-1.938	.075
	Kidney Disease	15.8	1.4		
Social Functioning	Healthy	95.0	14.5	3.284	.010
	Kidney Disease	62.5	19.9		
Overall Quality of Life	Healthy	82.1	3.3	3.019	.033
	Kidney Disease	51.6	11.8		
Sleep Quality	Healthy	4.5	11.2	-3.529	.006
	Kidney Disease	11.8	27.0		

Before the regression analysis, each variable was assessed for normality to determine if any transformations to the data were necessary. All tests of skewness and kurtosis indicated no need for transformations. Normal probability plots for each variable are shown in Appendix E.

For the kidney disease group, the relationship between each of the variables and depression was analyzed using SPSS's linear regression procedure. A univariate regression was conducted for each variable with depression. The results of these analyses are reported in Table 4.2. The individual analyses showed both social functioning ($p = .012$) and overall quality of life ($p = .007$) to be significantly negatively related to depression scores. Age ($p = .051$) was found to have a marginally significant negative relationship, while sleep quality ($p = .744$) and length of time on dialysis ($p = .193$) were not significant.

Table 4.2

Univariate Regression Analysis with Depression Results for Kidney Disease Participants

Factor	Pearson <i>r</i>	<i>p</i> -value	<i>t</i>	<i>p</i> -value
Social Functioning	-.755	.006	-3.252	.012
Overall Quality of Life	-.783	.004	-3.564	.007
Sleep Quality	.119	.372	.338	.744
Length of Time on Dialysis	-.514	.096	-1.468	.193
Age	-.630	.025	-2.294	.051

Next, multivariate analyses were conducted to determine if any combination of variables served as a stronger predictor than any individual variable alone. Using SPSS's linear regression procedure, a series of models were created to assess all combinations of the variables. Each model was compared on significance of the regression model, multiple *r*-square, and *r*-square change values to determine if the model added significantly to the previous model. Using this technique, 20 models were assessed, 7 of which were significant at a two-tailed *p*-value of less than .05. It was discovered that the model including social functioning, sleep quality, and age significantly predicted depression scores ($p = .007$) and accounted for the greatest amount of sample variance in the depression scores ($r^2 = .852$, adjusted- $r^2 = .778$) of all models. In this model, social functioning ($t = -3.939$, $p = .008$) and age ($t = -2.685$, $p = .036$) were significantly negatively related to depression scores, while sleep quality was marginally significant and positively related to depression scores ($t = 2.429$, $p = .051$).

Correlations of each variable are shown in Table 4.3. A model including the significant predictors from the univariate analysis (Social functioning, overall quality of life, age) was not significant, most likely due to multicollinearity (high correlation between variables). In a case of multicollinearity, the variable with the highest simple r is considered to have a stronger relationship. Therefore, if only one measure is available, the health related quality of life is the better measure in this study. In an additional note about the data analyses, sleep quality was not a significant predictor when used alone, however when controlling for two of the other variables (social functioning and age) it was. The variables that strengthen sleep quality's relationship with depression are called suppressor variables. With the relationship being positive, this finding indicates that when social functioning and age are equal, those who have low sleep quality (higher PSQI score) have high levels of depression.

Table 4.3

Simple Pearson r Correlations of Variables

	Depression	Social Functioning	Quality of Life	Sleep Quality	Time on Dialysis	Age
Depression	1	-.749	-.774	.308	-.514	-.569
Social Functioning	-	1	.907	-.026	.461	.225
Quality of Life	-	-	1	-.218	.280	.245
Sleep Quality	-	-	-	1	.026	.103
Time on Dialysis	-	-	-	-	1	.382
Age	-	-	-	-	-	1

Summary of Hypothesis Testing

H1: Perceived social functioning, as measured by the SF-36 subscale, was expected to have a significant negative relationship with depression scores. This hypothesis was supported by the data analyses. In both univariate and multivariate regression models, high levels of perceived social functioning were significantly related to lower depression scores in the sample.

H2: Overall health related quality of life, as measured by the SF-36, was expected to have a significant negative relationship with depression scores. This hypothesis was supported by the data analysis. Similar to social functioning, in both univariate and multivariate regression models, high levels of overall quality of life were significantly related to lower depression scores.

H3: Quality of sleep, as measured by the PSQI, was expected to have a significant negative relationship with depression scores. This hypothesis was partially supported by the data analysis. Quality of sleep was only significantly related to depression scores when its suppressor variables were included in a multivariate analysis. Social functioning, overall quality of life, as well as age acted as suppressor variables for sleep quality. When these factors were held constant, better quality of sleep was significantly related to lower depression scores.

H4: Length of time on dialysis was expected to have a significant positive relationship with depression scores. This hypothesis was not supported by the data analysis. In both univariate and multivariate regression models, length of time on dialysis was not significantly related to depression scores.

H5: Age was expected to have a significant negative relationship with depression scores. This hypothesis was supported by the data analysis. Although marginally significant ($p = .051$) in the univariate regression analysis, the multivariate analyses showed age to have a significant, negative relationship with depression scores, when social functioning and sleep quality were held constant.

H6: ESRD participants were expected to score significantly differently from the healthy controls on measures of depression, social functioning, health related quality of life, and sleep quality. The t-test analysis confirmed that in all measures except depression, the ESRD participants were significantly different from healthy controls ($p < .05$). In the measure of depression, ESRD participants scored only marginally significantly differently ($p = .075$) than healthy controls. In all measures, the ESRD participants scored worse than control participants (i.e. higher depression scores than healthy controls, lower social functioning scores than healthy controls, etc.)

CHAPTER V

DISCUSSION

Interpretation of Findings

The results of the t-test suggest some important factors that should be addressed when interpreting the findings of this study. While the ESRD group was marginally significantly different from the healthy group on the measure of depression, the mean of the ESRD group was only 15.8. The literature on the measure indicates that any score greater than or equal to 16 is considered showing clinical depression symptoms (Eaton et al., 2004). Therefore, while the ESRD participants may be different from the healthy control group, it is important to note that they are not showing very high symptoms of depression, as would be expected from the literature. This sample of ESRD participants may reflect a group of “super patients” that feel well enough to participate in a research study and may not be very representative of the ESRD population as a whole.

The results of the univariate regression analysis showed social functioning, overall quality of life, and age (marginally) to be significantly related to depression scores. For all of these factors the relationship to depression was negative, meaning that as social functioning, overall quality of life, or age increased, depression levels decreased. While many of these findings were expected based on the literature, the negative relationship between age and depression is interesting because the relationship is possibly counterintuitive compared to other studies on age effects in other populations. These results are consistent however with Laudanski

et al.'s (2013) findings that younger ESRD patients use more emotional preoccupation to cope with the disease than older ESRD patients. These results suggest it is possible that younger adults are more affected by the disease due to their life circumstances (i.e. taking care of their family) compared to older adults who may be less relied on by family members.

The results of the length of time on dialysis analyses were not significant; however, these results may warrant more consideration than other non-significant findings. The inclusion criteria listed in Appendix A, require the patients to be on dialysis for greater than three months. This criterion may have limited the sample to exclude a crucial period of time at first diagnosis where having ESRD can be the most impactful mentally. The length of time on dialysis may not be as much of a factor after being on dialysis for greater than three months, however, time since diagnosis may have an entirely different impact. The subjective response to being diagnosed may play a larger role in depression of ESRD patients, due to the substantial impact the disease treatment can have on one's life.

Multivariate analyses were used to determine the relationship between two or more variables while holding other variables in the analysis constant. This allows us to assess if the relationship is due to the variable, or other factors influencing the relationship. It also allows us to examine the relationship of a combination of the variables, to determine if a combination of variables has a stronger relationship to depression over any variable alone. The results of these analyses found the combination of social functioning, sleep quality, and age to account for the greatest amount of variability in the depression scores of the sample. The adjusted multiple r-square of .778 estimates what percentage of the differences that these variables would account for if applied to the population based on the number of predictors, and sample size. The high adjusted multiple r-square is particularly important in this study because of the unusually small

sample size, and suggests that these three factors could provide a focus for caretakers of ESRD patients. However, as mentioned previously, these results should be interpreted with caution due to the type of participants that were recruited for this study.

Limitations

The most outstanding limitation in the present study is the sample size of 10 for kidney disease participants and 5 for healthy controls. Sample sizes did not meet the projected amount during the data collection period due to withdrawals of consent, missed appointments, and difficulty of recruitment. As part of a larger study, recruitment and appointment scheduling involved many groups and individuals to be available, and required the participants to show up for their scheduled appointment. Along with a small sample size, the unequal distribution of males ($n = 8$) to females ($n = 2$) as well as the missing data on length of time on dialysis for two participants, made the analysis of gender as a factor unfeasible and any analysis that included length of time on dialysis was restricted to 8 participants, further shrinking an already small sample size. Furthermore, the sample used in this study was made up of ESRD patients that were willing and able to participate in the study. This factor may have influenced the results of the analysis as these ESRD patients might be considered “super subjects” that are healthier than other ESRD patients, and who may not be representative of the population as a whole consequently.

Another limitation of the present study involves the measures that were used. The SF-36 health related quality of life scale, and subscale measure of social functioning may not be the strongest measure of quality of life and social functioning in the ESRD population according to a review by Glover et al. (2011) comparing the content validity of six different quality of life

measures across various studies on quality of life in the ESRD population. Out of 378 articles reviewed, it was found that the SF-36 measure was the most commonly used, however, the KDQOL-SF had the highest content validity of all six measures reviewed. This disease specific measure may provide a more valid and accurate assessment of quality of life, compared to a generic measure, in ESRD patients specifically. However, while a disease specific measure will most likely be more valid in studying the ESRD population, there are some circumstances where a generic measure may also be appropriate, most notably in a comparison to other chronic disease populations. Disease specific measures do not allow for these comparisons across populations, therefore, in these circumstances a generic measure may be more appropriate. In these instances, the review by Glover et al. (2011) found the World Health Organization Quality of Life assessment, abbreviated version (WHOQOL-BREF) to be a more appropriate measure in respect to content validity compared to the other general health related quality of life questionnaires reviewed, including the SF-36. The authors suggest that the widespread use of the SF-36 in this population is the result of it being used commonly in studies of other chronic diseases and that its data is easy to compare across different groups. However, the authors caution the use of this measurement because it does not measure all aspects of quality of life of the ESRD population, and suggest the use of the WHOQO-BREF as it is similarly short, and easy to administer, while also providing a measure of the aspects of quality of life that the SF-36 misses (Glover et al., 2011). This review provides a claim that future studies should be used to strengthen the body of research on alternative quality of life measures for a better comparison between the many different measures.

Recommendations for Future Studies

Future studies should examine these factors in a larger sample size, using a disease specific measure of social functioning instead of a generic measure and subscales of quality of life. Although not all factors were significant, a larger sample size with more accurate measures could find vastly different results, while also providing more data on other quality of life measures in the ESRD population. These results could be used in comparison to other studies using a generic quality of life measure to determine if a disease specific measure provides more accurate results in studies on this population.

Furthermore, longitudinal studies examining the impact of these same factors included in the present study over a period of time would help determine which of these events was the original problem. With correlational data, no inference can be made about which factor caused which. Longitudinal analyses could answer some important questions, such as, “Does depression cause poor sleep quality? Or does poor sleep quality cause depression?” With answers to these questions, caretaking strategies could better focus on the original problem, rather than treating the symptoms.

Additionally, objective measures of social support, quality of life, sleep quality, and depression should be considered in future studies. All measures included in the present study were self-report. The discrepancy between perceived support or quality of life and actual support or quality of life as measured by family members and friends could provide more insight as to what treatments may be most effective. For example, increasing the presence of available social support may not be an effective treatment option if the patient claims to have a different level of support than what family members and friends report. The problem in these cases may be a

perception issue, rather than an actual level of support issue, which should be an important factor to consider when deciding treatment options for these patients.

Other studies could involve testing the effectiveness of interventions based on these results to determine if there are any effective augmentations to current depression treatments for kidney disease patients suffering from depression symptoms. An example of these studies include testing the effectiveness of interventions to increase sleep quality in kidney disease patients, a goal of the larger study (Tumlin et al., 2012) from which the present study was conducted. With the increasing life expectancy of these patients, it is crucial to conduct these studies to determine the safest and most efficient way to lowering depression prevalence and increasing quality of life in this population. Future studies looking at similar constructs could also be expanded to other chronic diseases with similar statistics as ESRD populations to determine if these factors are disease specific or can be generalized to other populations.

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APPENDIX A
INCLUSION/EXCLUSION CRITERIA

Inclusion Criteria:

- 1) Patient age > 18 and <85 years of age
- 2) Patients with CKD or ESRD with eGFR < 30 mls/min
- 3) If receiving hemodialysis, patients must be on treatment > 3 months
- 4) Normal healthy controls must be without a known history of CKD and be willing to have formal PSG test and plasma melatonin measurements

Exclusion Criteria:

- 1) Patients receiving outpatient hemodialysis for < 3 months
- 2) Patients with estimated GFR by Cockcroft Gault > 30 mls/min
- 3) Patients receiving beta blocker therapy within one month of randomization
- 4) Patients receiving Nifedipine therapy within one month randomization
- 5) Patients on peritoneal dialysis
- 6) Patient with chronic home oxygen supplementation
- 7) Patients receiving chronic home CPAP therapy
- 8) Patients actively receiving outpatient sleep medications
- 9) Patients with diabetic gastroparesis unresponsive to medication
- 10) Patients with known pregnancy or unwilling to use contraception during the course of the study
- 11) Patients with a functioning renal allograft
- 12) Patient currently receiving long-term immunosuppressive therapy. Patients receiving low dose prednisone (10mg or less per day) will not be excluded from this trial
- 13) Unable to give informed consent

APPENDIX B

SF-36 HEALTH RELATED QUALITY OF LIFE QUESTIONNAIRE (SF-36)

SF-36

Name _____

Date _____

Moderator _____

- 1) In general, would you say your health is: (circle one)
 - a) Excellent
 - b) Very good
 - c) Good
 - d) Fair
 - e) Poor

- 2) Compared to one year ago, how would you rate your health in general now? (circle one)
 - a) Much better now than one year ago
 - b) Somewhat better now than one year ago
 - c) About the same
 - d) Somewhat worse now than one year ago
 - e) Much worse now than one year ago

Place a check mark or “X” in the appropriate box. Only select one for each question.

In a typical day, does your health now limit you in these activities? If so, how much?	Yes, Limited a Lot	Yes, Limited a Little	No, Not Limited at All
3. Vigorous activities , such as running, lifting heavy objects, participating in strenuous sports			
4. Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf			
5. Lifting or carrying groceries			
6. Climbing several flights of stairs			
7. Climbing one flight of stairs			
8. Bending, kneeling, or stooping			
9. Walking more than one mile			

Place a check mark or “X” in the appropriate box. Only select one for each question.

In a typical day, does your health now limit you in these activities? If so, how much?	Yes, Limited a Lot	Yes, Limited a Little	No, Not Limited at All
10. Walking several blocks			
11. Walking one block			
12. Bathing or dressing yourself			

Place a check mark or “X” in the appropriate box. Only select one for each question.

During the past 4 weeks , have you had any of the following problems with your work or other regular daily activities as a result of your physical health ?	Yes	No
13. Cut down on the amount of time you spent on work other activities		
14. Accomplished less than you would like		
15. Were limited in the kind of work or other activities		
16. Had difficulty performing the work or other activities (for example, it took extra effort)		

Place a check mark or “X” in the appropriate box. Only select one for each question.

During the past 4 weeks , have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?	Yes	No
17. Cut down on the amount of time you spent on work other activities		
18. Accomplished less than you would like		
19. Were limited in the kind of work or other activities		

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

(Circle one)

- a) Not at all
- b) Slightly
- c) Moderately
- d) Quite a bit
- e) Extremely

21. How much **bodily** pain have you had during the **past 4 weeks**? (Circle one)

- a) None
- b) Very mild
- c) Mild
- d) Moderate
- e) Severe
- f) Very severe

22. During the **past 4 weeks**, how much **pain** interfered with your normal work (including both work outside the home and house work)? (Circle one)

- a) Not at all
- b) A little bit
- c) Moderately
- d) Quite a bit
- e) Extremely

Place a check mark or “X” in the appropriate box. Only select one for each question.

During the past 4 weeks ...	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little Bit of the Time	None of the Time
23. Did you feel full of pep?						
24. Have you been a nervous person?						
25. Have you felt so down in the dumps that nothing could cheer you up?						
26. Have you felt calm and peaceful?						
27. Did you have a lot of energy?						

Place a check mark or “X” in the appropriate box. Only select one for each question.

During the past 4 weeks...	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little Bit of the Time	None of the Time
28. Have you felt downhearted and blue?						
29. Did you feel worn out?						
30. Have you been a happy person?						
31. Did you feel tired?						

32. During the **past 4 weeks**, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?
(Circle one)

- a) All of the time
- b) Most of the time
- c) Some of the time
- d) A little of the time
- e) None of the time

Place a check mark or “X” in the appropriate box. Only select one for each question.

How true or false is each of the following statements for you?	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
33. I seem to get sick a little easier than other people					
34. I am as healthy as anybody I know					
35. I expect my health to get worse					
36. My health is excellent					

APPENDIX C
CENTER FOR EPIDEMIOLOGIC STUDIES DEPRESSION SCALE,
REVISED VERSION (CESD-R)

CESD-R

Name _____

Date _____

Moderator _____

Place a check mark or “X” in the appropriate box. Only select one for each question.

Below is a list of the ways you might have felt or behaved. Please check the boxes to tell me how often you have felt this way in the past week or so.	Last Week				Nearly every day for 2 weeks
	Not at all <i>or</i> Less than 1 day	1-2 days	3-4 days	5-7 days	
1) My appetite was poor.					
2) I could not shake the blues.					
3) I had trouble keeping my mind on what I was doing.					
4) I felt depressed.					
5) My sleep was restless.					
6) I felt sad.					
7) I could not get going.					
8) Nothing made me happy.					
9) I felt like a bad person.					
10) I lost interest in my usual activities.					
11) I slept much more than usual.					

12) I felt that I was moving too slowly.					
13) I felt fidgety.					
14) I wished I were dead.					

Place a check mark or "X" in the appropriate box. Only select one for each question.

Below is a list of the ways you might have felt or behaved. Please check the boxes to tell me how often you have felt this way in the past week or so.	Last Week				Nearly every day for 2 weeks
	Not at all <i>or</i> Less than 1 day	1-2 days	3-4 days	5-7 days	
15) I wanted to hurt myself.					
16) I was tired all the time.					
17) I did not like myself.					
18) I lost a lot of weight without trying to.					
19) I had a lot of trouble getting to sleep.					
20) I could not focus on the important things.					

APPENDIX D
PITTSBURGH SLEEP QUALITY INDEX (PSQI)

PSQI

Number _____

Date _____

During the past month,

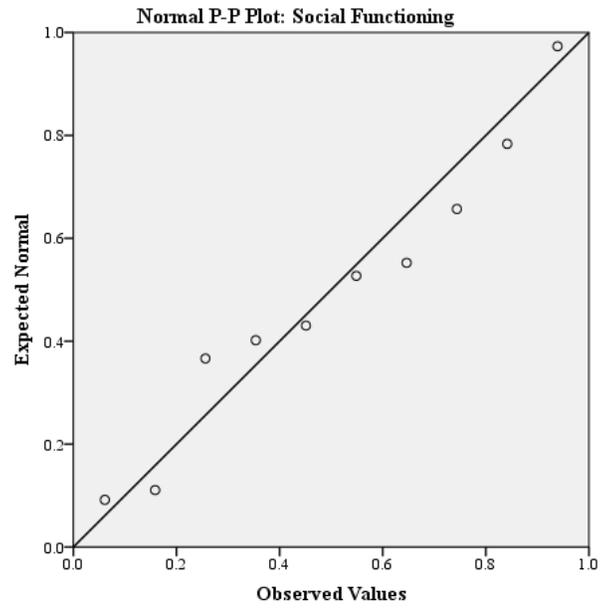
1. When have you usually gone to bed (what time)? _____
2. How long (in minutes) has it taken you to fall asleep each night? _____
3. When have you usually gotten up in the morning? _____
4. How many hours of actual sleep do you get at night? (This may be different than the number of hours you spend in bed) _____

5. During the past month, how often have you had trouble sleeping because you...	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Cannot get to sleep within 30 minutes				
b. Wake up in the middle of the night or early morning				
c. Have to get up to use the bathroom				
d. Cannot breathe comfortably				
e. Cough or snore loud				
f. Feel too cold				
g. Feel too hot				
h. Have bad dreams				
i. Have pain				
j. Other reason(s), please describe, including how often you have trouble sleeping because of this reason(s):				
6. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity				
8. During the past month, how much of a problem has it been for you to keep your enthusiasm to get things done?				

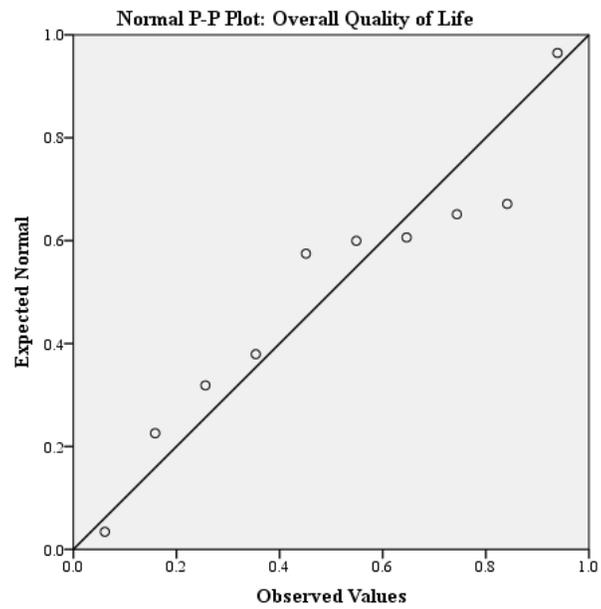
	Very Good	Fairly Good	Fairly Bad	Very Bad
9. During the past month, how would you rate your sleep quality overall?				

APPENDIX E
NORMAL PROBABILITY PLOTS OF VARIABLES

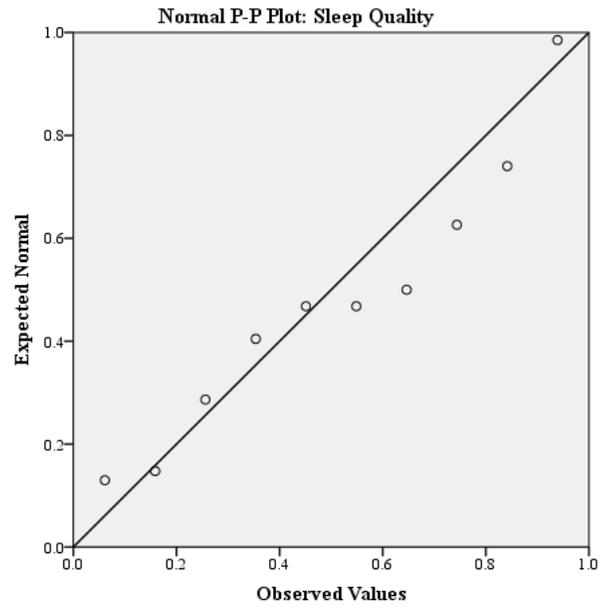
Social Functioning



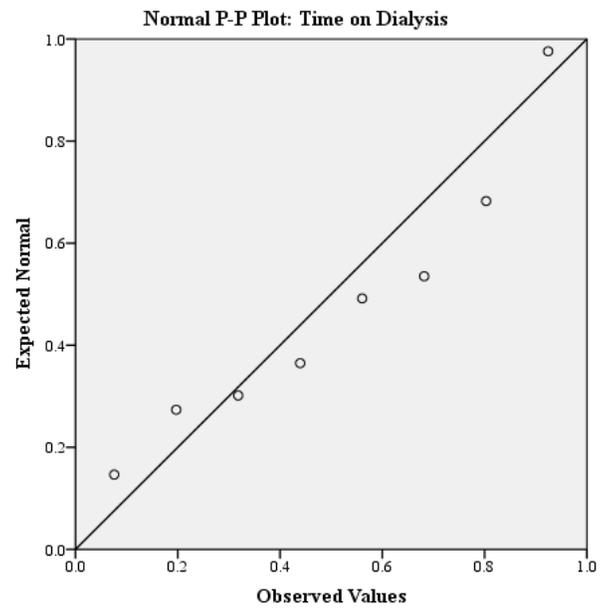
Overall Quality of Life



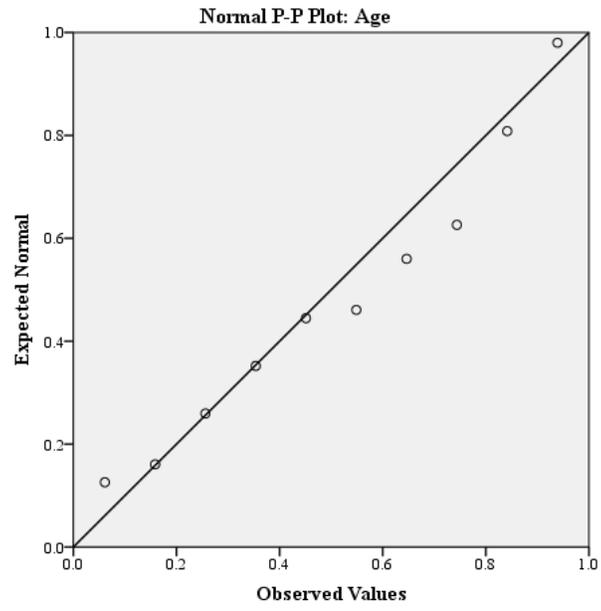
Sleep Quality



Time on Dialysis



Age



APPENDIX F
INFORMED CONSENT DOCUMENT

Informed Consent Form

While we hope that you will complete the attached study, your participation is voluntary. You may elect not to participate at any time. In addition, if you do not feel comfortable answering any of the questions you may leave that question blank and continue with the rest of the study. The information you provide will be anonymous and we do not ask you to identify yourself in any way. Boredom and Nasal Dryness are the only risks associated with your participation in this project. You will not receive any direct benefit from participating in the study.

This first part of the study will ask you to respond to questions about sleeping, general health, and recent feeling or behaviors. The second part of the study will ask you to identify smells located on scratch and sniff booklets. The third part will ask you to respond whether or not you detected an odor in a tube. The last thing the study asks you to do is fill out a demographic page. The demographic information will ask about age, gender, ethnicity, occupation, education, smoker vs. non-smoker, history with health illnesses, and any medications being taken. These questions will help us to interpret the results of the rest of the study.

We expect that it will take approximately 1 hour to participate in this study.

Remember, this is an anonymous survey, so please do not write your name anywhere other than this page.

You may also request a copy of this form for your records.

Who to Contact

If you have any questions or would like to obtain a report of this research study when the results have been completed, please contact Dr. Nicky Ozbek (423-425-4262), Department of Psychology, University of Tennessee at Chattanooga. This survey is being conducted as part of a Student Senior Research Project. This project meets the requirements for approval by the UTC IRB and contact can be made to the UTC IRB through Director Lindsay Pardue (423-425-4443) and Chair Dr. Bart Weathington (423-425-4289).

Thank you for participating in our research!

Name (Print) _____ **Date** _____

Signature _____ **Date** _____

APPENDIX G
IRB APPROVAL DOCUMENTS

MEMORANDUM

TO: Dr. Nicky Ozbek
Dr. James Tumlin **IRB # 12-196**

FROM: Lindsay Pardue, Director of Research Integrity
Dr Bart Weathington, IRB Committee Chair

DATE: November 28, 2012

SUBJECT: IRB Application # 12-196: Olfactory Sensitivity and Depression in Dialysis Patients

The IRB Committee Chair has reviewed and approved your application and assigned you the IRB number listed above. You must include the following approval statement on research materials seen by participants and used in research reports:

The Institutional Review Board of the University of Tennessee at Chattanooga (FWA00004149) has approved this research project # 12-196.

Since your project has been deemed exempt, there is no further action needed on this proposal unless there is a significant change in the project that would require a new review. Changes that affect risk to human subjects would necessitate a new application to the IRB committee immediately.

Please remember to contact the IRB Committee immediately and submit a new project proposal for review if significant changes occur in your research design or in any instruments used in conducting the study. You should also contact the IRB Committee immediately if you encounter any adverse effects during your project that pose a risk to your subjects.

For any additional information, please consult our web page <http://www.utc.edu/irb> or email us at: instrb@utc.edu.

Best wishes for a successful research project.

MEMORANDUM

TO: Dr. Nicky Ozbek IRB # 12-196

FROM: Lindsay Pardue, Director of Research Integrity
Dr. Bart Weathington, IRB Committee Chair

DATE: January 10, 2013

SUBJECT: IRB #:12-196: Olfactory Sensitivity and Depression in Dialysis Patients

The Institutional Review Board has reviewed and approved the following changes for the IRB project listed below:

- We would like to add the odor threshold test and the scratch and sniff cards for the odorant vanilla. Neither the WUTC odor threshold test nor the vanilla scratch and sniff cards had been available at the time of the original submission of the Melatonin grant profile. The addition of these tests instruments requires the patient consent form to include their administration in the consent. Approval of this modification has been obtained from the IRB of the UT College of Medicine scientific review board. A copy of the approval letter is attached.

You must include the following approval statement on research materials seen by participants and used in research reports:

The Institutional Review Board of the University of Tennessee at Chattanooga (FWA00004149) has approved this research project # 12-196.

Please remember that you must complete a Certification for Changes, Annual Review, or Project Termination/Completion Form when the project is completed or provide an annual report if the project takes over one year to complete. The IRB Committee will make every effort to remind you prior to your anniversary date; however, it is your responsibility to ensure that this additional step is satisfied.

Please remember to contact the IRB Committee immediately and submit a new project proposal for review if significant changes occur in your research design or in any instruments used in conducting the study. You should also contact the IRB Committee immediately if you encounter any adverse effects during your project that pose a risk to your subjects.

For any additional information, please consult our web page <http://www.utc.edu/irb> or email instrb@utc.edu

Best wishes for a successful research project.

VITA

Matthew McCurdy was born in Lebanon, Indiana to the parents of Kevin and Cheryl McCurdy. He graduated from Lebanon Senior High School in 2008, after which he attended Indiana University to study psychology. During his time studying psychology, he became interested in research and joined Dr. George Rebec's research lab gaining research experience. Matthew worked in Dr. Rebec's lab for two and a half years before graduating with a Bachelors of Science degree in psychology and moving on to a Master's program in research psychology at the University of Tennessee at Chattanooga in 2012. In the Master's program he worked with Dr. Nicky Ozbek for two years on the present thesis project studying depression in kidney disease patients. Matthew is expected to graduate with a Masters of Science degree in Research Psychology in May 2014. He plans to continue his education in research psychology by pursuing a Ph.D. degree at the University of Illinois at Chicago.