NEUROPSYCHOLOGICAL AND EVERYDAY PREDICTORS OF MEDICATION ADHERENCE AND EMPLOYMENT STATUS FOLLOWING KIDNEY TRANSPLANTATION

by

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ABSTRACT

The relative utility of traditional neuropsychological versus everyday cognitive measures in predicting specific functional outcomes is relatively unknown. I investigated the utility of both traditional neuropsychological and everyday measures of cognition in predicting medication adherence (n = 103) and employment status (n = 94) among kidney transplant (TX) recipients. Results indicated that both poorer performance on the Everyday Problem Solving test and a higher number of depressive symptoms were predictive of poorer self-reported medication adherence. Furthermore, being on antidepressant medication, having a higher number of depressive symptoms, and poorer performance on traditional neuropsychological measures were predictive of fewer hours worked. This study highlights the association of neurocognitive and psychosocial status with medication adherence and employment status following kidney transplantation, and the results suggest that the relative importance of traditional and everyday measures is dependent upon the outcome examined.

Keywords: kidney transplant; neuropsychological; ecological validity; medication adherence; employment

DEDICATION

To my son, Oliver, who, as a newborn, unknowingly put up with me finishing my dissertation.

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GLOSSARY

CES-D	Center for Epidemiological Studies Depression Scale
CKD	Chronic Kidney Disease
CVLT	California Verbal Learning Test – Second Edition
D-KEFS	Delis-Kaplan Executive Function System
ECB	Everyday Cognition Battery
EM	Electronic Monitoring
EPS	Everyday Problem Solving
GFR	Glomerular Filtration Rate
HL	Hosmer and Lemeshow
IADL	Instrumental Activities of Daily Living
MDRD	Modification of Diet in Renal Disease
MPR	Medication Possession Ratio
NP	Nuropsychological
RC	Refill Compliance
SFU	Simon Fraser University
SOT	Solid Organ Transplant
TBI	Traumatic Brain Injuries
TX	Transplant
TxEQ	Transplant Effects Questionnaire
VGH	Vancouver General Hospital

INTRODUCTION

Kidney disease is becoming an increasingly common chronic illness of middle and older adulthood. As of 2005, the prevalence rate of patients with kidney failure in Canada (i.e., requiring some form of kidney replacement therapy) was 162 per million population, representing a 36% increase from 1999 (2007 CORR Report). For a description of the stages and renal replacement therapy alternatives, see Appendix A. The fact that kidney disease appears to be associated with a high risk for cognitive difficulties further complicates the management of this illness. We recently reported that kidney transplant (TX) recipients exhibit significantly poorer verbal memory (i.e., ability to learn a list of words and recall as many as possible after a delay period) and executive abilities (in this case, the ability to inhibit responses to salient stimuli) in comparison to matched healthy controls (Gelb, Shapiro, Hill, & Thornton, 2008; see Appendix B). Furthermore, we found that TX recipients' performance was indistinguishable from that of individuals in the early stages of chronic kidney disease, a disorder also associated with diminished cognitive functioning (Kurella, Chertow, Luan, & Yaffe, 2004; Thornton, Shapiro, Deria, Gelb, & Hill, 2007).

While these findings suggest that reductions in cognitive performance may accompany kidney disease even after successful kidney TX, the implications remain unknown. For instance, to what extent is cognition predictive of difficulties with everyday tasks in kidney TX recipients? If cognitive performance is predictive of everyday outcomes, this could potentially influence treatment decisions, such as the need

for increased levels of education and support for TX recipients with cognitive impairments. To date, I am unaware of published research that has addressed the relationship between cognition and functional outcome in kidney TX recipients. The current study addresses this important knowledge gap by examining the utility of both traditional and everyday cognitive measures in predicting both medication adherence and employment status following successful kidney transplantation.

Ecological Validity

Recently, there has been increased interest in the relative ability of various neuropsychological tests to predict outcomes in everyday life (Burgess et al., 2006; LeBlanc, Hayden, & Paulman, 2000). Historically, neuropsychological tests were designed to aid in the localization of deficits and diagnosis of various conditions, but with advances in technology, the focus of neuropsychology has shifted toward providing clinical opinions on how cognitive impairments will affect an individual's ability to function in everyday life (Spooner & Pachana, 2006). If the results from a neuropsychological test are found to be predictive of some aspect of everyday functioning (e.g., ability to maintain employment), the test is said to have ecological validity. Unfortunately, neuropsychologists often equate poor cognitive performance with poor functioning in the real world without empirical evidence to support this link (Sbordone, 2001). Dissatisfied with the current state of practice, Burgess and colleagues (2006) argue that in clinical work it is imperative that we consider how cognitive performance in the laboratory relates to abilities in everyday life.

Despite these concerns, very few cognitive tests have been designed to predict real-world functioning (Sbordone, 2001). As a result, many question the ecological validity of traditional neuropsychological tests and there has been increased interest in developing new tests with ecological validity in mind (i.e., the everyday approach). Everyday measures include the Behavioral Assessment of the Dysexecutive Syndrome battery (Wilson, Alderman, Burgess, Emslie, & Evans, 1996), the Multiple Errands Test (Alderman, Burgess, Knight & Henman, 2003), the Rivermead Behavioural Memory Test (Wilson, Cockburn, & Baddeley, 2003), and the Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994). In addition, there is an extensive literature on everyday problem solving (EPS) that, to date, mainly focuses on adult developmental changes (Thornton & Dumke, 2005). Of course, the fact that a test on the surface appears similar to real-world demands does not ensure that the test is ecologically valid. Empirical validation for everyday measures is also necessary. To date, the relative degree of ecological validity in everyday measures compared to traditional neuropsychological tests has not been well established. Nonetheless, in a literature review, Chaytor and Schmitter-Edgecombe (2003) suggest that there is some preliminary evidence for the superiority of everyday cognitive measures over that of traditional neuropsychological tests among individuals with closed head injuries and multiple sclerosis.

Several challenges arise when considering the ecological validity of cognitive tests. The first involves determining acceptable measures of functional outcome or everyday behaviours. These can include caregiver reports, clinician ratings, and

interviews regarding cognitive functioning (e.g., Burgess, Alderman, Evans, Emslie, & Wilson, 1998). Chaytor and Schmitter-Edgecombe (2003) highlight two major categories of outcome in the literature: return to work and activities of daily living. As such, I chose to include both types of outcomes in the current study, with medication adherence falling into the latter domain.

Chaytor, Schmitter-Edgecombe, and Burr (2006) point out that another major challenge in assessing the ecological validity of cognitive tests is that environmental demands vary widely from one person to the next. For example, an individual's visual memory impairments may not cause difficulties if his or her environment does not place demands on visual memory (Chaytor & Schmitter-Edgecombe, 2003). Another question is whether a test could be ecologically valid in one population, but not another, or at one level of impairment, but not another (Chaytor & Schmitter-Edgecombe, 2003). If this is the case, it greatly complicates the assessment of ecological validity. To determine the stability of ecological validity across populations and levels of impairment, investigations are required that assess similar cognitive measures and target outcome variables in a variety of populations.

To address these issues, a number of recommendations have been made for ecological validity research. Chaytor and Schmitter-Edgecombe (2003) recommend that specific hypotheses be developed a priori in terms of the particular cognitive domains that are expected to predict the outcomes of interest, noting that most researchers have failed to do so in the past. In addition, they suggest that the state of ecological validity research has moved beyond asking whether cognitive tests are ecologically valid and that,

rather, researchers should be asking what tests have the greatest ecological validity in what circumstances, and in what ways can ecological validity be improved.

It is within this context that I chose to compare everyday and traditional cognitive measures in order to determine what approach results in the greatest ecological validity and for what types of circumstances, for which I considered two distinct outcomes (i.e., medication adherence and employment status). In terms of the everyday approach, within the adult developmental literature, the study of everyday problem solving (EPS) has been steadily garnering interest (e.g., Marsiske & Margrett, 2006; Thornton & Dumke, 2005). Everyday problem solving is a specific domain of everyday cognition, and has been defined by the following parameters: (a) a problem is identified that can be expected to commonly occur within the lives of individuals; (b) the problem solver is required to generate a solution or strategy to solve this problem; (c) the effective solution relies on accumulated experience; and (d) both the means and ends of the problem are salient, common, and familiar. Tasks that incorporate these parameters are commonly referred to as Everyday Problem Solving (EPS) measures, and it is this nomenclature and approach to the study of everyday cognitive function that propelled the current study. The study of EPS is premised upon the notion of ecological validity, and there is increasing evidence linking EPS to real-world outcomes (Diehl et al., 1995; Gilhooly et al., 2007).

While from a theoretical standpoint there are several reasons why EPS could potentially account for variance above and beyond that of traditional neuropsychological measures, research directly examining the relative utility of everyday and traditional cognitive measures has been sparse; however, emerging evidence suggests that measures of everyday cognition do account for unique variance above and beyond that of

traditional measures in predicting functional outcomes. Allaire and Marsiske (2002) compared the amount of variance in self-ratings of activities of daily living skills accounted for by measures of everyday cognition (i.e., the Everyday Cognition Battery (ECB), Allaire & Marsiske, 1999; Open-Ended Everyday Problems Test, Allaire, 1998) and traditional cognitive measures. They found that while poorer performances on all the measures were predictive of higher self-reported levels of independence in everyday functioning, everyday cognition measures accounted for 24% of variance and the traditional measures accounted for 5% of the variance in self-reported everyday functioning. Two studies have also assessed specific functional outcomes using measures of everyday cognition. Weatherbee and Allaire (2008) compared the ECB and traditional cognitive measures and found that both were predictive of mortality rates among older adults; furthermore, they found that one ECB subtest accounted for unique variance in mortality after accounting for traditional cognitive measures. Allaire and Willis (2006) found that poorer performance on the Everyday Problems Test for Cognitively Challenged Elderly (Willis, 1993) was associated with increased risk of mortality among the elderly after controlling for performance on the Mini-Mental State Examination (Folstein et al., 1975). In the current study, I wished to determine whether the relative advantages of EPS could be extended to additional functional outcomes (i.e., employment status and medication adherence) within another population (i.e., kidney TX recipients).

Medication Adherence

The importance of medication adherence among kidney TX recipients is highlighted by the fact that nonadherence in this population is associated with increased risk of acute graft rejection (Morrissey et al., 2005). In particular, Morrissey and

colleagues found that while only 4 of 47 episodes of early acute rejection episodes were associated with nonadherence (i.e., determined by patient interview), more than 50% of late acute rejection episodes (i.e., greater than 6 months post-kidney transplantation) were linked to nonadherence. In a meta-analysis of 36 studies, Butler and colleagues found that 22.3% of TX participants were considered nonadherent and that these participants were seven times as likely to lose their graft (Butler, Roderick, Mullee, Mason, & Peveler, 2004). In a literature review, Denhaerynck and colleagues (2005) found that the average estimated contribution of nonadherence to graft losses and late acute rejections was 16.3% and 19.9%, respectively.

A number of predictors of medication nonadherence in the kidney TX population have been identified, and are summarized in two recent reviews (Denhaerynck et al., 2005; Chapman, 2004). Interestingly, cognition was not taken into consideration in either review. This is, despite the fact, that significant associations have been identified between cognition and medication nonadherence in other populations (i.e., samples with HIV infection, schizophrenia, Type II diabetes).

Adherence Theories

A number of theories have been brought forth in an attempt to explain medication adherence behaviour. Parsons (2007) proposed that the health belief model (Rosenstock, 1974a; Rosenstock, 1974b), theory of reasoned action (Ajzen & Fishbein, 1980), and social learning theory (self-efficacy; Bandura, 1986) each help explain why cognition may play an important role in medication adherence. The health belief model was the first cognitive theory to be applied to adherence behaviours (Johnson, 2002), and it centers around the idea that adherence behaviours are motivated by a person's belief that:

(1) there is threat of illness; (2) they are susceptible to illness; and (3) there would be benefit to taking actions to reduce susceptibility (Rosenstock, Strecher, & Becker, 1988). Social learning theory was applied as an expansion of the health belief model (Rosenstock, Strecher, & Becker, 1988). In essence, social learning theory added the necessity of self-efficacy, the belief that one can successfully perform a behaviour and that the lack of self-efficacy creates a significant barrier to illness prevention. Finally, theory of reasoned action focuses on the importance of the intentions of an individual to perform a specific action (Johnson, 2002).

Interestingly, the aforementioned theories do not take into account the potential for cognitive impairments to have adverse consequences upon adherence behaviour, but more recent attempts have been made to incorporate the role of cognition. Rosen and colleagues (2003) suggest that a number of cognitive operations are necessary for proper adherence to medication regimens, such as understanding the task, encoding the task into long-term memory, and recall at the time when the medication is to be taken (i.e., prospective memory). Similarly, Park and Meade (2007) provide a social-cognitive model of adherence, and suggest that adherence initially requires effortful processing, which involves intentional effort to encode and process information (i.e., studying medical instructions and making a conscious effort to apply these instructions to a personal course of action). In the later stages of adherence, Park and Meade emphasize prospective memory, the ability to remember to perform an adherence task on a regular basis. Lastly, Johnson (2002), in her medication adherence model, emphasizes the crucial role of memory in establishing patterned behaviour, which is one of the three major

components to her model. In the current study, I hypothesize that the cognitive theories will provide additional clarity on adherence behaviours in the kidney TX population.

Assessing Adherence

The ideal measure of medication adherence would both prove and provide the timing of ingestion (Wetzels, Nelemans, Schouten, van Wijk, & Prins, 2006). While no such measure currently exists, there are a number of methods available for measuring medication adherence, and each has its advantages and drawbacks. Following is a summary of some of the most commonly used methods of measuring medication adherence. The relative efficacy of the approaches is also discussed.

Self-Report

This subjective approach is the most commonly used method of measuring medication adherence (Vitolins, Rand, Rapp, Ribisl, & Sevick, 2000). It includes questionnaires, interviews, and self-monitoring records. Perhaps the greatest advantage of self-report measures is that they are cost effective (DeGeest, Abraham, & Dunbar-Jacob, 1996). Some additional advantages of self-report measures include that they are fast and easy to administer, and have face validity (Vitolins et al., 2000). On the other hand, self-report measures are subject to response biases such as social desirability, recency effects, acquiescence, concern regarding consequences of candid answers, psychological factors (e.g., memory, health beliefs) and, for some, interviewer skills (Rand, 1990). Another issue with self-report can be the time frame that one is requested to refer to when reporting recent adherence (e.g., number of doses missed in the past week versus the past 2 months), with more recent time frames having better reliability and validity (Vitolins et

al., 2000). Although there are criticisms of self-report measures, several studies have found self-reported medication adherence to be strongly associated with virologic, immunologic, and clinical outcomes for persons with HIV-infection (see Mannheimer et al., 2006). Table C1 in Appendix C summarizes six self-report measures that have been developed, two of which specifically address adherence to immunosuppressive regimens for TX patients.

In addition, many studies use unstandardized questionnaires. In their research, Tucker and colleagues (2003) asked three questions about medication adherence in the past week: how many days they forgot to take a dose; purposely skipped a dose; or took a smaller dose than prescribed. Participants were described as non-adherent if they missed any dosages in the past week (Tucker, Burnam, Sherbourne, Fuan-Yue, & Gifford, 2003). Another approach, used by Chesney and colleagues (2000), is to ask participants to report the number of pills that they were supposed to take within a given time frame (usually 2 weeks) and how many pills they actually took. Ammassari and colleagues (2004) asked participants to identify the timing of the last missed dosage within the past four weeks (i.e., yesterday, last week, 1-2 weeks ago, 3-4 weeks ago, never). This was followed by 12 possible reasons (e.g., too busy, pills are unpleasant in taste, having side effects) for missing a dosage, which participants were asked to rate their relevance (not at all, a little, a fair amount, a lot).

Clinician Assessment

Questionnaires have also been developed for the healthcare provider to fill out regarding the patient's medication adherence. This approach to assessing adherence has many of the same advantages and disadvantages of self-report (DeGeest, Abraham, &

Dunbar-Jacob, 1996; see Miller et al., 2002 for a description of such a questionnaire). Like self-report, many studies have found that health professionals tend to overestimate patient adherence levels (see DeGeest, Abraham, & Dunbar-Jacob, 1996).

Assays/Markers

The advantages of assays/markers are that they are direct and objective (DeGeest, Abraham, & Dunbar-Jacob, 1996). An example is obtaining concentration levels of a particular medication in the bloodstream (i.e., serum) or urine. This is the only measure that can provide confirmatory evidence that a drug was ingested; however, biochemical measures are not available for all drugs, and concentration levels can be influenced by a number of factors, such as diet, absorption, other drugs, rate of excretion, and so forth (Farmer, 1999; Vitolins et al., 2000). For example, two patients could have similar serum concentrations of a given medication, but their pattern of medication adherence may be dissimilar (Farmer, 1999). In addition, assays/markers can be expensive and may be inconvenient (Vitolins et al., 2000; DeGeest, Abraham, & Dunbar-Jacob, 1996). Further issues are that patients may take their medications only just prior to clinic visits because they know that serum or urine levels of the drugs will be taken, which is known as "white-coat compliance" (Farmer, 1999; DeGeest, Abraham, & Dunbar-Jacob, 1996). In sum, the only information that can be gleaned from biochemical measures is a yes/no response for whether they took the medication near the time of their lab visit (Farmer, 1999).

In kidney TX recipients, serum cyclosporine and tacrolimus concentrations have previously been utilized as measures of medication adherence. DeGeest and colleagues (1996) point out that these measures have limited reliable time coverage (e.g., the half-

life of cyclosporine ranges from 10 to 27 hours), provide only global estimates of adherence, and likely underestimate compliance. Factors that can influence serum levels include within- and between-subject differences in pharmacokinetics and pharmacodynamics, the sample matrix (i.e., whole blood or serum), analytical techniques applied (e.g., radioimmunoassay), and the potential for drug interactions (DeGeest et al., 1996).

Chisholm, Mulloy, and DiPiro (2005) previously assessed medication adherence in kidney TX recipients using serum concentrations. They recorded serum concentrations of the immunosuppressants cyclosporine and tacrolimus monthly for one year. Serum concentrations of the immunosuppressants were classified as 'achieving target' or 'not achieving target'. The 'target' concentration of cyclosporine was 250 ng/mL or more and the 'target' tacrolimus concentration was 8 ng/mL or more.

Pharmacy Refill Records

This measure of adherence is derived from a patient's pharmacy records of medication refills. An advantage of using pharmacy refill records is that it does not influence adherence behaviour (Vitolins et al., 2000). In addition, it is objective and inexpensive (Wetzels et al., 2006), and it allows for measurement of adherence over a long period of time (DeGeest, Abraham, & Dunbar-Jacob, 1996). However, because it is an indirect method of measuring adherence (DeGeest et al., 1996), it does not guarantee medication ingestion. A participant may sometimes refill their prescriptions at other pharmacies, and refilling prescriptions does not guarantee that the participants are actually taking their medication (i.e., patients may have many un-opened bottles of medication at home; Vitolins et al., 2000; MacLaughlin et al., 2005). A number of factors unrelated to

adherence may also influence timing of refilling prescriptions, such as titrations of drug dosages, going on vacations, and hospitalizations (Andrade, Kahler, Frech, & Chan, 2006). Wetzels and colleagues suggest that pharmacy refill records provide an estimate of the upper bounds of the percentage that are considered adherent. In addition, it allows for identification of individuals who could not possibly be compliant because they have not obtained sufficient amounts of the medication (Steiner & Prochazka, 1997).

Several formulaes exist for calculating measures of adherence using pharmacy refill data. In a review of the literature, Hess, Raebel, Conner, and Malone (2006) identified eleven evaluable measures of pharmacy refill adherence. Andrade and colleagues (2006) found that a majority of studies use a medication possession ratio (MPR), which calculates an estimated percentage of the required supply of medication that an individual has obtained within a given time period. Even within the MPR approach, a number of different formulaes have been utilized to arrive at a 'percent adherence' level (e.g., continuous single-interval measure of compliance, continuous multiple-interval measure of compliance). Each of these measures provides essentially the same data with varying time periods, that is, the number of days of medication supply obtained is divided by the number of days in a specified interval of time in order to arrive at a 'percent adherence' level. (e.g., Chisholm, Mulloy, & DiPiro, 2005).

Typically, pharmacy databases include the following information about medication regimens: the name of the medication, dosage (milligrams/pill), quantity of medication dispensed, and the dates of prescription refills (Steiner & Prochazka, 1997; Chisholm et al., 2005). Hess and colleagues (2006) recommend careful identification of changes in prescription dosages during the monitored period and adjustments of

calculations accordingly. Andrade and colleagues (2006) point out that one must decide how to interpret oversupplies of medication (i.e., > 100% possession). While some truncate these values to 100%, Andrade and colleagues (2006) recommend that researchers allow percentages greater than 100% in order to treat the measure as a continuous variable, which, of course, is implausible.

Electronic Monitoring

Electronic monitoring (EM), which is a pill bottle cap that records when and how many times a medication is opened, is considered by many to be the gold standard for medication adherence (Russell et al., 2006). It provides a direct method of measuring adherence that is sensitive and objective, and provides extended reliable time coverage, patterns of adherence behaviour, and event data (DeGeest, Abraham, & Dunbar-Jacob, 1996). Even EM has its pitfalls, however. Perhaps the most frequently cited drawback to EM is that it is expensive (Farmer, 1999; Vitolins et al., 2000; DeGeest, Abraham, & Dunbar-Jacob, 1996) and, as a result, it is not widely used. In a meta-analysis of studies assessing adherence among kidney TX recipients, EM was used in only 2 of 36 studies (Butler, Roderick, Mullee et al., 2004). Due to its cost, it is unlikely that EM would be applied to more than one medication bottle at a time. In addition, a participant may ingest pills from an additional bottle of the same medication that does not have the EM cap on it (Butler, Roderick, Mullee et al., 2004; Russel et al., 2006), open the pill bottle and not take the pill (Butler et al., 2004; Farmer, 1999; Vitolins et al., 2000; Russel et al., 2006), or not completely close the cap (Choo et al., 1999). each of which may result in under-recording of adherence.

Another issue is the ‘white coat effect’, in that an individual’s awareness of the EM system could influence their adherence patterns (Butler et al., 2004; Vitolins et al., 2000). Wetzels and colleagues (2006) collected pharmacy refill data over a one-year period, which was followed by EM for a period of two months. Using the same criteria for non-adherence in both phases (i.e., adherence rates below 85% for at least one of the prescribed medications), 18.4% were considered non-adherent using the refill compliance data, and only 4% were classified as nonadherent by EM. Wetzels and colleagues (2006) suggest that awareness of EM may have resulted in improved adherence levels. Nonetheless, electronic monitoring provides detailed data on adherence patterns, is objective, and can increase the reliability and validity of medication adherence estimates (Vitolins et al., 2000).

Pill Counts

While pill counts are fairly straightforward, this method is subject to a number of drawbacks. In general, since it is an indirect measure (DeGeest et al., 1996), it does not confirm that the pills were actually ingested. For example, a participant may empty the bottle prior to the assessment (Murray et al., 2004; DeGeest et al., 1996), or may take the same types of pills from more than one bottle (Vitolins et al., 2000; DeGeest, Abraham, & Dunbar-Jacob, 1996). As well, the client must remember to bring their medications to the assessment (Vitolins et al., 2000). Pill counts have been found to overestimate adherence (see Farmer, 1999; DeGeest, Abraham, & Dunbar-Jacob, 1996).

Unless one is using a continuous measure of medication adherence, an issue that comes into play regardless of the type of adherence measurement is that of setting cut-off points for distinguishing between the adherent and non-adherent. Denhaercynck and

colleagues (2005) emphasize the need for a consensus as to what constitutes a clinically meaningful cut-off point for determining medication adherence. In a meta-analysis of studies considering adherence among kidney TX recipients, the criterion for nonadherence was only defined in 10 of 36 studies. Furthermore, for those that did define nonadherence, the definitions (i.e., the cut-off criteria for classifying participants as adherers or nonadherers) widely varied (Butler, Roderick, Mullee et al., 2004).

Relative Efficacy of Adherence Measures

Several studies have compared self-reported adherence to other approaches of measuring adherence. In a study of kidney TX recipients, the ability of self-report, clinician rating, interview self-report, and cyclosporine concentrations adherence levels to predict EM levels of adherence were assessed. It was found that self-reported adherence during the interview was a better predictor of EM adherence than clinician ratings, cyclosporine levels, or self-report questionnaires (Butler, Peveler, Roderick, Horne, & Mason, 2004).

Garber, Nau, Erickson, Aikens, and Lawrence (2004) compiled a literature review of the concordance of self-report with other measures of medication adherence (i.e., pill counts, EM, clinical opinions, and assays/markers). Concordance was categorized as high (i.e., Kappa > 0.6, $r > 0.8$, or < 10% difference), moderate, or low (i.e., Kappa < 0.4, $r <$ 0.4, or ≥ 25% difference). Overall, out of 86 comparisons, 43% of self-report measures were highly concordant with other methods of assessing adherence, and 70% had high or moderate concordance rates. In comparisons for which less than high concordance rates were found, higher adherence levels were seen on self-report measures compared to non-self-report measures. Concordance rates were found to vary depending on the type of

self-report measure. Interviews, diaries, and questionnaires were highly concordant 31%, 71%, and 55% of the time, respectively. While questionnaires were highly concordant with EM in only 2 of 9 studies (22%), there was high concordance between questionnaires and medication levels (e.g., serum concentrations) in all four studies making this comparison (Garber et al., 2004).

Steiner and Prochazka (1997) reviewed studies that compared refill compliance (RC) to other measures of adherence, including self-report, pill counts, serum drug levels, medical outcome measures (e.g., blood pressure), and other health outcomes (e.g., number of hospitalizations). Overall, there were mixed findings for associations between self-report and refill compliance. The one study that compared refill compliance to pill counts found a strong association between the two adherence measures. All three studies comparing refill compliance and serum drug levels found significant associations, and four of five studies comparing refill compliance to medical and health outcomes (e.g., uncontrolled hypertension, acute myocardial infarction, rates of hospitalization, health care costs) found significant associations between negative outcome and nonadherence (Steiner & Prochazka, 1997). For a review of several other efficacy studies, see Appendix C, Table C2.

In summary, the various types of medication adherence measures are typically significantly correlated with each other and predictive of outcomes. Although self-report measures tend to result in overestimated adherence levels, they have been identified as the preferred measure next to EM among kidney TX recipients (Butler et al., 2004). Furthermore, questions related to forgetfulness may be the most useful self-report items (e.g., Choo et al., 1999). While refill compliance has not been studied to the extent of

self-report measures, there is support for its validity as well. Lastly, serum concentrations tend to be correlated with other adherence measures. While such a measure cannot be used to calculate percent adherence levels, it is the only measure that can guarantee ingestion.

Adherence and Cognition

As previously stated, the relationship between cognitive performance and medication adherence has not been assessed in kidney TX recipients. Nonetheless, associations between cognition and medication adherence have been assessed in other clinical populations. Results from other studies can aid in the selection of appropriate cognitive domains to take into consideration in the present study. While most of the research has focused on persons with HIV, studies have also been done in other populations, including schizophrenia and other mental illness groups, type II diabetes, chronic obstructive pulmonary disease, older adults, individuals taking cholesterol-lowering agents, and individuals taking antidepressants (e.g., Hinkin, Hardy, Mason et al., 2004; Jeste, Patterson, Palmer et al., 2003; Rosen, Beauvais, Rigsby et al.. 2003; Incalzi, Gemma, Marra et al., 1997; Cooper, Carpenter, Katona et al., 2005; Stilley, Sereika, Muldoon, Ryan, & Dunbar-Jacob, 2004; Ayalon, Areán, & Alvidrez, 2005). Brief summaries of the findings in several studies of medication adherence and cognition can be found in Table C3 in Appendix C.

To provide an overall summary, the most frequent findings across the clinical populations are associations between poor executive functioning and nonadherence, followed closely by memory and processing speed. With mounting evidence of reduced verbal memory and executive functioning skills among kidney TX recipients (Bermond

et al., 2005; Gelb, Shapiro, Hill, & Thornton, 2008) and the necessity for such individuals to strictly adhere to a medication regimen, the value of assessing the role of cognition as a predictor of medication nonadherence is this population is evident.

It is important to recognize that the role of cognitive abilities in predicting medication nonadherence may vary according to the extent of cognitive impairment, the clinical population being assessed, and the cognitive measures utilized. For instance, in a clinical population that frequently exhibits executive functioning but not memory impairments, executive functioning performance may be a better predictor of medication adherence than memory. In sum, the type of cognitive impairment common to a given population may result in certain cognitive domains showing differential predictive utility. It should also be noted that most studies of cognition and adherence do not assess all cognitive domains (e.g., Vedhara et al. [2004] only assessed memory), and therefore the associations reported are limited by the domains most often assessed. Lastly, one should also be aware that I was unable to identify any studies comparing performance on everyday measures with medication adherence levels.

Other Variables Associated with Adherence

A number of factors likely influence an individual's level of adherence to medication regimens. Butler and colleagues (2004) identified modifiable risk factors associated with nonadherence to prednisone (i.e., an immunosuppressant commonly prescribed to kidney TX recipients). They found that having a lower belief of need for prednisone and/or other immunosuppressants and having received a TX from a live donor were related to EM nonadherence, while clinical depression was not (Butler, Peveler, Roderick, Smith et al., 2004). Chisholm, Lance, and Mulloy (2005) also identified a

number of risk factors including age (i.e., younger patients tend to be more adherent), income (i.e., those with lower incomes tend to be more adherent), and type of immunosuppressant (i.e., those on cyclosporine tended to be more adherent than those taking tacrolimus).

In a literature review, Denhaerynck and colleagues (2005) found that among kidney TX recipients, nonadherence is most consistently associated with living alone, being unmarried, external locus of control, lower belief of need for immunosuppressive medications, illegal drug dependency, and a recipient's experience of negative side-effects of medications. Additional factors that have also been associated with nonadherence include both younger or older age (i.e., the extremes on the spectrum), low perceived social support, lack of knowledge regarding the medication regimen, pre-TX nonadherence, depressive symptoms, nicotine dependency, diabetes, longer time since TX, being a living donor recipient, and more complex medication regimens. Factors that have consistently been found to *not* be associated with nonadherence are time on dialysis and being re-transplanted (Denhaerynck, Dobbels, Cleemput et al., 2005).

Depressive Symptoms. Depressive symptoms have been found to impact cognitive performance in both general populations (e.g., Brown, Scott, Bench, & Dolan, 1994) and those with medical conditions (e.g., Chamelian & Feinstein, 2006), and since depressive symptoms could also potentially mediate the relationship between cognition and medication adherence, its role is important to address. The relationship between depressive symptoms and medication adherence has previously been assessed among individuals with kidney disease. Frazier, Davis-Ali, and Dahl (1994) found that symptoms of depression and anxiety were significantly associated with poorer medication

adherence among kidney TX recipients. Furthermore, in participants with end stage renal disease, those who reported depressive symptoms were 3.44 times more likely to be nonadherent (DiMatteo, Lepper, & Croghan, 2000). Because of the common occurrence of hypertension and diabetes within the kidney TX population, the relationship between depressive symptoms and these conditions is also of interest. In a sample of hypertensive individuals in Pakistan, depressive symptoms were associated with poor medication adherence (Hashmi et al., 2007). Depressive symptoms have also been linked to nonadherence in individuals with type II diabetes (Kilbourne et al., 2005; Lin et al., 2004). Kilbourne and colleagues found that this association was still significant after adjusting for caregiver-reported cognitive impairment, binge drinking, age, and number of medications (Kilbourne et al., 2005). Nonetheless, Hill-Briggs and colleagues did not find a significant association between adherence and depression among African Americans with type II diabetes (Hill-Briggs et al., 2005).

Recent studies of other clinical populations have also linked depressive symptoms to medication nonadherence. A preponderance of the research has considered the relationship between these variables within the HIV-infected population, and several of these studies found higher levels of depressive symptoms to be significantly associated with poorer medication adherence (e.g., Avants, Margolin, Warburton, Hawkins, & Shi, 2001; Boarts, Sledjeski, Bogart, & Delahanty, 2006; Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000; Holzemer et al., 1999; Phillips et al., 2005; Tucker, Burnam, Sherbourne, Kung, & Gifford, 2003). However, only four of these studies considered depressive symptoms as a potential predictor of nonadherence in regression analyses, and of these studies, only one found depressive symptoms to be a significant predictor of

adherence (Boarts, Sledjeski, Bogart, & Delahanty, 2006) while three did not (Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000; Holzemer et al., 1999; Parsons, Rosof, & Mustanski, 2007).

Significant associations between depressive symptoms and medication adherence have also been identified in individuals with cardiovascular disease (Bane, Hughes, & McElnay, 2006; Carney, Freedland, Eisen, Rich, & Jaffe, 1995; Gehi, Haas, Pipkin, & Whooley, 2005; Rieckmann, Kronish, Haas et al., 2006), psychosis (Ascher-Svanum, Zue, Faires, Lacro, & Dolder, 2006; Elbogen, Swanson, Swartz, & Van Dorn, 2005), Parkinson's disease (Grosset, Bone, & Grosset, 2005), hypercholesterolemia (Stilley, Sereika, Muldoon, Ryan, & Dunbar-Jacob, 2004), and in older adults (Cooper et al., 2005). Gehi and colleagues found that major depression (i.e., defined according to the DSM-IV) in cardiovascular disease was independently associated with self-reported poor medication adherence, and that individuals with major depression were three times more likely to not be taking their medications as prescribed. Rieckmann and colleagues have also found that severity of depressive symptoms was related to medication adherence in a graded fashion (Rieckmann, Gerin, Kronish et al., 2006).

While several studies report associations between depressive symptoms and adherence, such associations are not always present (e.g., Insel, Morrow, Brewer, & Figueredo, 2006; Safren, Duran, Yovel, Perlman, & Sprich, 2007). Moreover, after the addition of other factors to a model, depressive symptoms may not remain a significant predictor of compliance (e.g., Stilley et al., 2004). Furthermore, the relationship between depressive symptoms and medication adherence has yet to be considered within a cognitive framework for kidney TX recipients. For these reasons, it is important to assess

the role of depressive symptoms in relation to cognitive performance and medication adherence for the current study.

Employment Status

In terms of employment, the literature estimates that 59 to 83% of kidney TX recipients will never return to work post-TX (see Wilkins, Bozik, & Bennet, 2003). Interestingly, while the relationship between cognitive performance and employment status has been widely studied in other clinical populations, I am not aware of any published research addressing this relationship in the kidney TX population. Cognitive impairment has previously been identified as one of the better predictors of unemployment (Rabkin, McElhiney, Ferrando et al., 2004). Given the increasing evidence of cognitive difficulties and high rates of unemployment among kidney TX recipients, the need for research in this area is readily apparent. McGurk and Mueser (2003) summarize a number of benefits of obtaining employment for individuals with severe mental illness, which could also apply to kidney TX recipients. These benefits include improved self-esteem and an increased sense of structure and purpose in one's life.

Assessing Employment

While employment is commonly assessed using a dichotomous measure (i.e., "employed" versus "unemployed"; Chaytor & Schmitter-Edgecombe, 2003), this variable can be indexed in a number of ways. Measures of employment include categorical data (e.g., working/working part-time/not working), number of hours worked (Rabkin et al., 2004), number of jobs held, and wages earned (McGurk & Mueser, 2006). Competitive

employment is often differentiated from other types of employment, and can be defined as employment in a position that pays at least minimum wage in an integrated community setting that is not set aside for persons with disabilities (McGurk & Mueser, 2006). Nonetheless, in a literature review of employment status post-kidney transplantation, van der Mei and colleagues (2006) noted that researchers frequently do not report the classification system that they have used for determining employment status. The variety of approaches to conceptualizing employment are illustrated in the scales that have been developed to ascertain employment status (see Appendix C, Table C4).

Employment and Cognition

A number of difficulties are unique to predicting employment outcomes with measures of cognition. Whereas the skills required for medication adherence are similar for most people, the abilities needed to maintain employment greatly depend on the type of position for which an individual is seeking employment. This will most definitely vary on an individual level, but may also vary on a group level. For instance, in a study of individuals with substance abuse problems, Mackin and colleagues (2005) found that performance on measures of sustained attention and learning and memory were predictive of employment problems while executive functioning performance was not. The researchers suggested that this was because most of the individuals assessed were employed in unskilled labour positions where executive functioning skills may not be as crucial (Mackin, Horner, Harvey, & Stevens, 2005). In contrast, a long-term follow-up study of individuals with schizophrenia in supported employment programs found that employment in an occupation requiring greater cognitive complexity was significantly associated with better performance on measures of executive functioning and verbal

learning and memory (McGurk & Mueser, 2006). Thus, depending on the types of employment individuals are seeking, certain cognitive domains may be more important than others.

Despite the great degree of heterogeneity in successful outcomes, research in this area has produced notable results. Neuropsychological performance as a predictor of employment has been assessed in a variety of clinical populations (e.g., traumatic brain injuries (TBI), substance abuse problems, severe mental illness, HIV infection, multiple sclerosis, and in healthy individuals; see Appendix C, Table C5). Furthermore, Kalechstein and colleagues (2003) recently completed a meta-analysis of the associations between neuropsychological abilities and employment status among individuals with epilepsy, HIV, severe traumatic brain injuries, and other various disorders. Using the guidelines outlined by Cohen (1992), the researchers found medium effect sizes for most cognitive domains (i.e., intellectual functioning, $d = 0.64$; attention/concentration, $d = 0.53$; visuospatial abilities, $d = 0.49$; verbal learning and memory, $d = 0.62$; nonverbal learning and memory, $d = 0.60$; motor/psychomotor speed, $d = 0.47$; executive functioning, $d = 0.62$), indicating that poorer performance on measures from each of these areas was associated with a greater likelihood of unemployment (Kalechstein, Newton, & van Gorp, 2003). Since the researchers grouped all studies together irrespective of differences in the cognitive battery used and the populations assessed, one cannot draw conclusions about whether some cognitive domains are better predictors of certain positions of employment for a given population. Nonetheless, there appears to be empirical support for neuropsychological performance predicting employment status.

Employment Status and Depressive Symptoms

Interestingly, relatively few studies have assessed the relationship between depression and unemployment in populations with chronic illnesses, and the findings are inconsistent. In Rabkin and colleagues' (2004) longitudinal study of men with HIV infection, current level of depressive symptoms and diagnosis of mood disorders over one's lifetime were independently predictive of the number of hours worked (Rabkin et al., 2004). In contrast, van Gorp and colleagues (2006) found that neither symptoms of depression nor diagnosed major depression were predictive of unemployment in a group of individuals with HIV infection (van Gorp, Rabkin, Ferrando et al., 2006). Similarly, Heaton and colleagues (1994) found that significantly fewer HIV infected individuals with neuropsychological impairments were employed, and that removing individuals with moderate to severe levels of depression did not change this relationship.

Results from studies of other populations also suggest disparate findings regarding the relationship between depression and employment status. In a longitudinal study in which individuals with TBI were assessed 2, 5, and 10 years post-injury, depressive symptoms were similar between employed and unemployed individuals at 2 and 10 years, but unemployed participants asserted a significantly higher number of depressive symptoms at 5 years post-injury (Franulic, Carbonell, Pinto & Sepulveda, 2004). Furthermore, for individuals with epilepsy, it is thought that depressive symptoms may be one of the strongest predictors of employment (Gilliam, Hecimovic & Sheline, 2003). In contrast, it was found that higher levels of depressive symptoms and anxiety during hospitalization were predictive of returning to work among individuals who suffered from myocardial infarctions (MÆland & Havik, 1987). In summary, while depressive symptoms may not consistently be predictive of employment status in clinical

populations, it is likely important to take this variable into account when studying predictors of employment status.

Additional Predictors of Employment Status

Employment Status

Relative Efficacy of Adherence Measures

In addition to the factors discussed above, other predictors of employment status may be specific to kidney TX populations. In a literature review of employment status post-kidney transplantation, van der Mei and colleagues (2006) highlighted pre-TX employment status as a consistent predictor of employment status post-TX. In addition, these researchers also noted that age, diabetes, and being less than 1 year post-TX were predictive of unemployment. In contrast, van der Mei and colleagues reported that TX donor source (i.e., living versus deceased) and type of kidney replacement therapy pre-TX were not significant predictors of employment post-TX.

Employment levels following kidney transplantation may, in part, particularly reflect pre-TX employment levels when individuals were on dialysis. Overbeck and colleagues (2005) found that similar percentages of dialysis patients and post-TX patients were employed or in training (i.e., 28% of dialysis patients and 25% of TX patients). Interestingly, however, a greater percentage of TX patients were permanently out of work on disability (i.e., 42%) compared to dialysis patients (i.e., 26%).

In summary, the literature provides support for a relationship between employment status and a number of cognitive and non-cognitive domains. Not surprisingly, in a review of the literature, Sbordone and Guilmette (1999) concluded that no individual neuropsychological test can be used to predict one's ability to work.

Nonetheless, based on Kalechstein and colleagues (2003) meta-analysis and more recent literature, the domains most strongly associated with employment appear to be intellectual functioning, learning and memory, and executive functioning. Furthermore, I was only able to identify one study that took into consideration the role of depressive symptoms when assessing the relationship between neuropsychological functioning and employment status. This was in a study of individuals with HIV infection, and this did not account for the findings between the latter variables (Heaton et al., 1994). It has been argued that the relationship between neuropsychological tests and employment status is moderate at best (Chaytor & Schmitter-Edgecombe, 2003; Sbordone & Guilmette, 1999) and Kalechstein and colleagues` meta analysis provides further support for these arguments. While it seems possible that everyday tests may result in larger effect sizes, our literature review did not reveal any studies assessing the ability of such measures to predict employment status.

OBJECTIVES AND HYPOTHESES

To better understand the implications of neurocognitive impairment among kidney TX recipients (Gelb et al., 2008) our overarching objective was to assess the utility of both traditional and everyday measures of cognitive abilities as predictors of medication adherence and employment status.

Primary Objectives

Our first objective was to assess the ability of traditional neuropsychological measures to predict medication adherence and employment outcomes following successful kidney transplantation. As a second part to the first objective, I wished to assess whether neuropsychological variables were still predictive of medication adherence and employment status after taking into consideration non-cognitive predictors (e.g., years since TX, depressive symptoms, diabetic status; the procedure for determining which variables would be added to analyses is outlined in the research methods section) of these two outcomes.

For our second objective, I wished to compare EPS to traditional neuropsychological performance as a predictor of medication adherence and employment status. There has been a growing focus on developing everyday measures, yet the relative advantages or disadvantages of such measures over that of traditional cognitive measures are not well understood. While it has previously been hypothesized that everyday measures will show greater associations with outcomes than traditional

neuropsychological measures, it is our understanding that such measures have not previously been applied to medication adherence and employment outcomes. As an additional part to the second objective, I wished to assess this same relationship after taking into consideration non-cognitive predictors of employment status and medication adherence.

Hypotheses

Based on the outcomes in other clinical populations, I hypothesized that memory, executive functioning, and processing speed would be predictive of medication adherence and employment status. Furthermore, because of its emphasis on practical problems that are believed to draw upon experience, accumulated knowledge and broader cognitive skills, I hypothesized that an everyday measure of EPS would account for unique variance above and beyond that accounted for by traditional neuropsychological measures.

1. a) It was anticipated that cognitive performance on traditional neuropsychological measures (i.e., measures of memory, executive functioning, and processing speed) would be predictive of medication adherence and employment status in kidney TX participants.

   b) After controlling for non-cognitive variables, I anticipated that neuropsychological performance would remain a significant predictor of medication adherence and employment status.

2. a) I expected that an everyday measure would account for unique variance in medication adherence and employment status above and beyond that of traditional neuropsychological measures.

b) After controlling for non-cognitive variables, I predicted that an everyday measure would account for unique variance in medication adherence and employment status above and beyond that of traditional neuropsychological measures.

METHOD

Participants

Data was collected in two phases from participants seen at the Solid Organ Transplant (SOT) Clinic at Vancouver General Hospital (VGH). In our lab, I conducted extensive cognitive and psychosocial assessments on 64 patients with kidney TXs from October of 2004 until October of 2006. The cognitive findings from the first phase have been previously reported (Gelb, Shapiro, Hill, & Thornton, 2008), and in the second phase (i.e., November of 2007 until June of 2008), I collected data from an additional 86 participants to address the current objectives.

Recruitment

All participants met the following inclusion criteria: (1) capable of giving informed consent; (2) not visually impaired (corrected vision must be at least 20/50) or hearing impaired (or other sensory or motor impairments which might interfere with the testing procedure); (3) fluent in the English language; (4) minimum of grade six education; (5) absence of psychosis; (6) absence of acute illness (e.g., metastatic cancer), neurological disease, and other major organ failure (e.g., end stage liver disease); (7) minimum six months or 1 year post-TX with a stable kidney graft for the medical adherence and employment analyses, respectively (i.e., stable kidney functioning with current estimated GFR above 14ml/minute per 1.73 m^2; information regarding how GFR stability was determined is presented in Appendix D); (8) less than 65 years of age for the

employment analyses. The decision to only include individuals at or after 1 year-post TX for the employment analyses is based on previous research regarding the length of time typically taken to return to work post-transplantation. For example, Sabb and colleagues (2007) found that, of the individuals in their study that were employed post-liver transplantation, 42.3% were able to return to work in less than 6 months post-TX, 21.8% returned between 6 and 11 months, and the remaining 33.3% returned after 1 year.

In the initial phase of testing, recruitment of TX participants occurred via two methods: (1) through in-person invitations from S. Gelb during their routine clinic visits; and (2) through a research study information letter and follow-up phone calls. In the second phase of testing, recruitment of TX participants occurred solely through a research study information letter and follow-up phone calls as necessary. I found that recruitment using the information letters and follow-up phone calls, which was initiated partway through the first phase, was more successful. Therefore, while the *overall* recruitment rate was approximately 21% in the first phase, 85% of persons contacted by phone agreed to participate. In the second phase of testing, where recruitment occurred through the study information letters, 7% called us and indicated a willingness to participate and 64% indicated willingness to participate after being contacted by phone. Besides not meeting eligibility criteria, common reasons for refusing to participate included medical problems (i.e., not directly related to their kidney TX), 'no interest', and 'too busy' (for further details on recruitment, see Appendix E).

However, only a portion of those who participated in the study were eligible for each of the analyses (i.e., employment and medication adherence analyses). Two reasons accounted for this. First, the eligibility criteria varied for the employment and medication

adherence analyses (i.e., as mentioned above, individuals had to be younger than 65 years of age and at least 1 year post-TX to be included in the employment analyses whereas these restrictions did not apply to the medication adherence analyses). Secondly, two measures were introduced after the first phase of data collection had begun. The Transplant Effects Questionnaire was implemented after about 20 individuals had already completed their participation; such individuals were not included in the medication adherence analyses. Furthermore, while the Employment Interview was implemented in the second phase of testing, I was able to perform employment interviews with many, but not all, of the individuals from the initial testing phase. For these reasons, 69% of those tested were eligible for the medication adherence analyses, and 62% were eligible for the employment analyses (for further details on eligibility, see Appendix F).

Participants received $40.00 as reimbursement for their transportation costs and time associated with the cognitive testing. All participants signed letters of informed consent and the study protocol was approved by the University of British Columbia and Simon Fraser University (SFU) research ethics boards.

Measures

According to standardized protocol, trained research assistants and graduate students individually administered and scored the tests. Participants were tested at the VGH SOT clinic or at the SFU Cognitive Aging Laboratory. All participants completed a 2-hour battery of tests and questionnaires. Information was gathered on demographics, health characteristics, and cognition. The selection of cognitive tests was based on a review of cognitive predictors of medication adherence and employment status in other clinical populations, their common use in clinical settings, and interest in assessing the

relative efficacy of an everyday measure compared to traditional neuropsychological tests in predicting functional outcomes. One or two variables were selected from each cognitive test in order to reduce the probability of Type I error. For the variables of interest, I selected time to completion in seconds for Trails Letter-Number Sequencing, time to completion in seconds for Color-Word Interference, total number of correctly copied symbols from Digit-Symbol Coding, and the raw scores from Trials 1-5 and Long Delay Free Recall from the California Verbal Learning Test – Second Edition (CVLT-II).

Demographics, Mood and Activities of Daily Living

Demographic information includes age, sex, ethnicity, education, and marital status. In order to assess depressive symptomatology, the Center for Epidemiological Studies Depression Scale (CES-D) was administered (Radloff, 1977). Responses on this 20-item inventory are rated on a 4-point Likert-type scale ranging from 0 (rarely or none of the time) to 3 (most or all of the time). In addition, there are four subscales: negative affect (e.g., felt sad), well-being (e.g., felt hopeful about future), somatic symptoms (e.g., appetite poor, tired), and interpersonal disturbance (e.g., people dislike me). Scores of greater than 15 out of 60 are considered indicative of clinically significant symptoms of depression. Responses to the CES-D has been found to have adequate internal consistency reliability in medical populations (Cronbach's $\alpha = .90$; Verdier-Taillefer, Gourlet, Fuhrer, & Alpérovitch, 2001). Furthermore, Lewinsohn, Seeley, Roberts, and Allen (1997) have found the CES-D to be resistant to the influences of age, sex, cognitive impairment, functional impairment, physical disease, and social desirability.

The Instrumental Activities of Daily Living questionnaire (IADL; Lawton & Brody, 1967) was also administered. The IADL questionnaire consists of eight skills that

are scored according to a hierarchical Guttman scoring format (i.e., less able versus more able to do a given task) with a dichotomous scale.

Medical Information

Medication information was gathered via three methods: self-report, laboratory measures, and medical chart review. The *Health Questionnaire* is a self-report measure that assesses medical history and current health concerns (i.e., cerebrovascular risk factors, medications). This measure, previously used with success in other studies of neuropsychological functioning (e.g., Raz et al., 1997, Gelb et al., 2008; Thornton, Deria, Gelb, Shapiro, & Hill, 2007), was used to identify exclusionary factors (e.g., neurological disease, brain injury) and to provide a description of the study population. Additional information was gathered from laboratory tests including hemoglobin levels (g/L), estimated GFRs, and immunosuppressant (e.g., tacrolimus) serum concentrations. The Modification of Diet in Renal Disease (MDRD) prediction equation was used to estimate GFR. The MDRD formula takes into account serum creatinine (umol/L), serum urea (mmol/L), and serum albumin (g/L) levels as well as age, ethnicity, and sex. The MDRD is one of two measures of GFR recommended by the National Kidney Foundation of the United States in the Kidney Disease Outcome Quality Initiative (National Kidney Foundation, 2002). Cognitive testing occurred within four weeks of the laboratory tests. Lastly, current medications and corresponding dosages, Chronic Kidney Disease (CKD) diagnosis, and information on co-morbidity was gathered from participants' medical records.

Cognitive Measures

The *California Verbal Learning Test - Second Edition* (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000) is a neuropsychological test used to assess verbal memory abilities including free recall and recognition memory. Participants are read a list of words and, immediately following, are asked to recall as many items as they can and again, after a delay period. As mentioned above, the learning and memory measures of interest for the present study are the raw scores for Trials 1-5 and Long Delay Free Recall. The sum of correct responses from Trials 1-5 indicates the total number of items an individual is able to recall after hearing the list five times and measures one's ability to learn verbal information (Delis et al., 2000). Long Delay Free Recall provides an estimate of the amount of verbal information an individual is able to retain after a delay of approximately 20 minutes. Trials 1-5 and Long Delay Free Recall are two of the most stable measures on the CVLT-II (test-retest reliability: r = .82 and .88, respectively; retesting took place 0-77 days after the initial testing)). Overall, the CVLT-II has adequate reliability and validity and is well tolerated by individuals with cognitive impairment (Delis et al., 2000). Performance on the CVLT has been found to be predictive of employment status in clinical populations including TBI (Kibby, Schmitter-Edgecombe, & Long, 1998) and substance abuse (Mackin et al., 2005). Furthermore, poor performance on the CVLT has been found to be associated with poor medication adherence in individuals with AIDS (Hinkin et al., 2004) and in older adults (Insel et al., 2006).

The *Delis-Kaplan Executive Function System* (D-KEFS; Delis, Kaplan & Kramer, 2000) provides an assessment of complex tasks that require cognitive flexibility. The

subtests that will be used from the system are the Trail Making Test and Color-Word Interference Test (i.e., Stroop task), which assess flexibility of thinking, and verbal inhibition of a dominant response, respectively (Delis et al., 2000). As stated earlier, the raw scores (time to completion in seconds) from the Letter-Number Sequencing Task and Color-Word Inhibition Task served as independent variables. Test-retest reliability of Trails Letter-Number Sequencing is .38, and Color-Word Inhibition is .75 (retesting took place 9-74 days after the initial testing). The cognitive complexity of executive functioning tasks appear to make these tests susceptible to greater performance variability, which may impact reliability estimates (Delis, Kramer, Kaplan, & Holdnack, 2004). Although test-retest reliability estimates are moderate, the measures were selected because of their theoretical utility and known sensitivity to executive function impairment (Delis et al., 2004). Both Trails B and the Stroop task performance have been found to be associated with medication adherence in individuals with diabetes mellitus (Rosen et al., 2003) and with number of hours worked in individuals with HIV infection (Rabkin et al., 2004).

Digit Symbol-Coding is a subtest from the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III), and it is typically considered a measure of processing speed. Individuals are asked to match numbers to symbols and copy them as quickly as they can. The Digit-Symbol Coding test is a well-established measure with adequate reliability and validity (Wechsler, 1997). Test-retest reliability was calculated separately for various age groups, and ranged from .83 (i.e., ages 16 – 29, 30 – 54, & 75-89) to .89 (i.e., for age 55-74; Wechsler, 1997). Poor Digit-Symbol Coding performance has previously been associated with unemployment among individuals with TBIs (Doctor et al., 2005) and

severe mental illness (McGurk & Mueser, 2003). The total number of correctly copied symbols served as the raw score for processing speed.

The *Everyday Problem Solving* (*EPS)* task consisted of six paper and pencil vignettes. These and similar vignettes have been used extensively in previous studies (Allaire & Marsiske, 2002; Artistico et al., 2003; Crawford & Channon, 2002; Denney & Palmer, 1981; Denney & Pearce, 1989; Haught, Hill, Nardi, & Walls, 2000; Heidrich & Denney, 1994; Marsiske & Willis, 1995; Thornton, Deria, Gelb, Shapiro, & Hill, 2007). For the current study, one problem was presented per each page. Participants were asked to read each problem carefully and to write down as many solutions as possible, even if it was a solution that they themselves would not adopt. In order to reinforce the instructions to generate as many solutions as they could, a prompt "*Please write down as many solutions as you can think of*" was printed on the top and bottom of every page. The scoring criteria was devised (Denney & Pearce, 1989) and adapted by previous authors (Marsiske & Willis, 1995) to incorporate both an individual's quantity and quality of ideas. Specifically, to receive a point, a solution had to satisfy the following criteria: 1) dealt directly with the problem at hand; 2) was *safe* for all individuals involved in the problem; and 3) was likely to be *effective* in resolving the problem for both the short and long term. The total number of conceptually distinct safe and effective solutions generated by each participant for each problem was combined into a total EPS score (i.e., the responses "*call a friend for help*" and "*call a relative for help*" would be considered as a single concept of "calling for help"). Inter-rater agreement using these criteria was determined to be very high among raters in our laboratory (r_{ic} = .85). The EPS vignettes used in the present study are provided in Appendix G.

Medication Adherence

Medication adherence was measured using a self-report questionnaire, prescription refill data, and serum concentrations of cyclosporine or tacrolimus as measured by the drug concentration 2 hours (C2) post dose. The self-report measure selected consists of the medication adherence subscale from the Transplant Effects Questionnaire (TxEQ; Ziegelmann et al., 2002). This subscale is comprised of 5 statements that the participant rates their level of agreement using a 5-point Likert type scale ranging from 'strongly agree' to 'strongly disagree', and assesses whether an individual sometimes does not take their immunosuppressants or believes that they do not need these medications. For example, one statement is "Sometimes I do not take my anti-rejection medications". Previous research has found the TxEQ to have acceptable internal consistency (Cronbach $\alpha = .79$) and test-retest reliability ($r = .77$; Ziegelmann et al., 2002). Among kidney TX recipients, the TxEQ adherence subscale has been found to be significantly correlated with the mental health composite score from the SF-36 (Jenkinson, Stewart-Brown, Petersen & Paice, 1999), a questionnaire which assesses health-related quality of life (Griva, Ziegelmann, Thompson et al., 2002).

In terms of pharmacy refill data, all of the kidney TX recipients at VGH obtain their immunosuppressant medications from the SOT Clinic pharmacy. The following information was obtained from the pharmacy database: the name of the medication; dosage (milligrams/pill); changes in dosages; quantity of medication on hand; quantity of medication dispensed; and the dates of prescription refills. While I aimed to collect the data for 6 months prior to testing, this was not always possible due to variations in how often TX recipients pick up their medications, missing data (i.e., amount of medication on hand when ordering a refill was frequently not recorded), and changes in primary

immunosuppressant type (i.e., changing from cyclosporine to tacrolimus). The data collected consists of a range of 3 to 9 months mostly prior to cognitive assessment of the participant (i.e., some individuals' refill data extends to after their cognitive assessment date). I used a medication possession ratio (MPR) as a measure of refill compliance (RC), which provides the percentage of supply of medication that an individual has obtained within a given time period in comparison to the supply of medication that the individual should have obtained.

For the last measure of medication adherence, immunosuppressant serum concentrations were collected from the participants' medical records. Serum concentrations are recorded on a minimum of a monthly basis at the SOT Clinic. In the current study, I collected the three most recent serum concentrations of the immunosuppressants cyclosporine and tacrolimus prior to cognitive testing. Serum concentrations of the immunosuppressants were classified as 'achieving target' if all three measurements reached the target range or 'not achieving target' if one or more measurements did not reach the target range of 450 ng/mL or more for cyclosporine (measured by the drug concentration at 2 hours (C2) post dose), and 4-8 ng/mL for tacrolimus (adjudicated on the trough (or c0) level). Target ranges were determined by those currently used at the VGH TX clinic.

Each of the medication adherence measures was considered for use as a dependent variable in regression analyses. If any two or all three of the measures were highly correlated, a composite medication adherence score was to be created by equally weighting each variable and used as the dependent variable in regression analyses.

Employment Status

In our study, I utilized one measure of employment. This consisted of a dichotomous measure of 'more employed' versus 'less employed'. The classification of 'more employed' included part-time work of at least 20 hours per week, and students who are taking at least half of a full credit load. Part-time students taking less than half a full credit load, part-time employed individuals working less than 20 hours per week, and unemployed individuals were classified as 'less employed'. This is similar to the classification system used by Dickerson and colleagues (2004). Individuals who were of retirement age (i.e., greater than 65 years of age) were not included in the analysis of employment status.

To our knowledge, there is no validated approach to assessing employment. Therefore, I chose to construct a semi-structured interview (see Appendix E) based on questions commonly asked in the existing literature (e.g., Matas et al., 1996; van der Mei et al., 2006) as well as additional questions that I felt might be useful in creating an employment outcome measure. Self-constructed employment interviews and/or questionnaires have previously been used in assessing employment among kidney TX recipients (e.g., Gross, Limwattananon, Matthees, Zehrer, & Savik, 2000; Simmons, Abress, & Anderson, 1988; Raiz, 1997).

Data Analysis

The dependent variables consist of measures of medication adherence and employment status. Independent variables include cognitive measures, demographic variables commonly reported in the neuropsychological literature (i.e., age, sex, and education), and non-cognitive variables either previously found to be associated with the

dependent variables (i.e., these have been summarized in the introduction of this dissertation) or those that could reasonably be expected to affect cognitive functioning (i.e., antidepressants, benzodiazepines and opiates, cerebrovascular diseases, and depressive symptoms (Ensrud et al., 2003; Pereira et al., 2005)). Since detailing neuropsychological functioning was not a focus of the current study, I conducted a principal component analysis with the five neuropsychological test scores (i.e., Digit Symbol Coding [total symbols correctly copied], CVLT Trials 1-5 and Long Delay, Trails Letter-Number Sequencing completion time, and Color-Word Inhibition completion time) in order to reduce the number of dependent variables. The smallest number of components that best fit the data was used in subsequent analyses.

According to Tabachnick and Fidell (2007), an adequate sample size for regression analyses can be calculated using the following formula: $(N) > 50 + 8m$ (where N = sample size and m = number of independent variables). Taking into consideration our sample sizes (i.e., adherence $N = 103$; employment $N = 94$), this would allow for seven independent variables in adherence analyses and five independent variables in employment analyses. Similarly, assuming a moderate effect size and $\alpha = .05$, Cohen (1992) recommends a sample size of 91 for 5 independent variables, and 102 participants for 7 independent variables. A priori, I decided to limit the number of non-cognitive variables added to each analysis to meet these recommendations. The criteria I used for selecting non-cognitive variables are outlined below.

Data analysis involved a number of steps. First, data were examined for normality of distribution, homogeneity of variance, and extreme values. Transformations were performed and considered where necessary. Since our outcome variables were

continuous and dichotomous for medication adherence and employment status, respectively, different regression analyses procedures were required. The procedures for these analyses are considered separately in the next two sections.

Medication Adherence

Prior to conducting the analyses, data were examined for violations of assumptions necessary for regression analyses, and necessary transformations were performed and considered. Bivariate and residual scatterplots were assessed for the presence of linear or curvilinear relationships. I also conducted bivariate correlations between the medication adherence measure and non-cognitive variables including depressive symptoms, clinical factors, and other variables previously found to be associated with medication adherence (e.g., living situation, marital status, age, sex, diabetes, longer time since TX, being a living donor recipient; Denhaerynck et al., 2005). Although years of education has previously been identified as an inconsistent predictor of adherence (Denhaerynck et al., 2005), this variable was considered alongside age and sex because I wished to evaluate how cognitive measures fared after inclusion of standard demographic measures that are often found to be associated with neuropsychological performance (Delis, Kramer, Kaplan & Ober, 2000; Delis, Kaplan, & Kramer, 2001; Wechsler, 1997). To reduce the possibilities of capitalizing on chance associations, I chose to add non-cognitive variables to the model that resulted in group differences at a level of $p < .01$.

Hierarchical regression analyses were used to assess the relationships between the independent variables and medication adherence. In each set of analyses, ΔR^2 values were assessed with *F*-tests in order to determine whether any of the subsequent steps

significantly added to the prediction of outcome beyond the variables added in earlier steps.

For the first objective, demographic variables were entered in Step 1 of the hierarchical regression analysis, and the neuropsychological composite was entered in Step 2. Next, demographics were entered in Step 1, non-cognitive variables were added in Step 2, and the neuropsychological composite was entered in Step 3.

For the second objective, demographics, the neuropsychological composite, and EPS were entered in the first through third steps, respectively, of the hierarchical regression model. Next, non-cognitive variables were entered in a separate step between the demographic variables and the neuropsychological variable.

The relative explanatory importance of the predictors was assessed using two separate methods. In the first, one predictor variable was entered in the step prior to the other in the regression analysis. This was also performed in the reverse order, and the ΔR^2 values were compared. Secondly, I tested the difference of the co-efficients (i.e., is $\beta_1 = \beta_2$?), using a procedure outlined by Cohen (2003), in order to determine the relative explanatory importance of each of the individual cognitive variables.

Employment Status

Prior to conducting the regression analyses, data were examined for violations of the assumptions of the regression model. Independent sample *t* tests and chi-square analyses were used to test for differences between individuals employed at least 20 hours per week and individuals employed less than 20 hours per week on demographics, cognition, and non-cognitive variables of interest (i.e., variables previously found to be associated with employment among kidney TX recipients; van der Mei et al., 2006). In

order to reduce the possibilities of capitalizing on chance associations, I chose to add predictors to the model that resulted in group differences at a level of $p < .01$. Similar to the medication adherence analysis, though age, education, and sex were not previously identified as predictors of employment among kidney TX recipients (van der Mei et al., 2006), these variables were considered because I wished to evaluate how cognitive measures faired after inclusion of standard demographic measures.

Sequential binomial logistic regression analyses were used for the dichotomous employment status variable in order to determine if any of the cognitive measures or other non-cognitive variables were independently predictive of the employment outcome measure. The Hosmer and Lemeshow (HL) goodness-of-fit test was examined in order to determine if the model was a good fit, and if not, adjustments were made accordingly. I then examined residual plots for points of influence (i.e., changes in deviance plotted against predicted probabilities, and Analog of Cook's influence plotted against predicted probabilities) in order to determine whether any participants should be removed from the analysis. Changes in Nagelkerke's R^2 values are reported (i.e., overall null deviance accounted for) and the significance of individual variables as predictors of employment status are tested with Wald statistics. Odd's ratios (i.e., Exp(B)) and confidence intervals are also reported for ease of interpretability.

For the first objective, demographic variables were entered in the first step of sequential logistic regression analysis, and the neuropsychological composite was entered in the second step. Next, demographics were entered in the first step, non-cognitive variables were added in the second step, and the neuropsychological composite was entered in the third step.

For the second objective, demographics, the neuropsychological composite, and the EPS variable was entered in the first through third steps, respectively, of the logistic regression model. Next, the non-cognitive variables were entered in a separate step between the demographic variables and the neuropsychological composite.

All analyses were conducted using SPSS 15, and all *p*-values reflect two-tailed tests with a *p*-value less than .05 considered statistically significant. Confidence intervals for R^2 were calculated using R2 (Steiger & Fouladi, 1992). Lastly, estimates of effect sizes are reported for hierarchical regression models using R^2 values; corresponding f^2 values were calculated using the procedures outlined in Cohen's Power Primer (1992) in order to determine the magnitudes of these effect sizes. I calculated effect sizes (i.e., Cohen's *d*) for cognitive variables within the employment analysis using the Effect Size (ES) version 1.0 (Shadish, Robinson, & Lu, 1999).

RESULTS

Participant Characteristics

Participant characteristics, including demographics, diagnoses, medications, and self-reported depressive symptoms, are presented in Table 1. Since inclusion criteria and respective participants for the medication adherence and employment analyses differ, the means and frequencies for various demographic and clinical characteristics are shown separately for the two analyses in Table 1. In addition, descriptives for the independent and dependent variables are presented in Table 2. On the IADL, TX participants in the medication adherence analysis scored 6, 7, or 8 with a mean of 7.94 (*SD* = .31), and TX participants in the employment analysis received a score of 7 or 8 on the IADL with a mean of 7.96 (*SD* = .25). Thus, all participants can be considered functionally independent for daily living skills.

Medications. As is shown in Table 1, the percentage of individuals on these medications vary from 1% (opiates) to 13.6% (antidepressants) for the medication adherence analysis and 1.1% (opiates) to 13.8% (antidepressants) for the employment analysis.

Co-morbidity. Diabetes and hypertension are commonly occurring conditions among individuals with CKD, and, as mentioned earlier, past research has implicated a relationship between these conditions and poor cognitive performance. Past history of diabetes becomes an important variable when taking into account that ten (9.7%) of the participants in the medication adherence analysis and 10 (10.6%) in the employment

analysis also received a pancreas TX, and, as a result, were no longer considered diabetic. Pancreas TX's effectively reversed Type 1 diabetes for these participants, and though they no longer have the condition, the history of diabetes remains an important vascular risk factor for these individuals. For this reason, the combined number and percentage of people with either diabetes at time of testing or a history of diabetes is also presented (see Table 1).

Additionally, both coronary artery disease and hypercholesterolemia are co-morbid conditions that may be associated with compromised cognition (see Pliskin et al., 2001). There were no significant differences between the rates of coronary artery disease and hypercholesterolemia in the employment analysis (see Table 6), and self-reported adherence was not significantly associated with these two conditions (r = .08, *ns*; r = .12, *ns*, respectively).

Clinical characteristics of TX participants. The causes of kidney disease for participants in both analyses are listed in Table 3. This is typically determined by clinical diagnosis and is most often not biopsy-confirmed.

Medication Adherence

I conducted hierarchical regression analyses to assess our prediction that EPS would emerge as a unique predictor of medication adherence over and above traditional neuropsychological abilities. Normality of data were assessed by looking at skewness, kurtosis, histograms, Q-Q plots, and boxplots. The CES-D scores were not normally distributed (skewness = 1.33; kurtosis = 1.56); therefore a number of transformations were applied to this measure and the square root transformation resulted in the best distribution (skewness = .151; kurtosis = -.316). Since the use of the CES-D square root

measure did not result in any substantial changes from the original data, I chose to present the results with the original CES-D measure for ease of interpretability.

Principal components analysis was conducted with the traditional neuropsychological variables (i.e., Digit Symbol Coding, CVLT Trials 1-5 and Long Delay, Trails Letter-Number Sequencing, and Color-Word Inhibition) in order to determine whether I could reduce the number of cognitive variables in the regression analyses. Principal components analysis revealed the presence of one component with an eigenvalue exceeding 1.0, explaining 61% of the variance. This component, which I labeled 'neuropsychological (NP) composite', included measures of learning and memory, processing speed, and executive functioning. The NP composite was used in subsequent analyses[1].

Self-reported Adherence

Similarly, though skewness and kurtosis were within normal limits for the TxEQ adherence measure, visual examination of the normality plots suggested non-normality. I therefore ran a number of transformations and found that the TxEQ to the power of two ($TxEQ^2$) resulted in an improved distribution. Nonetheless, after checking assumptions, and conducting all subsequent analyses (i.e., descriptives, histograms, Q-Q plots, plots of the residuals against the dependent variables) with both the original TxEQ measure and the transformed TxEQ measure, I did not observe any substantial differences in the results. For this reason, I have maintained the original TxEQ adherence measure in the analyses presented herein.

Serum Concentrations

As previously stated, I classified participants as either reaching or not reaching target serum concentration levels of tacrolimus and cyclosporine. Of the participants in the medication adherence sample, 85 participants were taking either cyclosporine or tacrolimus. Forty-four participants (52%) reached target levels of the immunosuppressant for each of the last three measurements, and forty-one (48%) did not (i.e., target levels were not reached for at least one of the three measurements). Using independent sample *t* tests and chi-square tests, I compared the two groups on standard demographics (i.e., age, sex, and education), cognitive performance, and non-cognitive variables (i.e., primary immunosuppressant, donor type, living situation, marital status, and diabetic status, antidepressants, benzodiazepines, and opiates, hypertension, and depressive symptoms), and these groups did not reliably differ (*ns*). Furthermore, a Kendall's tau-b correlation was conducted between the TxEQ adherence measure and the serum target variable, and it was found that the two variables were not significantly correlated (r = -.10, *ns*).

Prescription Refill Data

I was able to collect refill prescription data and calculate medication adherence (MPR) ratios for the primary immunosuppressant (i.e., cyclosporine or tacrolimus) for 83 of the participants. Adherence rates were relatively high (M = 94.02% adherence, SD = .21). By conducting Pearson and Kendall's tau-b bivariate correlations for continuous and dichotomous data, respectively, I took into consideration the association between refill compliance data, and standard demographics (i.e., age, sex, and education), cognitive performance, and non-cognitive variables (i.e., primary immunosuppressant, donor type, living situation, marital status, and diabetic status, antidepressants, benzodiazepines and

opiates, hypertension, and depressive symptoms). No significant associations were identified between adherence to primary immunosuppressants and these variables (p = *ns*). Furthermore, Pearson bivariate correlations conducted between the TxEQ adherence measure and the refill adherence data revealed that the variables were not significantly associated ($p > .05$). In addition, refill adherence data was unrelated to target immunosuppressant serum concentration levels ($r = .08$, p = *ns*). Therefore, I did not create a composite measure of adherence. Because self-reported adherence has been found to better predict EM levels of adherence than other alternatives among kidney TX recipients (Butler et al., 2004), I selected this measure of adherence as the dependent variable for the regression analyses.

TxEQ Adherence Analyses

Bivariate correlations were conducted between the continuous TxEQ medication adherence variable and standard demographic characteristics (i.e., age, years of education, sex), cognitive subtests, and variables previously found to be associated with medication adherence (Denhaerynck et al., 2005). Pearson bivariate correlations and Kendall's tau-b correlations were conducted for continuous and categorical data, respectively (see Table 4). Significant associations were observed between poorer self-reported medication adherence and higher self-reported depressive symptoms, more time since TX, and absence of diabetes (current diabetes or a history of the condition). Of the non-cognitive variables, self-reported depressive symptoms (i.e., CES-D) were significantly associated with adherence at the a priori criterion of $p < .01$, and therefore this variable was included in the regression analyses.

Examination of simple scatterplots of the relationship between the TxEQ Adherence measure and demographics (i.e., age, education), non-cognitive variables (i.e., depressive symptoms), and cognitive variables (i.e., NP composite variable and EPS) suggested linear relationships between the variables. Furthermore, examination of linear regression plots, histograms, Q-Q plots, and standardized residual plots suggested that the data met the assumptions necessary for regression analyses.

Objective 1. In order to address the first part of Objective 1, I entered age, education, and sex in Step 1 and the NP composite in Step 2 as independent predictors of TxEQ Adherence. Step 1 was not predictive of medication adherence (R^2 = .05), F (3, 98) = 1.60, *ns*), and Step 2 did not significantly add to the prediction of adherence ($\Delta R^2 < .01$, *ns*). The full model accounted for 5.1% of the variance in medication adherence, but was not significant (95% confidence limits from 0.00 to 0.14). Examination of the beta values shows that there were no significant predictors of medication adherence (see Table 5, Part I(A)). The effect size for the overall model was small (R^2 = .05; Cohen, 1992).

I proceeded with the second part of the first objective, which was to enter age, education, and sex in Step 1, depressive symptoms in Step 2, and the NP composite variable in Step 3. While depressive symptoms significantly added to the prediction of adherence ($\Delta R^2 = .09$, $p < .01$), the NP composite did not ($\Delta R^2 < .01$, $p > .05$). The full model accounted for 13.2 % of the variance (95% confidence limits from 0.01 to 0.24) in self-reported adherence. Examination of the beta values reveals that older age and more depressive symptoms were significant predictors of poorer self-reported medication adherence (see Table 5, Part I [B]). The effect size for the overall model was medium (R^2 = .13).

Objective 2. For the second objective, I entered demographics on Step 1, the NP composite in Step 2, and EPS in Step 3 of the hierarchical regression analysis. The EPS measure significantly added to the prediction of adherence beyond the demographic variables ($\Delta R^2 = .07$, $p < .01$). The full model accounted for 12.3% of the variance (95% confidence limits from 0.01 to 0.23) in self-reported adherence. Examination of Table 5, Part II (A) reveals that poorer EPS performance emerged as the only significant predictor of poorer medication adherence in the model. The effect size for the model was medium ($R^2 = .12$).

I then added depressive symptoms in Step 2, followed by the NP composite in Step 3, and EPS in Step 4. Depressive symptoms significantly added to the prediction of adherence ($\Delta R^2 = .09$, $p < .01$), as did EPS ($\Delta R^2 = .06$, $p < .01$). This model accounted for 19.2% of the variance (95% confidence limits from 0.04 to 0.31). Examination of beta values indicates that older age, more depressive symptoms, and poorer EPS performance were significant predictors of poorer medication adherence (see Table 5, Part II [B]). The effect size for the model was medium ($R^2 = .19$).

Secondary Analyses. Since both depressive symptoms and EPS emerged as predictors of adherence, I wished to assess whether one variable accounted for unique variance above and beyond that of the other. To do so, I looked at ΔR^2 values and the test of the difference of co-efficients. Age, education and sex were entered in Step 1, and EPS or depressive symptoms entered in Step 2. Both EPS and the depressive symptoms models significantly added to the prediction of adherence ($\Delta R^2 = .075$, $p < .01$; $\Delta R^2 = .084$, $p < .01$, respectively). Furthermore, a test of the difference of the co-efficients (Cohen, 2003; i.e., is β for depressive symptoms = β for EPS?) revealed a significant

difference between the β values (t = -3.56, p < .05), thereby suggesting that depressive symptoms account for unique variance above and beyond that of EPS. Nonetheless, both variables remained significant independent contributors to the final model, resulting in 18.4% of variance being accounted for (95% confidence limits from 0.03 to 0.30; see Table 5, Part III[A]).

Since depressive symptoms emerged as an important predictor of medication adherence, I wished to better elucidate how this variable was contributing to the model. When I applied Radloff`s (1977) criteria of scores of 16 or higher considered indicative of clinically significant symptoms of depression, I found 22 (21.4%) of the medication adherence sample to be endorsing symptoms exceeding that criteria. When I removed these 22 individuals from the analysis and ran the model with demographics, depressive symptoms, NP composite, and EPS entered in steps 1 through 4, respectively, the results remained similar. Depressive symptoms and EPS significantly added to the prediction of adherence (ΔR^2 = .06, p < .05; ΔR^2 = .08, p < .01, respectively). The final model accounted for 22.1% of the variance (95% confidence limits from 0.06 to 0.34). This is similar to the final model that included those endorsing clinically significant levels of depressive symptoms, which accounted for 19.2% of the variance (95% confidence limits from 0.04 to 0.31). Examination of individual beta values in Table 5, Part III (B) reveals that older age, lower education, higher number of depressive symptoms, and lower EPS performance significantly predicted poorer adherence. The effect size for the overall model was medium to large (R^2 = .22).

I then considered the subscales of the CES-D (i.e., negative affect [e.g., felt sad], well-being (e.g., felt hopeful about future), somatic symptoms (e.g., appetite poor, tired),

and interpersonal disturbance [e.g., people dislike me]), and their relationship with the TxEQ adherence subscale by conducting Pearson bivariate correlations. More self-reported negative affect and more somatic symptoms were significantly associated with poorer self-reported adherence (r = -.21, p < .05; r = -.34, p < .01). When I entered these two subscales as separate variables in the second step of the hierarchical regression model with both the reduced and the full sample (demographics, depressive symptoms, NP composite, EPS in steps 1 through 4, respectively), the step with the negative affect and somatic symptom variables significantly added to the prediction of adherence (see Table 5, Part III [C]). The final model with the full sample accounted for 24.3% of the variance (95% confidence limits from 0.07 to 0.36) and the final model with the reduced sample (i.e., not including those meeting the criteria for clinically significant symptoms of depression) accounted for 28.6% of the variance (95% confidence limits from 0.10 to 0.40). In summary, a regression model containing (1) only participants with clinically non-significant levels of depressive symptoms (i.e., less than a score of 16 for CES-D total) and (2) with the two subscales from the CES-D that were significantly associated with self-reported adherence as dependent variables (i.e., negative affect and somatic symptoms) resulted in a model that accounted for more variance (i.e., an additional 9.4% variance) than the original model.

Employment

I conducted logistic regression to assess our prediction that EPS would emerge as a unique predictor of employment status above and beyond that of traditional neuropsychological abilities. Because the sample composition for the employment analyses was slightly different than that of the medication analyses, data was re-examined

for normality of distribution, homogeneity of variance, and extreme values. Normality of data was assessed by looking at skewness, kurtosis, histograms, Q-Q plots, and boxplots. Although skewness and kurtosis were within normal limits for the CES-D, visual examination of the normality plots suggested non-normality. I applied a number of transformations to the CES-D scores and the square root transformation resulted in an improved distribution. I checked assumptions, and ran all subsequent analyses with both the original CES-D measure and the CES-D square root measure. Since the use of the CES-D square root measure did not result in any substantial changes from the original data, I chose to present the results with the original CES-D measure for ease of interpretability.

For our main analysis, I considered several different classification systems for employment.[2] I decided that a dichotomous measure of employment most appropriately fit our data. I dichotomized the group variable on the basis of number of hours worked, in which 'more employed' consisted of individuals working an average of 20 hours or more work per week and 'less employed' consisted of unemployed individuals and individuals working an average of less than 20 hours work per week.

I conducted independent sample *t* tests to compare the two groups on demographic, cognitive, and non-cognitive variables previously found to be associated with employment in kidney TX recipients (i.e., van der Mei et al., 2006; see Table 6). Significant group differences were observed, with participants working less than 20 hours per week tending to be older, reporting a higher number of depressive symptoms, more likely to have a history of or current diabetes, taking more diabetic medications, taking more benzodiazepine and/or antidepressant medications. For non-cognitive variables,

depressive symptoms and antidepressant medication usage met the criterion of $p < .01$, and therefore were included in the specified regression analyses. In addition, participants working less than 20 hours per week performed significantly worse on each of the traditional neuropsychological measures. The effect sizes were small to medium for EPS (d = -.33), medium for Color-Word and Digit Symbol Coding (d = .46; d = -.55, respectively), and medium to large for the Learning and Memory composite, Trails, and NP composite (d = -.61; d = .63; d = -.73, respectively; Cohen, 1992).

Examination of residual plots (i.e., Analog of Cook`s and Changes in Deviance plotted against the predicted probabilities) for the subsequent regression analyses repeatedly suggested points of influence that were of potential concern. Further exploration suggested that scores on the traditional cognitive tests were responsible for these points of influence. Therefore, where necessary, the traditional cognitive variables were winsorized (Wilcox, 1995). This was achieved by calculating Tukey's Hinges, and bringing outliers in (i.e., winsorizing) to the outer bounds of the hinge spread (i.e., values from the first to third quartiles).

As described above, I conducted principal components analysis with the traditional neuropsychological variables for the employment analysis sample (i.e., Digit Symbol Coding, CVLT Learning and Memory, Trails Letter-Number Sequencing, and Color-Word Inhibition) to reduce the number of cognitive variables in the regression analyses. Principal components analysis revealed the presence of one component with an eigenvalue exceeding 1.0, explaining 60% of the variance. This component, referred to as the 'neuropsychological composite' was used in all subsequent analyses[1].

Objective 1. In order to ensure adequate statistical power to test the hypotheses of interest, I initially conducted sequential binomial logistic regression with age, sex, and education to determine whether any demographic variables could be removed from the model. The overall multivariate model was significant, χ^2 (3, N = 94) = 9.41, p <.05. Results showed that age was the only significant predictor of employment status (odds ratio [OR] = .96, p < .05). Therefore, I retained age for subsequent analyses.

I entered age on the first step and the NP composite on the second step. Examination of the Hosmer and Lemeshow (HL) goodness-of-fit test suggested a good fit at each step of the model (χ^2 = 8.26, p > .05; χ^2 =11.75, p > .05, respectively). For the final model, 16.4% of the null deviance was accounted for (Nagelkerke's R^2 = .164). Examination of Table 7, Part I (B) reveals that poorer neuropsychological performance was a significant predictor of fewer hours worked.

I then entered age on Step 1, non-cognitive variables (i.e., antidepressant medication and self-reported depressive symptoms) on Step 2, and the NP composite into Step 3 of logistic regression. The HL goodness-of-fit test suggested a good fit at each step of the model (χ^2 = 7.68, *ns*; χ^2 = 7.16, *ns*; χ^2 = 12.11, *ns*; χ^2 = 2.76, *ns*, respectively). Thirty-one percent of the null deviance was accounted for by the final set of predictors in Step 2 (Nagelkerke's R^2 = .312). Examination of Table 7, Part I (B) reveals that more depressive symptoms and taking antidepressants were significant predictors of fewer hours worked, while poorer neuropsychological performance was a marginal predictor of fewer hours worked.

Objective 2. For the second objective, I entered age on Step 1, the NP composite on Step 2, and EPS on Step 3. The HL goodness-of-fit test suggested a good fit for each

of the steps of the model (χ^2 = 8.26, *ns*; χ^2 = 11.75, *ns*; χ^2 = 12.29, *ns*, respectively). Seventeen percent of the null deviance was accounted for by the final set of predictors in Step 2 (Nagelkerke's R^2 = .166). Examination of Table 7, Part II (A) reveals that poorer neuropsychological performance was a significant predictor of fewer hours worked.

For the second part of the second objective, I entered age, antidepressants and depressive symptoms, the neuropsychological composite, and EPS on steps one through four, respectively. The HL goodness-of-fit test suggested a good fit at each step of the model (χ^2 = 7.68, *ns*; χ^2 = 7.16, *ns*; χ^2 = 2.76, *ns*; χ^2 = 9.89, *ns*, respectively). Thirty-two percent of the null deviance was accounted for by the final set of predictors in Step 4 (Nagelkerke's R^2 = .318). Examination of Table 7, Part II (B) revealed that more depressive symptoms and taking antidepressant medication were significant predictors of fewer hours worked, and poorer neuropsychological performance was a marginal predictor of fewer hours worked.

Since age and EPS were not significant predictors in the final model, I also conducted logistic regression analysis without these two variables. The HL goodness-of-fit test suggested a good fit (χ^2 = 6.72, *ns*). Twenty-nine percent of the null deviance was accounted for by the set of predictors (Nagelkerke's R^2 = .294). Examination of the Wald statistics in Table 7, Part II (C) reveal that a higher number of depressive symptoms, taking antidepressants, and poorer performance on the neuropsychological composite were predictive of fewer hours worked.

Secondary Analyses. Since depressive symptoms emerged as a significant predictor of employment status, I wished to better elucidate how this variable was contributing to the model. When I applied the cut-off criteria established by Radloff

(1977), with those scoring 16 or higher considered to be exhibiting clinically significant symptoms of depression, 24 (25.5%) participants scored above the cut-off point. I ran a sequential logistic regression analysis with these 24 individuals removed from the sample (non-cognitive variables, and NP composite entered in Step 1 and Step 2, respectively). The HL goodness-of-fit test suggested a good fit ($\chi^2 = 6.81$, *ns*; $\chi^2 = 7.86$, *ns*, respectively). The final model accounted for 24.4% of the null deviance (Nagelkerke's $R^2 = .244$). Interestingly, as can be seen in Table 7, Part III, only poorer neuropsychological performance was predictive of fewer hours worked.

I then considered the subscales of the CES-D (i.e., negative affect [e.g., felt sad], well-being[e.g., felt hopeful about future], somatic symptoms [e.g., appetite poor], and interpersonal disturbance [e.g., people dislike me]), and their relationship with employment by conducting Kendall's tau-b bivariate correlations. Higher scores on the negative affect, well-being, and somatic symptoms subscales were significantly associated with less hours worked ($r = -.21$, $p < .05$; $r = -.21$, $p < .05$; $r = -.22$, $p < .05$, respectively). Using the full sample (i.e., not excluding participants with CES-D scores equal or greater to 16) I entered these three subscales as separate variables in the first step of the model and the NP composite in the second step; however, none of the CES-D subscales were significantly predictive of fewer hours worked. Similarly, when I conducted the same analysis in the reduced sample (i.e., participants with CES-D scores of 16 or more removed from the sample), the three CES-D subscales were not predictive of employment status.

DISCUSSION

Summary of Findings

I considered the relative role of traditional and everyday cognitive measures as predictors of medication adherence and employment status in a population previously found to have compromised cognition (Gelb et al., 2008). To my knowledge, this is the first study to assess the role of cognitive performance as a predictor of medication adherence and employment status among kidney TX recipients. Furthermore, to my knowledge, it is the first study to compare the relative utility of an everyday cognitive test (i.e., EPS) versus traditional neuropsychological measures to predict either medication adherence or employment status in any population.

My first objective was to assess the ability of traditional neuropsychological measures to predict medication adherence and employment status. I had predicted that better neuropsychological performance would be associated with greater adherence to medication regimens and more hours worked post-TX. Counter to our initial hypotheses, the traditional neuropsychological composite was not predictive of self-reported adherence. In contrast, better performance on the traditional neuropsychological composite was predictive of being employed post-TX.

The current results counter those of previous research that found a composite measure of traditional neuropsychological functioning to be predictive of medication adherence (e.g., Albert et al., 1999; Hinkin et al., 2004). Not only was the composite NP measure not predictive of adherence, but the individual traditional cognitive measures

were not correlated with self-reported adherence either, a finding that is in contrast to a great deal of studies (e.g., Rosen et al., 2003; Barclay et al., 2007; Albert et al., 1999; Avants et al., 2001). One potential reason for these discrepant findings may be that the current population exhibits a lesser degree of cognitive compromise than the above-mentioned studies. For example, in our previous study (Gelb et al., 2008) I found that 28% of the kidney TX participants scored 1.5 standard deviations below the mean of controls in terms of performance on the CVLT. In contrast, using the same memory measure, Hinkin and colleagues (2004) found that 57% of their participants scored 1.5 standard deviations below the mean. Perhaps if I were to assess medication adherence among TX participants that exhibited a greater degree of cognitive impairment, our findings would have been more similar to the results found in other studies (e.g., Hinkin et al., 2004).

Our second objective was to assess the relative ability of an everyday measure to predict our outcome measures. I anticipated that an everyday measure would account for variance above and beyond that of traditional neuropsychological measures. Our predictions were partially supported. For the medication adherence outcome measure, better performance on EPS (i.e., after accounting for age and traditional neuropsychological performance) was found to be predictive of higher self-reported medication adherence, but not employment status.

It could be argued that there is no benefit to assessing everyday cognition unless is provides some sort of additive value or unique information beyond that which is gained through traditional cognitive testing (Marsiske & Margrett, 2006; Weatherbee & Allaire, 2008). Marsiske and Margrett (2006) outline three ways in which the additive value of

everyday cognitive measures could surface: (1) as a better predictor of outcomes; (2) as a more efficient way of capturing variance than an extensive cognitive battery; (3) through encouraging self-efficacy in that the tasks may seem more relevant and familiar to the examinee. The current study lends further support to a growing body of research (e.g., Weatherbee & Allaire, 2008; Allaire & Marsiske, 2002; Allaire & Willis, 2006) suggesting that everyday cognitive testing is a better predictor of at least certain outcomes (e.g., self-reported adherence). Our findings support the first two ways outlined above in which everyday cognitive measures can provide something unique above and beyond that of traditional cognitive testing.

An additional concern that has been raised is whether measures of everyday cognition are simply tasks that require one to integrate the basic cognitive domains that are tested using a traditional neuropsychological battery (Marsiske & Margrett, 2006). While I found EPS to be significantly associated with both self-reported adherence and three of the four traditional neuropsychological measures (Digit-Symbol Coding r = .32; Trails r = -.34; Color-Word Interference r = -.23), the traditional measures were not significantly associated with medication adherence. Similar to Allaire and Marsiske's (2002) research, our study suggests that EPS is more than a measure of compiled cognition and provides unique information about an individual's cognitive functioning.

The EPS measure requires people to come up with as many practical, safe and effective solutions to everyday problems as they can. Based on its theoretical tenets, one would expect that EPS is predictive of adherence because of its emphasis on practical problems that rely on experience, accumulated knowledge, and broader cognitive skills (Marsiske & Margrett, 2006). It may be that an individual who is able to generate several

safe and effective solutions is better able to apply their knowledge to a problem (e.g., 'If I don't take my immunosuppressants, I stand a significant chance of losing my kidney transplant') and come up with a number of solutions (e.g., 'I should get my spouse to remind me or I could leave a note on the bathroom mirror as a reminder to take my medications') that they have found to be useful from previous experience (e.g., 'If I get in the habit of taking my medications at the same time every day, I will be less likely to forget to take them').

The current study suggests that the ability to adhere to a medication regimen and to work full-time rely on different cognitive capacities for kidney TX recipients. Chaytor and Schmitter-Edgecombe (2003) suggest that functional outcomes can be thought of as belonging to one of two categories: employment status, which tends to have a moderate relationship (i.e., using the standards outlined by Cohen (1992) r = .10 equals a small effect size, or *low* relationship, and r = .30 equals a medium, or *moderate,* effect size) with neuropsychological functioning; and activities of daily living, which have low to moderate relationships with neuropsychological functioning. Medication adherence is one example of an activity of daily living, and the low to moderate relationships previously found between activities of daily living and cognition may aid in explaining why medication adherence was not predicted by traditional neuropsychological measures in the current study. In fact, using the standards outlined by Cohen (1992), the magnitude of the effect sizes for correlations between medication adherence and traditional neuropsychological measures tended to be small (r values range from .05 to .18, see Table 4), whereas the magnitude of the effect size for the relationship between adherence and EPS approached medium (r = .26). The finding that EPS is predictive of adherence

behaviours suggests that everyday measures may be more useful than traditional neuropsychological measures in predicting activities of daily living following kidney transplantation. This is consistent with findings from the cognitive aging literature, in which measures of EPS account for unique variance above and beyond that of than traditional measures in predicting independence in daily living skills (Allaire & Marsiske, 2002) and mortality (Weatherbee & Allaire, 2008; Allaire & Willis, 2006).

An additional reason that traditional neuropsychological measures were better predictors of employment than EPS may lie in the fact that the skills needed to maintain employment greatly depends on the type of position in which an individual is employed in or seeking employment (Mackin et al., 2005). Chaytor, Schmitter-Edgecombe, and Burr (2006) support this argument, stating that varying environmental cognitive demands may act as a mediator of the relationship between cognitive performance and everyday functioning. Perhaps in a large-scale study including individuals from a broad range of occupations one would identify some occupations for which EPS is a better predictor of employment than traditional neuropsychological measures. Such research might lead to findings that allow clinicians to take into consideration an individual's unique environmental demands and select cognitive tests accordingly, which may, in turn, lead to more accurate prediction of functional consequences.

Non-cognitive Predictors

Medication adherence. I was able to take into consideration a number of additional variables that have previously been linked to medication adherence among kidney TX recipients (Denhaerynck et al., 2005), including living situation, marital status, age, sex, depressive symptoms, diabetes, time since TX, and type of organ donor

recipient. Of these variables, the current study only revealed significant associations between adherence and depressive symptoms, time since TX, and diabetes, and because of the entry criterion of $p < .01$, only depressive symptoms were added into main model. In future research, it may be interesting to look at the contribution of the additional variables that were significantly associated with medication adherence, but did not meet our criterion of $p < .01$.

Independently accounting for 9% of the variance in self-reported medical adherence, depressive symptoms appear to be an important predictor of adherence among kidney TX recipients. While a number of studies of other clinical populations have reported an association between depressive symptoms and adherence (e.g., Avants et al., 2001; Catz et al., 2000), few studies have identified depressive symptoms as a significant predictor of adherence (e.g., Boarts et al., 2006). Our findings stress the importance of assessing depressive symptoms among individuals at risk for poor adherence to medication regimens.

It is interesting to note that the Somatic Symptoms subscale from the CES-D appears to account for the relationship between depressive symptoms and adherence. In fact, the model including only the Negative Affect and Somatic Symptoms subscales of the CES-D accounted for more variance than the model including the CES-D total score, and of the two subscales only the Somatic Symptoms subscale was significantly predictive of adherence. The individual questions that comprise the Somatic Symptoms subscale include 'I was bothered by things that usually don't bother me', 'I did not feel like eating; my appetite was poor', 'I felt that everything I did was an effort', 'My sleep was restless', and 'I could not get "going" '. Most of these questions suggest lethargy

rather than specifically pointing towards a depressed mood, and it seems possible that in a medical population such as kidney TX recipients may experience lethargy for reasons other than depression. This is supported by the fact that the same relationship between somatic symptoms and adherence was observed after removing from the sample participants who reported clinically significant levels of depressive symptomatology. Further research will be necessary in order to determine exactly how depressive symptomatology contributes to the prediction of medication adherence.

Since depressive symptoms emerged as an important predictor of adherence, I wished to assess whether EPS or depressive symptoms was a better predictor of adherence. While a test of the difference of the co-efficients suggests that depressive symptoms account for significantly more unique variance in self-reported adherence than EPS, the fact that EPS independently accounted for 6% of the variance (i.e., after accounting for age, sex, education, and depressive symptoms) suggests that EPS is still a useful tool in identifying kidney TX recipients who are at risk for poor adherence.

Employment status. It is also interesting that our findings revealed an association between both higher number of self-reported depressive symptoms and taking antidepressant medications, and few hours worked. One potential explanation for this finding is that certain individuals may have initially stopped working because of depression, and then did not return to work once their depression symptoms diminished. To our knowledge, antidepressant medication use has not previously been taken into consideration as a potential predictor of employment in any population, and may be worthy of future study.

Unlike with the adherence outcome variable, no single subscale of the CES-D was predictive of employment. This suggests that it is the collective contribution of the various types of depressive symptoms (i.e., negative affect, lack of well-being, somatic symptoms, interpersonal disturbances) that is predictive of employment. As mentioned earlier, there is a growing body of literature assessing the associations between depressive symptoms and employment status, and while the findings are not unequivocal, depressive symptoms appear to be an important variable to take into consideration among at least some clinical populations including kidney TX recipients, and persons with HIV, TBIs, and epilepsy (Rabkin et al., 2004; Franulic et al., 2004; Gilliam et al., 2003).

Limitations

It is important to consider our results within the context of various limitations. While some consider EM to be the 'gold standard' in measuring medication adherence (Russell et al., 2006), the high cost of this method has limited its utility (Butler et al., 2004) In fact, self-reported adherence has been found to better predict EM levels of adherence than other alternatives among kidney TX recipients (Butler et al., 2004). Although associations between a health-related quality of life measure and the TxEQ adherence subscale have previously been identified (Jenkinson et al., 1999), it is our understanding that the current study is the first to use the TxEQ Adherence subscale as an outcome measure of medication adherence. I feel that the use of a subscale derived from a standardized, psychometrically sound measure strengthens our findings, as several earlier studies have relied on unstandardized questionnaires (e.g., Tucker, Burnam, Sherbourne, Fuan-Yue, & Gifford, 2003; Chesney et al., 2000).

I also planned to utilize serum concentrations of immunosuppressants and refill prescription data as additional medication adherence measures. In contrast to previous research (Garber et al., 2004; Steiner & Prochazka, 1997), refill adherence data, target serum levels, and self-reported adherence were not significantly associated with each other in the current sample. Therefore, I did not create a composite measure. Interestingly, neither target immunosuppressant serum concentrations nor refill adherence data was associated with any of the main variables of interest (i.e., demographics, cognition, and the non-cognitive variables outlined in Table 4). Since self-reported adherence has been found to better predict EM levels of adherence than other alternatives among kidney TX recipients (Butler et al., 2004), I chose to use this as our adherence outcome measure.

It was interesting to note the limited range of the refill compliance data (i.e., 33% of participants were over 100% adherent to tacrolimus or cyclosporine). While the refill adherence data for the current study suggests that kidney TX recipients seen at VGH are mainly adherent to their immunosuppressants, it may be that this adherence measurement only provides an indication of the maximum adherence rate a patient could possibly keep if they correctly took all of the prescribed medication that they had on hand. Nonetheless, the current study's mean refill compliance rate of 94% adherence to cyclosporine/tacrolimus is in sharp contrast to the existent literature, which suggests adherence rates below 50% (e.g., Butler et al., 2004; Chisholm, Mulloy & DiPiro, 2004) for kidney TX recipients. If our data accurately represents the adherence rates of the participants in the study, this suggests that the kidney TX population at VGH is more

adherent to immunosuppressant medications than many of the populations reported previously in the kidney TX literature.

Regarding the employment analyses, one limitation that would apply to most studies of unemployment risk factors is the lack of established methods for assessing or classifying employment. As noted by van der Mei and colleagues (2006), researchers frequently do not state the classification system that they have used for determining employment status. Furthermore, while employment is commonly assessed using a dichotomous measure (i.e., "employed" versus "unemployed"; Chaytor & Schmitter-Edgecombe, 2003), it is typically unclear where part-time employed individuals fit into such a dichotomy. It was for this reason that I chose to classify individuals as 'more employed' if they worked an average of 20 hours or more per week, and 'less employed' if they worked none or an average of less than 20 hours per week. I feel that this transparency is important and useful in the interpretation of the study results. Lastly, if I had a much larger sample size, I could have included classifications such as part-time employed, homemaker, and student. For the current study, however, such a classification system would have resulted in cell sizes of 6 or less, thereby precluding its usefulness in statistical analyses.

It is important to note that the cross-sectional nature of this study precludes one from making inferences regarding whether poor cognitive functioning actually causes poor medication adherence or failure to return to work. While the current study shows that cognitive performance is associated with the two outcomes, further research is necessary to determine the direction of this relationship. Such research might include longitudinal studies of individuals throughout the stages of kidney disease, as well as

assess the possible cognitive side effects of medication utilized, and reasons for difficulties returning to work.

Furthermore, there are additional noncognitive variables that might influence the relationship between cognitive performance and medication adherence and employment status. For instance, the level of environmental support (e.g., compensatory strategy use, social support) may mediate the relationship between cognition and the two outcomes of interest in the current study. In fact, in a mixed population (i.e., participants with traumatic brain injuries, epilepsy, and other medical conditions), researchers found that by controlling for the variance accounted for by compensatory strategy, the ecological validity of executive functioning tests was improved (Chaytor, Schmitter-Edgecombe & Burr, 2006). The role of environmental support in relation to cognitive performance has not previously been considered in the kidney TX population.

An additional noncognitive variable that we did not take into consideration is fatigue. As previously mentioned, self-reported somatic symptoms of depression emerged as a significant predictor of adherence, for which many of the subscale items suggest a general lethargy. Therefore, assessing for fatigue may be useful in sorting out the relative contribution of depressive symptoms over and above that of low energy to predicting adherence.

Conclusions

In terms of the clinical practice of neuropsychology, there is a critical need for a better understanding of the functional implications of reduced cognitive performance in chronic illness populations such as kidney disease. The current results suggest that EPS is

predictive of medication adherence and performance on traditional neuropsychological measures and taking antidepressant medication is predictive of employment status. Furthermore, self-reported depressive symptoms are predictive of both outcome variables. These findings highlight the potential benefits of formal evaluation of cognition and psychosocial functioning in order to predict individuals at risk for difficulties returning to work and adhering to medication regimens.

In addition, the results from this study have important implications for kidney TX recipients in terms of treatment planning. Since traditional and everyday measures are predictive of medication adherence and employment status, respectively, healthcare professionals may wish to consider routine assessments of cognitive capabilities in order to identify individuals who might benefit from additional services and increased support following kidney transplantation. Additional services might include education, increased monitoring of medication adherence, simplified medication regimens (Chapman, 2004), and supported return to work services. Educational programs could involve health education and teaching compensatory techniques, such as utilizing memory notebooks or alarms as reminders to take medications. In general, helping individuals be more prepared for the challenges that they may face as a result of cognitive difficulties could aid in successfully transitioning individuals into life post-kidney transplantation.

My study resulted in a number of other interesting findings apart from our primary objectives, including identification of other non-cognitive predictors of medication adherence and employment status, and the relationship among three measures of medication adherence in a kidney TX population. The role of depressive symptoms

cannot be overlooked, and the current study stresses the importance of this variable in predicting both adherence and employment status.

This is one of the first studies to test the hypothesis that everyday measures are better predictors of specific real-world outcomes than traditional neuropsychological measures. Since EPS was found to be a stronger predictor of medication adherence than traditional neuropsychological measures, the need to further develop everyday tests of cognition is reinforced. While there has recently been a significant emphasis on the development of such measures (e.g., Burgess et al., 2006), relatively little is known about the benefits of these tests (Chaytor & Schmitter-Edgecombe, 2003), especially in terms of specific outcome measures such as medication adherence and employment status. Our findings suggest that different types of cognitive measures (i.e., everyday vs. traditional) are better at predicting different outcomes (i.e., adherence vs. employment). Therefore, it may not be sufficient to look at general outcome measures such as self- or caregiver-reported cognitive functioning; instead, identifying specific predictors of specific outcomes appears to be necessary. Such research will allow clinicians to make educated recommendations regarding the meaning of neuropsychological assessments in terms of particular functional outcomes.

APPENDICES

Appendix A

While compromised cognition has long been reported in persons undergoing dialysis treatment (e.g., Teschan et al., 1979; Kurella, Chertow, Luan, & Yaffe, 2004), accumulating evidence suggests that individuals may be at increased risk for cognitive difficulties relatively early in the course of the disease, even before kidney failure occurs (Thornton, Shapiro, Deria, Gelb, & Hill, 2007; Kurella et al., 2004). Chronic Kidney Disease (CKD) can be briefly described as a decrease in kidney function due to kidney damage (for a detailed review, see Levey et al., 2003). Untreated CKD results in the gradual development of uremia, which is thought to be a result of the accumulation of metabolic waste products, some of which are thought to be neurotoxic (Burn & Bates, 1998). Glomerular Filtration Rate (GFR), an estimation of the filtration capacity of the functioning nephrons (i.e., the ability of the kidney to filter substances from the blood), is the best overall indicator of level of kidney function (Levey et al., 2003). Lower GFR levels indicate either a decrease in the filtration rate of the nephrons or a decline in the number of nephrons in the kidneys (Stevens & Levey, 2005). Kidney failure, also referred to as End Stage Renal Disease (ESRD), occurs when GFR drops below 15mL/min per 1.73 m^2. When a patient enters a state of kidney failure, they must begin kidney replacement therapy to survive (Levey et al., 2003).

To date, there are three major forms of kidney replacement therapy: hemodialysis, peritoneal dialysis, and kidney transplantation (Pliskin, Kiolbasa, Hart, & Umans, 2001). The first form of dialysis, hemodialysis, involves an exchange of solutions across a semi-permeable membrane which filters metabolic wastes from the blood. Hemodialysis is the most prevalent treatment and involves a clinical visit three times a week for several hours each time (Gonzalez-Perez, Stearns, & Wordsworth, 2005). Even with this treatment, individuals may still experience severe kidney insufficiency. The concept of peritoneal dialysis is similar, but it involves the use of the patient's own peritoneal membrane to filter metabolic wastes. This treatment is self-administered, either nightly or four to five times daily. The patient on peritoneal dialysis may also remain in a state of severe renal insufficiency (Kidney Disease Outcome Quality Initiative (K/DOQI; National Kidney Foundation, 2002).

The last treatment modality is kidney transplantation. When successful, transplantation usually stabilizes kidney functioning at 60-70% of normal levels (R. J. Shapiro, personal communication, June 28, 2006). Between 1996 and 2005, there were 10,693 kidney transplants in Canada (2007 CORR Report). Of these, 63% were received from deceased donors and the remaining transplants were from living donors (2007 CORR Report). The 1-year patient survival rates have improved from 85.8% in 1996 to 92.3% in 2000 for recipients of organs from deceased donors, while 5-year survival rates for recipients of organs from living donors has remained relatively stable (i.e., 94.9% in 1996; 95.1% in 2000). Furthermore one-year patient survival rates are very high 98.9% and 99.7% in 2005 for recipients of organs from deceased and living donors, respectively; 2007 CORR Report). Relative to dialysis, kidney transplantation provides

an improvement in long-term survival rates (Polkoff-Rubin & Goes, 2004). Although the recipient must remain on immunosuppressive drugs for life, this is still a highly preferred treatment modality because it usually prevents kidney disease from progressing and stabilizes or improves kidney functioning (Pliskin et al., 2001).

Appendix B

ANOVA Results for Cognitive Performance

Cognitive Measures	Group	N	M	(SD)	F	df
CVLT - Trial 1	CKD	47	5.19	(1.66)	3.53*	(2, 139)
	TX	43	5.16	(1.95)		
	Control	52	6.10	(2.26)		
Learning & Memory	CKD	47	40.47	(8.88)	15.11**	(2, 138)
	TX	42	41.78	(9.79)		
	Control	52	50.00	(9.40)		
Trails-Letter-Number Sequencing	CKD	47	107.68	(48.22)	5.95**	(2,137)
	TX	41	95.98	(39.21)		
	Control	52	80.06	(31.62)		
Color-Word Inhibition	CKD	47	64.11	(17.23)	7.99**	(2,133)
	TX	37	62.44	(15.43)		
	Control	52	53.76	(12.70)		

Appendix C

Table C1. Summary of self-report approaches to assessing medication adherence

Measure	Format	Sample Questions	Scoring	Reliability	Validity
Medication Adherence Scale (MAS; Morisky et al., 1986)	Interview: Four Questions	"Do you ever forget to take your medication?"	1 point for each no response Total Scores 1 = low adherence 2-3 = moderate adherence 4 = high adherence	*r* = 0.61	Predictive Validity: Hypertensive individuals scoring high on the MAS were more likely to have well-controlled hypertension; *r* = 0.58, *p* < .01. Sensitivity: 81% Specificity: 44%
General Adherence Scale (GAS; Sherbourne et al., 1992)	Question-naire: five questions rated on a Likert scale	"I had a hard time doing what the doctor suggested I do"	Sum of Likert scale points	Internal Consistency: Cronbach α = 0.80 Test-Retest: *r* = 0.41 (over 2 years)	- GAS correlated with initial adherence, avoidance coping style, and health distress
Center for Adherence Support Evaluation (CASE) Adherence Index (Manheimer et al., 2006)	Question-naire: three questions rated on a Likert scale	"How often do you feel that you have difficulty taking HIV medications on time? By 'on time' we mean no more than two hours before or two hours after the time your doctor told you take it"	Sum of Likert scale points. Total score range: 3 to 16. > 10 = good adherence ≤ 10 = poor adherence	not provided	- CASE Adherence Index more strongly associated with HIV virologic outcomes than self-reported three day adherence data Sensitivity: 74% Specificity: 99% (in relation to 3 day adherence data)

Measure	Format	Sample Questions	Scoring	Reliability	Validity
Brief Medication Questionnaire (BMQ) – Regimen Screen (Svarstad et al., 1999)	Self-report questionnaire: Seven questions	"How many days did you take it?"	Responses indicating non-adherence are scored "1" and "0" for no indicators of non-adherence. Rates of dose omission are also calculated.	Not provided	Validity Highly correlated with EM rates of dose omission in past week (r = 0.67, p < 0.01)and past month (r = 0.89, p < 0.01) Repeat Non-adherence Sensitivity: 80% Specificity: 100% Sporadic Non-adherence Sensitivity: 0% Specificity: 37.5%
Transplant Effects Questionnaire (TxEQ; Ziegelmann et al., 2002)	Self-report questionnaire: Five questions rated on a 5-point Likert scale	"Sometimes I do not take my anti-rejection medicines"	Total score range: 5-25.	Internal Consistency: Cronbach α = .79 Test-Retest: r = .77	Not provided
Immuno-suppressant Therapy Adherence Scale (ITAS; Chisholm et al., 2005)	Self-report questionnaire: Five questions rated on a 4-point Likert scale	One question asks how often the patient forgets to take their immunosuppressant therapy (IST) medications	Individual item scores range 0-3	Internal Consistency: Cronbach α = .81	Significantly correlated with prescription refill rates and serum immunosuppressant concentrations (p < .01). Item scores negatively associated with increased serum creatinine levels (p < .05).

Table C2. Summary of studies assessing the concurrent validity of medication adherence measures

Study	Population	Comparisons	Results
Waterhouse, Calzone, Mele & Brenner (1993)	Cancer	Self-report, pill counts, & EM	Self-report and pill counts resulted in significantly higher adherence rates than EM
Straka, Fish, Benson, & Suh (1997)	Coronary Artery Disease	Self-report diary measure & EM	Self-report resulted in significantly higher rates of adherence. Approximately 84% of self-reported compliance rates differed from EM.
Liu, Golin, Miller et al. (2001)	HIV Infection	Interview, pill counts, EM, and composite adherence score	The composite adherence score (i.e., interview, pill count, and EM composite) was the strongest predictor of virologic response.
Arnsten, Demas, Farzadegan et al. (2001)	HIV Infection	Self-report & EM	Self-report and EM significantly correlated. Self-report resulted in significantly higher adherence rates. Both self-report and EM were significantly correlated with HIV load; more of those with EM adherence ≥ 90% achieved virologic suppression.
Hamilton (2003)	Hypertension	Self-report, clinician report, pill counts, urinary potassium levels, and EM	EM was significantly correlated with self-report and pill counts. Urinary potassium levels were not significantly correlated with any of the adherence measures.
Svarstad, Chewning, Sleath & Claesson (1999)	Mixed clinical population	Self-report (BMQ-Regimen Screen (RegS) and Recall Screen (RecS)) & EM	Using EM as the referent standard, the RegS had good sensitivity (80%) and excellent specificity (100%) for the repeat non-adherence pattern and poor sensitivity (0%) and specificity (37.5%) for the sporadic non-adherence pattern. The RecS had poor sensitivity (40%) and specificity (40%) for repeat non-adherence and good sensitivity (90%) and specificity (80) for sporadic non-adherence.
Chisholm, Mulloy, and DiPiro (2005)	Kidney TX	RC & serum levels	Significantly more nonadherent participants had below target immunosuppressant concentrations.
Wetzels et al. (2006)	Hypertension & Diabetes	RC & EM	Nonadherence rates were 18.4% for RC and 4% EM.
Paes, Bakker, and Soe-Agnie (1998)	Diabetes	RC, pill count, self-report & EM	Refill compliance and EM were significantly correlated while pill count was not; RC resulted in more individuals classified as adherent than EM.
Choo et al. (1999)	hypertension	RC, self-report, pill count, & EM	Self-report, RC, & pill count were significantly associated with EM. One self-report item was independently predictive of EM.

Table C3. Summary of studies assessing the association between medication adherence and cognition

Study	Population	Cognitive Domains Assessed	Outcome Measures	Results
Rosen et al. (2003)	Type II Diabetes	Processing speed, working memory, motor skills, executive functioning (EF)	Electronic Monitoring (EM)	EF was independently associated with medication adherence.
Vedhara et al. (2004)	Type II Diabetes (65 years or older)	Prospective Memory	EM	Adherence rates were significantly higher for individuals who performed better on a prospective memory task.
Barclay et al. (2007)	HIV Infection	Memory, EF, verbal fluency, attention, working memory, motor functioning	EM	Memory and EF significantly associated with poor adherence.
Hinkin et al. (2004)	HIV Infection	Memory, EF, verbal fluency, attention, working memory, motor functioning	EM	Memory and EF significantly associated with poor adherence. Global neuropsychological impairment impairment (i.e., average score ≥ to 1.5 standard deviation below the mean) was independently predictive of poor medication adherence.
Albert et al. (1999)	HIV Infection	EF, attention, psychomotor skills, verbal fluency, learning and memory, attention	Self-report	Poorer memory was significantly associated with poor adherence. Overall neuropsychological performance was a significant predictor of adherence.
Ammassari et al. (2004)	HIV Infection	EF, attention, psychomotor skills, verbal fluency, learning and memory, attention	Self-report	No significant findings.
Avants, Margolin, Warburton, Hawkins, & Shi (2001)	Drug-using individuals with HIV infection	Intelligence, learning and memory, psychomotor speed, EF	Self-report	Poor adherence was associated with poor performance in all cognitive domains. None of the measures independently predicted poor adherence.
Waldrop-Valverde et al. (2006)	Drug-using individuals with HIV infection		Self-report	Poorer psychomotor speed was significantly associated with poor adherence.
Wagner, Kanouse, Koegel & Sullivan (2004)	Dual diagnosis: HIV and serious mental illness	Learning and memory, EF, processing speed	EM	No significant findings.

Study	Population	Cognitive Domains Assessed	Outcome Measures	Results
Robinson et al. (2002)	1st episode of schizophrenia or schizoaffective disorder	Extensive neuropsychological battery of 41 tests	Medication dis-continuation	Discontinuation was significantly associated with poor EF performance.
Jeste et al. (2003)	Schizophrenia and schizoaffective disorder	Dementia screening instrument	Role-play medication management	Conceptualization and memory subscales independently predicted MMAA performance.
Pratt, Mueser, Driscoll, Wolfe & Bartels (2006)	Severe mental illness	memory, working memory, verbal fluency, EF	Pill count, self-report, informant ratings	No significant findings.
Verdoux, Liraud, Assens, Abalan, & van Os (2002)	Early psychosis	EF, verbal fluency, processing speed, memory	Medication dis-continuation	Poor performance on an EF measure (Wisconsin Card Sorting Test; Heaton, 1993) was associated with better medication adherence.
Insel, Morrow, Brewer & Figuerdo (2006)	Older adults taking antihypertensives, lipid-lowering agents, and antiarthritic agents.	EF, working memory, cued recall, and recognition memory	EM	A composite of EF and working memory performance was a significant predictor of adherence.
Cooper et al. (2005)	Older adults	Mini-Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975)	Self- or caregiver-report	Greater cognitive impairment was predictive of nonadherence
Ayalon, Areán, & Alvidrez (2005)	Older adults (Black and Latino) taking antidepressants	MMSE	Self-report	Cognitive performance was not predictive of intentional nonadherence, but was predictive of unintentional nonadherence.
Incalzi et al. (1997)	Chronic obstructive pulmonary disease	Verbal memory and a cognitive screening battery	Self- or caregiver-report	Poor performance on delayed recall and the screening battery associated with non-adherence.
Stilley, Sereika, Muldoon, Ryan, & Dunbar-Jacob (2004)	Adults taking cholesterol-lowing medications	Attention, EF, visuospatial/con-struction skills, IQ, memory	EM	All domains except memory associated with poor medication adherence. Estimated IQ was the most powerful predictor of medication adherence, even when including non-cognitive factors.

Table C4. Summary of approaches used to assess employment

Study	Measure	Format	Population
Meyer, Bond, Tunis & McCoy (2002)	The Work Placement Scale	1) Unemployed 2) Prevocational training 3) Sheltered workshop/volunteer work 4) Group placement (i.e., paid job for persons with disabilities) 5) integrated employment (i.e., competitive community employment)	Schizophrenia Spectrum-Disorders
Rabkin et al. (2004)	Hollingshead-Redlich Scoring System	1) Unemployed 2) Part-time, at least 4 hours/week 3) Employed, at least 35 hours/week	Men with HIV/AIDS
Dickerson et al. (2004)	N/A	1) Unemployed or no current work activity 2) Current participation in volunteer work, sheltered work, part-time competitive work (less than 20 hours/week) or part-time student status 3) Current participation in full-time competitive work (at least 20 hours/week) or full-time student status	Bipolar Disorder
Wood & Rutterford (2006)	N/A	1) Full-time employed 2) Part-time employed 3) Unemployed 4) Student 5) Retired	Traumatic Brain Injury
Machamer, Temkin, Fraser, Doctor & Dikmen (2005)	N/A	1) Unemployed 2) Work ≤50% of the time 3) Work 51-89% of the time 4) Work ≥ 90% of the time	Traumatic Brain Injury
Matas et al. (1996(	N/A	Full-time employment, part-time employment, full-time college student, part-time college student, part-time employment plus part-time student, pre-college student, receiving disability benefits, retired, independent homemaker, other	Kidney Transplant

Table C5. Summary of studies assessing the association between employment and cognition

Study	Population	Cognitive Domains Assessed	Results
Wood & Rutterford (2006)	TBI	verbal ability, information processing speed, visuospatial reasoning, executive functioning, nonverbal memory, verbal memory, and working memory	Cognitive performance explained 18.5% of the variance in employment status. No single cognitive domain significantly contributed to employment status.
Machamer et al. (2005)	TBI	intellectual functioning, processing speed, executive functioning, and memory	Better performance in each cognitive domain significantly associated with more time spent working and maintenance of employment. Employment stability best predicted by neuropsychological functioning, pre-injury annual earnings, and a pre-injury arrest record.
Doctor, Castro, Temkin, Fraser, & Machamer (2005)	TBI	Intellectual functioning, processing speed, & executive functioning	Poorer performance in each cognitive domain associated with greater risk of unemployment.
Kibby Schmitter-Edgecombe, & Long (1998)	TBI	Executive functioning & verbal learning and memory	Cognitive performance not significantly associated with employment status. Memory performance significant predictor of work performance.
Mackin, Horner, Harvey, & Stevens (2005)	Substance Abuse	Attention, memory, & executive functioning	Attention and memory predictors of employment problem severity.
Rabkin, McElhiney, Ferrando, Van Gorp, & Lin (2004)	HIV infection	Processing speed, verbal learning and memory, executive functioning, & visuomotor skills	Better executive functioning predictive of greater number of hours worked.
Dickerson et al., 2004	Bipolar Disorder	Working memory, attention, and neurocognitive screen	All cognitive domains significantly associated with employment status
McGurk & Mueser (2006)	Severe Mental Illness	Academic achievement, attention, working memory, psychomotor speed, verbal learning and memory, & executive functioning	Employment in an occupation requiring greater cognitive complexity significantly associated with better performance on measures of executive functioning and verbal learning and memory.

Study	Population	Cognitive Domains Assessed	Results
Gold et al. (2002)	Severe Mental Illness	Intellectual functioning, academic achievement, working memory, memory, verbal fluency, motor functioning, executive functioning	Neuropsychological functioning predicted total number of hours worked. No differences in cognitive performance between those who were employed and those who were not. Authors concluded that cognitive performance is a predictor of job tenure but not job attainment.
Evans, Bond, Meyer et al. (2004)	Severe Mental Illness	Verbal learning and memory, executive functioning, working memory, and information processing speed.	Cognitive performance better among competitively employed individuals compared to those in supported employment settings. Work habits, work quality, cooperativeness and personal presentation associated with verbal learning and memory. Personal presentation associated with executive functioning.
Benedict, Cookfair, Gavett et al. (2006)	Multiple Sclerosis	Language, spatial processing, processing speed, learning and memory, working memory, executive functioning	Verbal memory, executive functioning, and working memory/processing speed found to be significant predictors of employment.
Ready, Stierman & Paulsen (2001)	Healthy Persons	language, processing speed, and executive functioning	Language, processing speed, and executive functioning significantly associated with work behaviour and accounted for 15% of variance in this outcome.

Appendix D

Stability of GFR

The same procedures for assessing stability of kidney functioning will be used as in the initial project (Gelb, Shapiro, Hill, & Thornton, in press). To date, the most current GFR (GFR1; the GFR closest to the time of testing), and the two most recent GFRs (GFR2 = 2nd most recent, and GFR3 = 3rd most recent) have been collected for TX participants. This data was then analyzed to identify, if any, major concerns regarding kidney stability, including decreases in kidney functioning to the point of ESRD. In the interpretation of this data, it is important to note that kidney functioning in kidney TX recipients is rarely restored to a level of normal kidney function. This may be because TX recipients typically have only one functioning kidney rather than two. Therefore, even if a patient is considered to have a successful kidney TX, GFR levels would represent a degree of kidney insufficiency in a majority of the cases.

GFR1-GFR2

The difference scores were calculated between GFR1 and GFR2 (GFR2-GFR1) as well as overall means. Difference scores were approximately normally distributed. The mean difference score was 4.72 (*S.D.* = 3.74). GFR difference scores that were greater than one standard deviation below the mean at the time of testing were identified (i.e., indicating a relative drop in GFR and overall kidney functioning). Two individuals were within this range (T19, T22). Both of these individuals at the time of testing had stage 2

kidney damage (mild damage; GFR between 59 and 90). The same two individuals also met the criterion of 2 standard deviations below the mean.

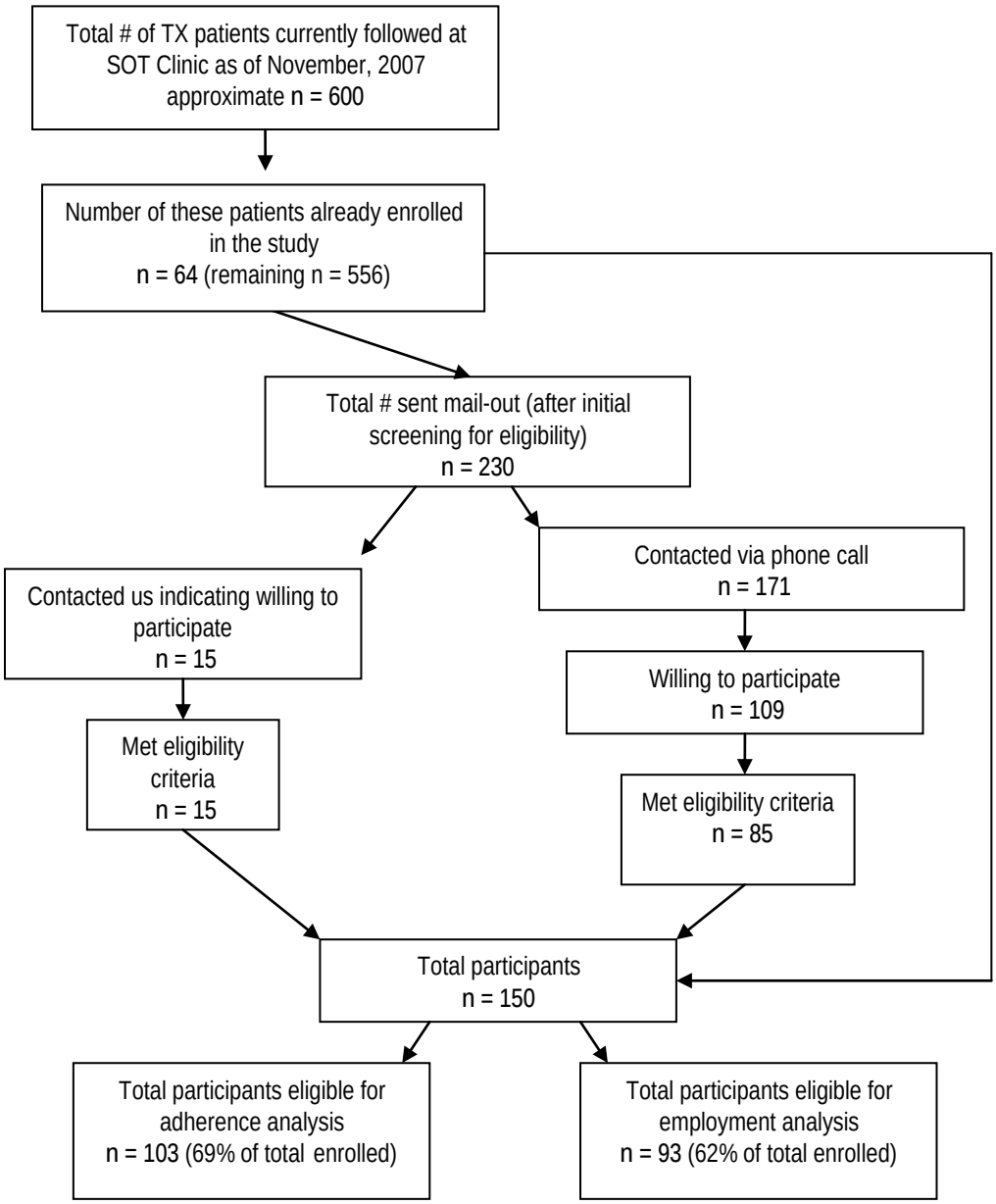
GFR1-GFR3

I used similar procedures for GFR1 and GFR3 (GFR1-GFR3). Again, difference scores were approximately normally distributed. The mean difference score was 5.79 (*S.D.* = 5.47). Two individuals were identified who were one standard deviation below the mean (T22 & T40). Once again, at the time of testing both individuals were at the level of stage 2 kidney damage (i.e., mild). When the criterion was set at 2 standard deviations below the mean, only one individual was within this range (T22).

Individuals with Stage 4 Kidney Damage

For individuals with stage 4 kidney disease, additional qualifications were applied: (1) Their GFR levels must not have decreased more than 1 SD below the mean; and (2) none of the past three measurements of GFR could be within the range of stage 5 kidney disease (i.e., kidney failure). At time of testing, none of the three individuals with stage 4 kidney damage showed a decrease of kidney functioning of one standard deviation or more below the mean in comparison with the two most recent measures of GFR. However, one of three participant's GFR levels fell in the range of stage 5 kidney disease. This participant was excluded from further analyses, while the other two participants remained in the study.

Appendix E


Total # of TX patients currently followed at SOT Clinic as of November, 2007 approximate n = 600
Number of these patients already enrolled in the study n = 64 (remaining n = 556)
Total # sent mail-out (after initial screening for eligibility) n = 230
Contacted us indicating willing to participate n = 15
Contacted via phone call n = 171
Met eligibility criteria n = 15
Willing to participate n = 109
Met eligibility criteria n = 85
Total participants n = 150
Total participants eligible for adherence analysis n = 103 (69% of total enrolled)
Total participants eligible for employment analysis n = 93 (62% of total enrolled)

Appendix F

Employment Interview

Have you been employed since receiving your transplant? Yes No
(If NO, skip to p. 2)

Are you currently employed? Yes No

If employed post-TX, please ask these questions about the most recent job:

Job Title:
Start Date (month, year): _____, _____
Average number of hours worked per week:
For how many months/years have you been working this number of hours k? ___ months ___ years
Description of job:

Other jobs held since receiving kidney TX:

Description (starting w/most recent) **Date of employment** (--/-- to --/--)

_____ _____ full-time part-time

_____ _____ full-time part-time

_____ _____ full-time part-time

_____ _____ full-time part-time

_____ _____ full-time part-time

Were you employed prior to receiving your kidney transplant? Yes No

If yes, please ask these questions about the last job prior to TX:

Job Title:
Start Date (month, year): _____, _____
Average number of hours worked per week:
For how many months/years have you been working this number of hours k? ___ months ___ years
Description of job:

Was there a time prior to receiving your kidney transplant when you were unable to maintain employment because of your kidney problems? Yes No

(If yes) **How long was this for**? ___ years/___ months *OR* date: ____/__ to ____/__

(If no) **Was there a time prior to receiving your kidney transplant when you had to reduce the number of hours you worked each week because of your kidney problems?**

Yes No *(If yes)* **How long was this for**? ___ years/___ months

(If not currently employed) **What best describes your current status?**

__ Homemaker **__ On Disability** short-term long –term

__ Student: full-time part-time **__ Unemployed**

__ Retired (at what age did you retire? ____)

__ Other (please describe) **_____**

How long have you been in this position (e.g., homemaker, student, retired)? ____/____
month year

If you are a homemaker, on average, how many hours per week do you spend in this position? _____

If you are a student, how many credits are you currently taking? _____
part-time full- time

How long have you been in school? ____ months ____ years

Appendix G

Everyday problem solving vignettes used in the current study (adapted from Artistoco et al., 2003; Denney & Palmer, 1981; Denney & Pearce, 1989).

1. NOW LET'S SAY THAT ONE EVENING YOU GO TO THE REFRIGERATOR AND YOU NOTICE THAT IT IS NOT COLD INSIDE, BUT RATHER IT'S WARM. WHAT WOULD YOU DO?

2. LET'S SAY THAT YOU LIVE IN A HOUSE WITH A BASEMENT. ONE NIGHT THERE IS A FLASH FLOOD AND YOU NOTICE THAT YOUR BASEMENT IS BEING FLOODED BY THE WATER COMING IN THE WINDOW WELLS. WHAT WOULD YOU DO?

3. LET'S SAY THAT AN ELDERLY COUPLE IS LIVING ON SOCIAL SECURITY AND THAT THEY HAVE NO OTHER SOURCE OF INCOME. ONE WINTER THEY FIND THAT THE HEATING BILLS ARE SO HIGH THAT THEY CANNOT PAY THEM. WHAT SHOULD THEY DO?

4. LET'S SAY THAT YOU ARE A PARENT OF AN EIGHT-YEAR-OLD DAUGHTER. ONE DAY YOU ARRIVE AT HOME FIFTEEN MINUTES AFTER YOUR DAUGHTER COMES HOME ON THE SCHOOL BUS. WHEN YOU GET HOME, YOUR DAUGHTER IS NOT THERE. YOU WAIT FOR HER TO CALL OR COME HOME, WHICH SHE USUALLY DOES WITHIN ABOUT THIRTY MINUTES. YOU WAIT FOR AN HOUR AND THIRTY MINUTES AND YOU'VE STILL NOT HEARD FROM HER. IT'S BEGINNING TO GET DARK. WHAT WOULD YOU DO?

5. AN ELDERLY MAN HAS JUST RETIRED. HE DOESN'T HAVE ANY HOBBIES BECAUSE HE HAS NEVER HAD TIME FOR THEM BEFORE. NOW HE IS REALLY BORED. WHAT SHOULD HE DO?

6. LET'S SAY THAT A 68-YEAR-OLD WOMAN IS TAKING CARE OF HER 93-YEAR-OLD MOTHER. THE MOTHER IS IN VERY POOR HEALTH AND NEEDS CONSTANT CARE. THE WOMAN, HOWEVER, IS NOT IN VERY GOOD HEALTH EITHER AND IS UNDER DOCTOR'S ORDERS TO TAKE IT EASY AND GET A LOT OF REST. WHAT SHOULD SHE DO ABOUT CARING FOR HER MOTHER?

Footnotes

1. In order to examine whether individual traditional neuropsychological measures would be superior independent predictors of medication adherence and employment status, I entered individual subtest scores from Digit Symbol Coding, Trails, Color Word, and Learning and Memory into multivariate and binomial logistic regression analyses, respectively. In terms of medication adherence, the overall model was not significant (R^2 = .22, F (4, 97) = 1.30, $p > .05$), nor were any of the variables independently predictive of adherence. With regards to employment status, the overall multivariate model was significant, χ^2 (4, N = 94) = 12.40, $p < .05$; however, none of the variables made independent, statistically significant contributions to the model.

2. As one of our measures of employment, I proposed to use a categorical classification system. Categories that I intended to include were as follows: (1) unemployed or no current work activity, (2) part-time competitive work (less than 20 hours per week) or part-time student status, (3) current participation in full-time competitive work (at least 20 hours per week) or full-time student status, and (4) homemaker. As is shown in the table below (i.e., Classification 2), there were only 6 individuals classified as part-time employed/part-time students and 5 homemakers; therefore, the size of these two groups precluded us from conducting any additional analyses using this classification system.

Classifications of Employment

Classification 1	Unemployed (n; %)	33 (35.1%)
	Part-time Employment or Student (n; %)	12 (12.8%)
	Full-time Employment or Student (n; %)	49 (52.1%)
Classification 2	Unemployed (n; %)	28 (29.8%)
	Part-Time Employment or Student (< 20 hrs/week) (n; %)	6 (6.4%)
	Full-Time Employment or Student (≥ 20 hrs/week) (n; %)	55 (58.5%)
	Homemaker (n; %)	5 (5.3%)
Classification 3	Less than 20 hours/week (n; %)	39 (41.5%)
	More than 20 hours/week (n; %)	55 (58.5%)
Classification 4	Full-time Employed (n; %)	49 (52.1%)
	Unemployed or Part-time Employed (n; %)	45 (47.9%)

Table 1. Demographic and Clinical Variables

Participant Characteristics	TxEQ Analysis (*n* = 103)	Employment Analysis (*n* = 94)
Age (mean ±SD)	50.07 ± 12.38	46.85 ± 10.58
Female (n; %)	49 (47.6%)	45 (47.9%)
Right Handedness (n; %)	94 (91.3%)	84 (89.4%)
Ethnicity		
Caucasian (n; %)	*75 (72.8%)*	*70 (74.5%)*
Asian (n; %)	*17 (16.5%)*	*14 (14.9%)*
Other (n; %)	*11 (10.7%)*	*10 (10.6%)*
Education (mean years ±SD)	13.93 ± 2.12	13.84 ± 2.05
Depressive Symptoms (mean score ±SD)	10.70 ± 9.85	11.07 ± 9.56
Smoke cigarettes (n; %)	3 (2.9%)	3 (3.2%)
Hypertension (n; %)	80 (77.7%)	74 (78.7%)
Diabetes mellitus (n; %)	17 (16.5%)	13 (13.8%)
DM & History of DM (n; %)	27 (26.2%)	23 (24.5%)
Coronary Artery Disease (n; %)	11 (10.7%)	35 (37.2%)
Hypercholesterolemia (n; %)	37 (35.9%)	35 (37.2%)
Anti-depressants (n; %)	14 (13.6%)	13 (13.8%)
Benzodiazepines (n; %)	6 (5.8%)	6 (6.4%)
Opiates (n; %)	1 (1.0%)	1 (1.1%)
Anti-cholesterol agents (n; %)	39 (37.9%)	33 (35.1%)
Anti-hypertensives (n; %)	75 (72.8%)	71 (75.5%)
Anti-diabetic medications (n; %)	14 (13.6%)	11 (11.7%)
Time since transplant (years; mean ± SD)	7.96 ± 6.25	7.35 ± 5.83
Kidney and Pancreas transplant %	10 (9.7%)	10 (10.6%)
Dialysis History %	93 (90.3%)	82 (87.2%)
Hemodialysis	*51 (49.6%)*	*44 (46.8%)*
Peritoneal Dialysis	*21 (20.4%)*	*19 (20.2%)*
Both	*21 (20.4%)*	*19 (20.2%)*
Time Spent on Dialysis (years; mean ± SD)	2.78 ± 3.03	2.64 ± 3.00
Immunosuppressant Type[#]		
Cyclosporine (n; %)	*22 (21.4%)*	*18 (19.1%)*
Tacrolimus (n; %)	*72 (69.9%)*	*68 (72.3%)*
Deceased Donor[#]	58 (56.3%)	50 (53.2%)
Previously on Dialysis (n; %)	*56 (96.6%)*	*48 (96.0%)*
Living Donor %	45 (43.7%)	44 (46.8%)
Previously on Dialysis (n; %)	*37 (82.2%)*	34 (77.3%)
# of Kidney Transplants		
1 Transplant (n ;%)	89 (86.45)	80 (85.1%)
2 Transplants (n;%)	14 (13.6%)	14 (14.9%)

[#]deceased vs. living donors previously on dialysis: χ^2=5.94, p <.05 & χ^2=7.37, p <.01 for adherence and employment samples, respectively.

Table 2. Descriptives for Independent and Dependent Variables

	M ± SD	Skewness	Kurtosis	α
Medication Adherence Sample (*n* = 103)				
Age (mean ±SD)	50.07 ± 12.38	-.22	-.44	—
Education (mean years ±SD)	13.93 ± 2.12	.09	-.86	—
CES-D Total	10.70 ± 9.85	1.33	1.56	.91
Somatic Symptoms	3.22 ± 3.03	1.26	1.26	.75
Negative Affect	2.25 ± 2.97	1.45	1.43	.83
Well-being	2.65 ± 2.65	.73	-.33	.75
Interpersonal Disturbance	.55 ± 1.09	2.45	6.94	.75
Digit-Symbol Coding	67.78 ± 15.80	.26	.48	—
CVLT Trials 1-5	47.67 ± 11.31	.10	-.52	—
CVLT Long Delay	10.70 ± 3.46	-.46	-.35	—
Trails Letter-Number Sequencing	83.72 ± 31.54	1.06	.72	—
Color Word Interference	56.13 ± 12.30	.45	.19	—
Everyday Problem Solving	25.61 ± 8.90	.84	1.47	—
Transplant Effects Questionnaire	20.80 ± 3.60	-.73	-.12	.74
Employment Sample (*n* = 94)				
Age (mean ±SD)	46.85 ± 10.58	-.45	-.48	—
Education (mean years ±SD)	13.84 ± 2.05	.08	-.78	—
CES-D	11.07 ± 9.56	.95	.15	.91
Somatic Symptoms	3.26 ± 3.05	1.11	.77	.76
Negative Affect	2.30 ± 2.84	1.32	1.09	.80
Well-being	2.87 ± 2.77	.63	-.62	.79
Interpersonal Disturbance				.63
Digit-Symbol Coding	69.41 ± 16.07	.12	.43	—
CVLT Trials 1-5	48.48 ± 11.35	.08	-.52	—
CVLT Long Delay	10.84 ± 3.39	-.58	.02	—
Trails Letter-Number Sequencing	83.54 ± 33.27	1.29	1.48	—
Color Word Interference	55.80 ± 13.23	.72	.66	—
Everyday Problem Solving	25.76 ± 8.86	.99	1.66	—

Table 3. Renal Disease Diagnoses

1.1.1.1 **Participant Diagnoses**	**Adherence analysis (n = 103)**	**Employment analysis (n = 94)**
Diabetic Nephropathy	17 (16.5%)	14 (14.9%)
Hypertensive Nephrosclerosis/Ischemic Nephropathy	3 (2.9%)	3 (3.2%)
Both Diabetes and Hypertension	1 (1.0%)	1 (1.1%)
GN (e.g., IgA, FS, FSGS)	47 (45.6%)	48 (51.1%)
Glomerulonephritis (GN)	14	12
Focal Glomerulosclerosis	6	7
IgA Nephropathy	16	18
Latent GN	1	1
Membranous GN	1	1
Chronic Interstitial Nephritis	2	2
Reflux Nephropathy	3	3
Henoch-Schonlein Nephritis I	2	2
Hypoplastic GN	1	1
Fibrillary Nephritis	1	1
Cystic Kidney Disease	13 (12.6%)	7 (7.4%)
Unknown	12 (11.7%)	12 (12.8%)
Other	10 (9.7%)	9 (9.6%)
Cysteinuria		1
Alport's Syndrome	2	2
Amyloidosis		1
Cholesterol Emboli	1	
Goodpasture`s Syndrome	1	
Lupus	3	3
Kidney Stones	1	
Spina Bifida	1	1
Strep Throat	1	1

Table 4. Intercorrelations among variables for the medication adherence analysis

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1. AG	--																	
2. ED	-.08	--																
3. DS	-.06	.10	--															
4. TS	.29^{+}	-.07	-.02	--														
5. DC	-.39^{+}	.14	-.24*	.01	--													
6. LM	-.39^{+}	.03	-.21*	-.06	.45^{+}	--												
7. TS	.33^{+}	-.17	.26^{+}	.18	-.56^{+}	-.38^{+}	--											
8. CW	.39^{+}	-.08	.08	.06	-.59^{+}	-.79^{+}	.39^{+}	--										
9. NP	-.48^{+}	.12	-.25*	-.07	.84^{+}	.75^{+}	-.74^{+}	-.79^{+}	--									
10. EP	-.15	.44^{+}	-.17	-.13	.32^{+}	.15	-.34^{+}	-.23*	.32^{+}	--								
11. TR	-.19$^{\#}$	-.01	-.27^{+}	-.23*	.09	.18	-.16	-.05	.14	.26^{+}	--							
12. SE	-.03	-.08	-.14	.04	.11	.31^{+}	.12	-.08	.14	.04	.10	--						
13. IM	.21*	-.23*	-.08	.39^{+}	-.09	-.08	.26^{+}	.06	-.13	-.14	.04	.29^{+}	--					
14. DT	-.17*	.09	-.03	-.25^{+}	.19*	.16*	-.16*	-.20*	.21^{+}	.08	.08	.06	-.11	--				
15. LS	-.10	.01	-.01	-.03	.17*	.14	.01	-.04	.10	-.02	-.12	-.03	-.17	.10	--			
16. MS	.10	-.02	-.09	.06	.15	.05	.05	.02	.05	-.01	-.07	.01	-.06	.08	.67^{+}	--		
17. DM	.07	-.04	.09	-.13	-.28^{+}	-.06	-.01	.18*	-.17*	.07	.19*	-.17$^{\#}$	-.07	-.21*	-.23*	-.15	--	
18. AD	-.05	-.18*	-.10	.09	.13	.09	.11	-.13	.09	-.13	-.09	.04	.05	.18$^{\#}$	.14	.06	-.22*	--
19. BE	-.14$^{\#}$	.11	-.03	.06	.04	.06	.11	-.10	.03	-.03	-.12	.07	.04	.05	.12	.02	-.04	.26^{+}

Note. n = 103; *p < .05, $^{+}$$p$ < .01, $^{\#}$ p < .10. AG = age; ED = education; DS = depression symptoms; TS = time since transplant; DC = digit symbol coding; LM = learning and memory; TS = Trails – sequencing; CW = Color-Word Inhibition; NP = neuropsychological composite; EP = everyday problem solving; TR = TxEQ – Adherence; SE = sex; IM = immunosuppressant (i.e., cyclosporine vs. tacrolimus); DT = donor type (i.e., cadaveric vs. living); LS = living situation (i.e., living alone vs. living with others); MS = marital status (i.e., spouse vs. no spouse); DM = diabetes (i.e., current or history of diabetes vs. no diabetes); AD = antidepressants; BE = benzodiazepines.

Table 5. Multiple Regression Analyses Predicting Self-Reported Medication Adherence

I. *Objective 1*

A.

Variables entered	Step 1	Step 2				
	β	β	*F*	R^2	ΔR^2	ΔF
Age	-.186#	-.154				
Education	-.011	-.018				
Sex	.103	.092	1.599	.047		
NP Composite		.070	.282	.050	.004	.364

*p < .05, +p < .01, # p < .10

B.

Variables entered	Step 1	Step 2	Step 3				
	β	β	β	*F*	R^2	ΔR^2	ΔF
Age	-.193#	-.230*	-.243*				
Education	-.030	-.066	-.064				
Sex	.085	.057	.061	1.570	.046		
CES-D		-.296+	-.304+	3.625+	.131	.085	9.382+
NP Composite			-.223	2.881*	.132	.000	.050

*p < .05, +p < .01, # p < .10. CES-D = Center for Epidemiological Studies Depression Scale.

II. *Objective 2*

A.

Variables entered	Step 1	Step 2	Step 3				
	β	β	β	*F*	R^2	ΔR^2	ΔF
Age	-.186#	-.154	-.164				
Education	-.011	-.018	-.143				
Sex	.101	.092	.102	1.599	.047		
NP Composite		.070	-.025	1.283	.050	.004	.364
EPS			.316+	2.702*	.123	.073	8.011+

*p < .05, +p < .01, # p < .1

B.

Variables entered	Step 1 β	Step 2 β	Step 3 β	Step 4 β	*F*	R^2	ΔR^2	ΔF
Age	-.193#	-.230*	-.243*	-.248*				
Education	-.030	-.066	-.064	-.175#				
Sex	.085	.057	.061	.073	1.570	.046		
CES-D		-.296+	-.304+	-.288+	3.625+	.131	.085	9.382+
NP Composite			-.026	-.108	2.881*	.132	.000	.050
EPS				.288+	3.735+	.192	.061	7.080+

*p < .05, +p < .01, # p < .10. CES-D = Center for Epidemiological Studies Depression Scale.

III. *Secondary Analyses*

A.

Variables entered	Step 1 β	Step 2 β	Step 3 β	*F*	R^2	ΔR^2	ΔF
Age	-.184#	-.151	-.243*				
Education	-.013	-.146	-.064				
Sex	.107	.103	.061	1.614	.047		
EPS		.307+	-.304+	3.389*	.122	.075	8.335+
Age	-.191#	-.228*	-.195*				
Education	-.033	-.069	-.176#				
Sex	.088	.061	.063	1.584	.046		
CES-D		-.295+	-.259+	3.644+	.131	.084	9.419+
EPS			.260*	4.317+	.184	.053	6.223*

*p < .05, +p < .01, # p < .10. CES-D = Center for Epidemiological Studies Depression Scale.

B.

Variables entered	Step 1 β	Step 2 β	Step 3 β	Step 4 β	*F*	R^2	ΔR^2	ΔF
Participants with CES-D < 16								
Age	-.203#	-.203#	-.241#	-.254*				
Education	-.112	-.120	-.112	-.239*				
Sex	.150	.094	.097	.113	2.127	.078		
CES-D		-.253*	-.273*	-.286*	2.997*	.139	.061	5.244*
NP Composite			-.070	-.170	2.424*	.142	.003	.251
EPS				.327+	3.420+	.222	.079	7.349+

*p < .05, +p < .01, # p < .10. CES-D = Center for Epidemiological Studies Depression Scale.

C.

Variables entered	Step 1	Step 2	Step 3	Step 4				
	β	β	β	β	*F*	R^2	ΔR^2	ΔF
Full Sample								
Age	-.193#	-.223*	-.228*	-.236*				
Education	-.030	-.111	-.110	-.224*				
Sex	.085	.048	.050	.062	1.570	.046		
Negative Affect		.020	.018	.024				
Somatic Symptoms		-.388+	-.389+	-.385+	4.143+	.179	.133	7.678+
NP Composite			-.011	-.099	3.418+	.179	.000	.010
EPS				.295+	4.267+	.243	.064	7.865+
Participants with CES-D < 16								
Age	-.203#	-.200#	-.233#	-.247*				
Education	-.112	-.149	-.141	-.256*				
Sex	.150	.079	.085	.103	2.127	.078		
Negative Affect		-.109	-.122	-.145				
Somatic Symptoms		-.335+	-.340+	-.329+	3.879+	.210	.132	6.075+
NP Composite			-.061	-.158	3.233+	.212	.002	.211
EPS				.317+	4.071+	.286	.074	7.382+

*$p < .05$, +$p < .01$, # $p < .10$

Table 6. Demographic, Clinical, and Cognitive Variables in Employment Sample

Participant Characteristics	Employed < 20 hours/week	**Employed ≥ 20 hours/week**	p-value
	(*n* = 39)	(*n* = 55)	
Age (mean ±SD)	49.77 ± 10.30	44.78 ± 10.37	< .05
Female (n; %)	22 (56.4%)	23 (41.8%)	*ns*
Right Handedness (n; %)	35 (89.7%)	49 (89.1%)	*ns*
Ethnicity (n; %)			*ns*
Caucasian	31 (79.5%)	40 (72.7%)	
Asian	4 (10.3%)	10 (18.2%)	
Other	4 (10.2%)	5 (9.1 %)	
Education (mean years ±SD)	13.41 ± 2.04	14.15 ± 2.02	< .10
Depressive Symptoms (mean ±SD)	14.44 ± 10.38	8.63 ± 8.19	< .01
Smoke cigarettes (n; %)	2 (5.1%)	1 (1.8%)	*ns*
Hypertension (n; %)	28 (71.8%)	46 (83.6%)	*ns*
Diabetes mellitus (DM) (n; %)	9 (23.1%)	4 (7.3%)	<.05
DM & History of DM (n; %)	14 (35.9%)	9 (16.4%)	<.05
Coronary Artery Disease (n; %)	7 (17.9%)	4 (7.3%)	*ns*
Hypercholesterolemia (n; %)	16 (41.0%)	19 (34.5%)	*ns*
GFR (mean ±SD)	56.03 ± 21.58	61.15 ± 20.89	*ns*
Haemoglobin (g/L) (mean ±SD)	133.54 ± 13.03	133.71 ± 15.68	*ns*
EPREX (n; %)	2 (5.1%)	4 (7.4%)	*ns*
Anti-depressants (n; %)	10 (25.6%)	3 (5.5%)	<.01
Benzodiazepines (n; %)	5 (12.8%)	1 (1.8%)	<.05
Opiates (n; %)	0 (0%)	1 (1.8 %)	*ns*
Anti-cholesterol agents (n; %)	16 (41.0%)	17 (30.9%)	*ns*
Anti-hypertensives (n; %)	27 (69.2%)	44 (80.0%)	*ns*
Anti-diabetic medications (n; %)	8 (20.5%)	3 (5.5%)	<.05
Oral agents	3 (7.7%)	1 (1.8%)	< .10
Injectable agents	5 (12.8%)	2 (3.6%)	*ns*
Digit Symbol Coding (mean ±SD)	64.42 ± 14.59	72.85 ± 16.26	<.05
Learning and Memory (mean ±SD)	46.70 ± 8.98	52.34 ± 9.42	< .01
Trails (mean ±SD)	95.59 ± 36.83	75.00 ± 27.80	< .01
Color-Word (mean ±SD)	59.36 ± 13.93	53.27 ± 12.22	< .05
EPS (mean ±SD)	24.08 ± 8.66	26.95 ± 8.89	*ns*

p-values derived from independent sample *t* tests for continuous data; *p* values derived from χ^2 for categorical data.

Table 7. Binary Logistic Regression Analyses Predicting Employment Status

I. *Objective 1*

A.

Variable	B	SE	Wald	*df*	*p*	Odds ratio	95% CI_{or}	
							Lower	Upper
Step 1								
Age	-.046	.022	4.435	1	.035	.955	0.915	0.997
Step 2								
Age	-.021	.024	.771	1	.383	.979	.934	1.026
NP composite	.695	.273	6.465	1	.011	4.095	1.173	3.422

B.

Variable	B	SE	Wald	*df*	*p*	Odds ratio	95% CI_{or}	
							Lower	Upper
Step 2								
Age	-.051	.024	4.435	1	.035	.950	0.907	0.996
CES-D	-.078	.027	8.617	1	.003	.925	0.877	0.975
Anti-depressants	-1.713	.728	5.541	1	.019	.180	0.043	0.751
Step 3								
Age	-.033	.027	1.528	1	.216	.968	.918	1.020
CES-D	-.067	.027	6.013	1	.014	.935	0.887	0.986
Anti-depressants	-1.698	.738	5.288	1	.021	.183	0.043	0.778
NP Composite	.479	.289	2.740	1	.098	1.615	0.916	2.845

CES-D = Center for Epidemiological Studies Depression Scale.

II. *Objective 2*

A.

Variable	B	SE	Wald	*df*	*p*	Odds ratio	95% CI_{or}	
							Lower	Upper
Step 3								
Age	-.022	.024	.790	1	.374	.979	0.933	1.025
NP Composite	.658	.285	5.334	1	.021	1.930	1.105	3.376
EPS	.012	.028	.172	1	.678	1.012	0.958	1.069

CES-D = Center for Epidemiological Studies Depression Scale.

B.

Variable	B	SE	Wald	*df*	*p*	Odds ratio	95% CI_{or}	
							Lower	Upper
Step 4								
Age	-.033	.027	1.539	1	.215	.967	0.918	1.020
CES-D	-.066	.027	5.688	1	.017	.937	0.888	0.987
Anti-depressants	-1.787	.748	5.703	1	.017	.167	0.039	0.725
NP Composite	.416	.298	1.954	1	.162	1.517	0.845	2.718
EPS	.023	.032	.538	1	.463	1.024	0.961	1.089

CES-D = Center for Epidemiological Studies Depression Scale.

C.

Variable	B	SE	Wald	*df*	*p*	Odds ratio	95% CI_{or}	
							Lower	Upper
CES-D	-.059	.026	5.154	1	.023	.943	0.896	0.992
Anti-depressants	-1.778	.745	5.692	1	.017	.169	0.039	0.727
NP Composite	.662	.265	5.522	1	.019	1.863	1.153	3.259

CES-D = Center for Epidemiological Studies Depression Scale.

III. *Secondary Analyses*

Variable	B	SE	Wald	*df*	*p*	Odds ratio	95% CI_{or}	
							Lower	Upper
Step 1								
CES-D	-.086	.058	2.186	1	.139	.917	0.819	1.028
Anti-depressants	-1.623	.765	4.494	1	.034	.197	0.044	0.884
Step 2								
CES-D	-.056	.062	.813	1	.367	.946	0.837	1.068
Anti-depressants	-1.499	.789	3.613	1	.057	.223	0.048	1.049
NP composite	.703	.331	4.514	1	.034	2.020	1.056	3.864

CES-D = Center for Epidemiological Studies Depression Scale.

Reference List

2007 Report. *Canadian Organ Replacement Register* (2007). Canadian Institute for Health Information: Ottawa, Ontario.

Albert, S. M., Weber, C., Todak, G., Polanco, C., Clouse, M., McElhiney, M. et al. (1999). An observed performance test of medication management ability in HIV: relation to neuropsychological status and medication adherence outcomes. *AIDS and Behaviour, 3*, 121-128.

Alderman, N., Burgess, P. W., Knight, C., & Henman, C. (2003). Ecological validity of a simplified version of the multiple errands shopping test. *Journal of the International Neuropsychological Society, 9*, 31-44.

Allaire, J. C., & Marsiske, M. (2002). Well- and ill-defined measures of everyday cognition: Relationship to older adults' intellectual ability and functional status. *Psychology and Aging, 17*(1), 101-115.

Allaire, J. C., & Willis, S. L. (2006). Competence in everyday activities as a predictor of cognitive risk and mortality. *Aging, Neuropsychology, and Cognition, 13,* 207-224.

Ajzen, I. (1985). From intentions to action: A theory of planned behavior. In J. Kuhl & J. Beckmann (Eds.). *Action control: From cognition to behavior* (pp. 11-39). New York: Springer.

Ammassari, A., Antinori, A., Aloisi, M. S., Trotta, M. P., Murri, R., & Bartoli, L. (2004). Depressive symptoms, neurocognitive impairment, and adherence to highly active antiretroviral therapy among HIV-infected persons. *Psychosomatics, 45*(5), 394-402.

Andrade, S. E., Kahler, K. H., Frech, F., & Chan, K. A. (2006). Methods for evaluation of medication adherence and persistent using automated databases. *Pharmacoepidemiology and drug safety, 15,* 565-574.

Army Individual Test Battery (1944). *Manual of directions and scoring.* Washington, DC: War Department.

Arnsten, J. H., Demas, P. A., Farzadegan, H., Grant, R. W., Gourevitch, M. N., Chang, C. et al. (2001). Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: Comparison of self-report and electronic monitoring. *HIV/AIDS, 3,* 1417-1423.

Artistico, D., Cervone, D., & Pezzuti, L. (2003). Perceived self-efficacy and everyday problem solving among young and older adults. *Psychology & Aging, 18(1),* 68-79.

Avants, S. K., Margolin, A., Warburton, L. A., Hawkins, K. A., & Shi, J. (2001). Predictors of nonadherence to HIV-related medication regimens during methadone stabilization. *The American Journal on Addictions, 10,* 69-78.

Ayalon, L., Areán, P. A., & Alvidrez, J. (2005). Adherence to antidepressant medications in black and latino elderly patients. *American Journal of Geriatric Psychiatry, 13*(7), 572-580.

Bandura, A. (1986). Social foundations of thought and action: A social cognitive theory. Englewood, NJ: Prentice-Hall.

Bane, C., Hughes, C. M., & McElnay, J. C. (2006). The impact of depressive

symptoms and psychosocial factors on medication adherence in cardiovascular disease. *Patient Education and Counseling, 60*(2), 187-193.

Barclay, T. R., Hinkin, C. H., Castellon, S. A., Mason, K. M., Reinhard, M. J., Marion, S. D. et al. (2007). Age-associated predictors of medication adherence in HIV-positive adults: health beliefs, self-efficacy, and neurocognitive status. *Health Psychology, 26*(1), 40-49.

Benedict, R. H. B., Cookfair, D., Gavett, R., Gunther, M., Munschauer, F., Garg, N. et al. (2006).Validity of the minimal assessment of cognitive function in multiple sclerosis. *Journal of the International Neuropsychological Society, 12,* 549-558.

Benton, A. L. (1951). *The Visual Retention Test.* New York: The Psychological Corporation.

Benton, A. L., Hamsher, K., and Sivan, A. B. (1983). *Multilingual Aphasia Examination* (3rd ed.). Iowa City, IA: AJA Associates.

Bermond, B., Surachno, S., Lok, A., ten Berge, I. J. M., Plasmans, B., Kox, C., et al. (2005). Memory functions in prednisone-treated kidney transplant patients. *Clinical Transplantation, 19*(4), 512-517.

Boarts, J. M., Sledjeski, E. M., Bogart, L. M., & Delahanty, D. L. (2006). The differential impact of PTSD and depression on HIV disease markers and adherence to HAART in people living with HIV. *AIDS and Behavior, 10*(3), 253-261.

Boone, K. B., Miller, B. L., Lesser, I. M., & Hill, E. (1990). Performance on frontal lobe tests in healthy, older individuals. *Developmental Neuropsychology, 6,* 215-223.

Bowie, C. R., & Harvey, P. D. (2005). Cognition in schizophrenia: Impairments, determinants, and functional importance. *Psychiatric Clinics of North America, 28*(3), 613-633.

Brands, A. M. A., Van Den Berg, E., Manschot, S. M., Biessels, G. J., Kappelle, L. J., De Haan, E. H. F. et al. (2007). A detailed profile of cognitive dysfunction and its relation to psychological distress in patients with type 2 diabetes mellitus. *Journal of the International Neuropsychological Society, 13,* 288-297.

Brown R. G., Scott, L. C., Bench, C. J., & Dolan, R. J. (1994). Cognitive function in depression: Its relationship to the presence and severity of intellectual decline. *Psychological Medicine, 24*(4), 829-847.

Burgess, P. W., Alderman, N., Forbes, C., Costello, A., Coates, L. M., Dawson, D. R., et al. (2006). The case for the development and use of "ecologically valid" measures of executive function in experimental and clinical neuropsychology. *Journal of the International Neuropsychological Society, 12,* 194-209.

Butler, J. A., Peveler, R. C., Roderick, P., Horne, R., & Mason, J. C. (2004). Measuring compliance with drug regimens after renal transplantation: Comparison of self-report and clinician rating with electronic monitoring. *Transplantation, 77*(5), 786-789.

Butler, J. A., Peveler, R. C., Roderick, P., Smith, P. W. F., Horne, R., & Mason, J. C. (2004). Modifiable risk factors for non-adherence to immunosuppressants in renal transplant recipients: a cross-sectional study. *Nephrology, Dialysis Transplantation, 19*(12), 3144-3149.

Butler, J. A., Roderick, P., Mullee, M., Mason, J. C., & Peveler, R. C. (2004). Frequency and impact of nonadherence to immunosuppressants after renal transplantation: A systematic review. *Transplantation, 77*(5), 769-789.

Carney, R. M., Freedland, K. E., Eisen, S. A., Rich, M. W., & Jaffe, A. S. (1995). Major depression and medication adherence in elderly patients with coronary artery disease. *Health Psychology, 14*(1), 88-90.

Catz, S. L., Kelly, J. A., Bogart, L. M., Benotsch, E. G., & McAuliffe, T. L. (2000). Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. *Health Psychology, 19*(2), 124-133.

Chamelian, L., & Feinstein, A. (2006). The effect of major depression on subjective and objective cognitive deficits in mild to moderate traumatic brain injury. *Journal of Neuropsychiatry & Clinical Neurosciences, 18*(1), 33-38.

Chapman, J. R. (2004). Compliance: The patient, the doctor, and the medication? *Transplantation, 77*(5), 782-786.

Chaytor, N., & Schmitter-Edgecombe, M. (2003). The ecological validity of neuropsychological tests : A review of the literature on everyday cognitive skills. *Neuropsychology Review, 13*(4), 181-197.

Chaytor, N., Schmitter-Edgecombe, M., & Burr, R. (2006). Improving the ecological validity of executive functioning assessment. *Archives of Clinical Neuropsychology, 21,* 217-227.

Chisholm, M. A., Mulloy, L. L., & DiPiro, J. T. (2005). Comparing renal transplant patients' adherence to free cyclosporine and free tacrolimus immunosuppressant therapy. *Clinical Transplantation, 19,* 77-82.

Chisholm, M. A., Lance, C. E., & Mulloy, L. L. (2005). Patient factors associated with adherence to immunosuppressant therapy in renal transplant recipients. *American Journal of Health-System Pharmacy, 62,* 1775-1781.

Choo, P. W., Rand, C. S., Inui, T. S., Lee, M. T., Cain, E., Cordeiro-Breault, M. et al. (1999). Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy. *Medical Care, 37*(9), 846-857.

Cohen, J. (1992). A Power Primer. Psychological Bulletin, 112(1), 155-159.

Cohen, J., Cohen, P., West, S. G., & Aiken, L. S. (2003). Applied multiple regression/correlation analysis for the the behavioral sciences (3rd Edition). Mahway, New Jersey: Lawrence Erlbaum Associates, Publishers.

Coker, L. H., & Shumaker, S. A. (2003). Type 2 diabetes mellitus and cognition: An understudied issue in women's health. *Journal of Psychosomatic Research, 54*(2), 129-139.

Cooper, C., Carpenter, I. , Katona, C.,, Schroll, M., Wagner, C., Fialova, D. et al. (2005). The AdHOC study of older adults' adherence to medication in 11 countries. *The American Journal of Geriatric Psychiatry, 13*(12), 1067-76.

Cramer, J. A., Scheyer, R. D., & Mattson, R. H. (1990). Compliance declines between clinic visits. *Archives of Internal Medicine, 150,* 1509-1510.

De Geest, S., Abraham, I., & Dunbar-Jacob, J. (1996). Measuring transplant patients' compliance with immunosuppressive therapy. *Western Journal of Nursing Research, 18*(5), 595-605.

D'Elia, L., Satz, P., Uchiyama, C. L., and White, T. (1996). *Color trails 1 and 2.* Odessa, FL: Psychological Assessment Resources.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A (1987). *CVLT Adult Version:*

California Verbal Learning Test Manual, Version 1. San Antonio, TX.: The Psychological Corporation, Harcourt Brace & Company.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A (1987). *CVLT Research Edition Manual. Adult Version:* San Antonio, TX: The Psychological Corporation.

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). Delis-Kaplan Executive Function System. San Antonio, TX: The Psychological Corporation.

Delis, D. C., Kramer, J . H., Kaplan, E., Ober, B. A. (2000). Manual for the *California Verbal Learning Test – Second Edition* (CVLT-II). San Antonio, TX: The Psychological Corporation.

Denhaerynck, K., Dobbels, F., Cleemput, I., Desmyttere, A., Schäfer-Keller, P., Schaub, S., & De Geest, S. (2005). Prevalence, consequences, and determinants of nonadherence in adult renal transplant patients: a literature review. *Transplant International, 18*(10), 1121-1133.

Denney, N. W., & Palmer, A. M. (1981). Adult age differences on traditional and practical problem-solving measures. *Journal of Gerontology, 36(3),* 323-328.

Denney, N. W., & Pearce, K. A. (1989). A developmental study of practical problem solving in adults. *Psychology & Aging, 4*, 438-442.

Dickerson, F. B., Boronow, J. J., Stallings, C. R., Origoni, A. E., Cole, S., & Yolken, R. H. (2004). Association between cognitive functioning and employment status of persons with bipolar disorder. *Psychiatric Services, 55*(1), 54-58.

Diehl, M., Willis, S. L., & Schaie, K. W. (1995). Everyday problem solving in older adults: Observation assessment and cognitive correlates. *Psychology and Aging, 10*, 478-491.

DiMatteo, M. R., Lepper, H. S., & Croghan, T. W. (2000). Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of Internal Medicine, 160,* 2101-2107.

Doctor, J. N., Castro, J., Temkin, N. R., Fraser, R. T., Machamer, J. E., & Dikmen, S. S. (2005). Workers' risk of unemployment after traumatic brain injury: A normed comparison. *Journal of the International Neuropsychological Society, 11*, 747-752.

Dywan, J., & Segalowitz, S. (1996). Self and family ratings of adaptive behavior after traumatic brain injury: Psychometric scores and frontally generated ERPs. *Journal of Head Trauma Rehabilitation, 11*, 79-95.

Elbogen, E. B., Swanson, J., Swartz, M. S., & Van Dorn, R. (2005) Medication nonadherence and substance abuse in psychotic disorders: Impact of depressive symptoms and social stability. *The Chicago Journal of Nervous and Mental Disease 193*(10), 673-679.

Ekstrom, R. B., Harmon, D., & Derman, D. (1976). *Manual for kit of factor-referenced cognitive tests*. Princeton, NJ: Educational Testing Services.

Ensrud, K. E., Blackwell, T., Mangione, C. M., Bowman, P. J., Bauer, D., C., Schwartz, A., et al. (2003). Central nervous system active medications and risk for fractures in older women. *Archives of Internal Medicine, 163*(8), 949-957.

Evans, J. D., Bond, G. R., Meyer, P. S., Kim, H. W., Lysaker, P. H., Gibson, P. J. et al.

(2004). Cognitie and clinical predictors of success in vocational rehabilitation in schizophrenia. *Schizophrenia Research, 70*, 331-342.
Farmer, K. C. (1999). Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clinical Therapeutics, 21*(6), 1074-1090.
Flowers, K. A., & Robertson, C. (1985). The effects of Parkinson's disease on the ability to maintain a mental set. *Journal of Neurology, Neurosurgery, and Neuropsychiatry, 48,* 517-529.
Folstein, M. F, Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state: A practical guide for grading the cognitive states of patients for the clinician. *Journal of Psychiatry Ressearch, 12,* 189-198.
Franulic, A., Carbonell, C. G., Pinto, P., & Sepulveda, I. (2004). Psychosocial adjustment and employment outcome 2, 5 and 10 years after TBI. *Brain Injury, 18*(2), 119-129.
Frazier, P., Davis-Ali-, S., & Dahl, K. (1994). Correlates of noncompliance among renal transplant recipients. *Clinical Transplantation, 8,* 550-557.
Garber, M. C., Erickson, S. R., Aikens, J. E., & Lawrence, J. B. (2004). The concordance of self-report with other measures of medication adherence: A summary of the literature. *Medical Care, 42*(7), 649-652.
Gehi, A., Haas, D., Pipkin, S., & Whooley, M. A. (2005). Depression and medication adherence in outpatients with coronary heart disease. *Archives of Internal Medicine, 165,* 2508-2513.
Gelb, S. R., Shapiro, R. J., Hill, A., & Thornton, W. L. (2008). Cognitive and psychosocial outcome following kidney transplantation. *Nephrology Dialysis Transplantation, 23*(3), 1032-1038.
Gilhooly, M. L., Gilhooly, K. J., Phillips, L. H., Harvey, A. B., & Hanlon, P. (2007). Real-world problem solving and quality of life in older people. British Journal of Health Psychology, 12, 587-600.
Gilliam, F., Hecimovic, H., & Sheline, Y. (2003). Psychiatric comorbidity, health, and function in epilepsy. *Epilepsy & Behavior, 4*(S4), 26-30.
Gold, J. M., Goldbert, R. W., McNary, S. W., Dixon, L. B., & Lehman, A. F. (2002). Cognitive correlates of job tenure among patients with severe mental illness. *American Journal of Psychiatry, 159*(8), 1395-1402.
Golden, C. J. (1978) *The Stroop Color and Word Test: A manual for clinical and experimental uses.* Stoelting Company: Chicago, IL.
Goldstein, G., McCue, M., Rogers, J., & Nussbaum, P. D. (1992). Diagnostic differences in memory test based predictions of functional capacity in the elderly. *Neuropsychological Rehabilitation, 2,* 307-317.
Gross, C. R., Limwattananon, C., Matthees, B., Zehrer, J. L., & Savik, K. (2000). Impact of transplantation on quality of life in patients with diabetes and renal dysfunction. *Transplantation, 70,* 1736-1746.
Grosset, K. A., Bone, I., & Grosset, D. G. (2005). Suboptimal medication adherence in Parkinson's disease. *Movement Disorders, 20*(11), 1502-1507.
Hamilton, G. A. (2003). Measuring adherence in a hypertension clinical trial. *European Journal of Cardiovascular Nursing, 2*(3), 219-228.
Shadish, W. R., Robin, L., & Lu, C. (1999). ES: A Computer Program for Effect Size

Calculation. St. Paul, MN: Assessment Systems Corporation.
Hasmi, S.K., Afridi, M. B., Abbas, K., Sajwani, R. A., Saleheen, D., Frossard, P. M. et al. (2007).Factors associated with adherence to anti-hypertensive treatment in Pakistan. *Plos ONE, 2,* e280.
Heaton, R. K., Grant, I., & Matthews, C. G. (1991). *Comprehensive norms for an expanded Halstead-Reitan battery: Demographic corrections, research findings, and clinical applications.* Odessa, FL: Psychological Assessment Resources.
Heaton, R. K., Chelune, G. J., Talley, J. L. et al. (1993). *Wisconsin Card Sorting Test Manual.* Odessa, FL: Psychological Assessment Resources.
Heaton, R. K., Velin, R. A., McCutchan, J. A., Gulevich, S. J., Atkinson, J. H., Wallace, M. R. et al. (1994). Neuropsychological impairment in human immunodeficiency virus-infection: Implications for employment. *Psychosomatic Medicine, 56,* 8-17.
Hess, L. M., Raebel, M. A., Conner, D. A., & Malone, D. C. (2006). Measurement of adherence in pharmacy administrative databases: A proposal for standard definitions and preferred measures. *The Annals of Pharmacotherapy, 40,* 1280-1287
Hill-Briggs, F., Gary, T. L., Bone, L. R., Hill, M. N., Levine, D. M., & Brancati, F. L. (2005). Medication adherence and diabetes control in urban African Americans with Type 2 diabetes. *Health Psychology, 24*(4), 349-357.
Hinkin, C. H., Castellon, S. A., Durvascula, R. S., Hardy, D. J., Lam, M. N., Mason, K. I., et al. (2002). Medication adherence among HIV+ adults: Effects of cognitive dysfunction and regiment complexity. *Neurology, 59,* 1944-1950.
Hinkin, C. H, Hardy, D. J., Mason, K. I., Castellon, S. A., Durvasula, R. S., Lam, M. N., et al. (2004). Medication adherence in HIV-infected adults: Effect of patient age, cognitive status, and substance abuse. *AIDS, 18*(s1), 19-25.
Hogan, T. P., Awad, A. G., & Eastwood, R. A. (1983). A self-report scale predictive of drug compliance in schizophrenics: Reliability and discriminative validity. *Psychological Medicine, 13,* 177-183.
Holzemer, W. L., Corless, I. B., Nokes, K. M., Turner, J. G., Powell-Cope, G. M., Inouye, J. et al. (1999). Predictors of self-reported adherence in persons living with HIV disease. *AIDS patient care and STDs, 13*(3), 185-197.
Incalzi, R. A., Gemma, A., Marra, C., Capparella, O., Fuso, L., & Carbonin, P. (1997). Verbal memory impairment in COPD: Its mechanisms and clinical relevance. *Chest, 112,* 1506-1513.
Insel, K., Morrow, D., Brewer, B., & Figueredo, A. (2006). Executive function, working memory, and medication adherence among older adults. *Journal of Gerontology: Psychological Sciences, 61B,* 102-107.
Jarvis, P. E., & Barth, J. T. (1994). The Halstead-Reitan Neuropsychological Battery: A guide to interpretation and clinical applications. Odessa, FL: Psychological Assessment Resources.
Jeste, S. D., Patterson, T. L., Palmer, B. W., Dolder, C. R., Goldman, S., & Jeste, D. V. (2003). Cognitive predictors of medication adherence among middle-aged and older outpatients with schizophrenia. *Schizophrenia Research, 63*(1-2), 49-58.
Johnson, J. L. (1994). Episodic memory deficits in Alzheimer's disease: A behaviorally anchored scale. *Archives of Clinical Neuropsychology, 9,* 337-346.
Johnson, M. J. (2002). The Medication Adherence Model: A guide for assessing

medication taking. *Research and Theory for Nursing Practice: An International Journal, 16*(3), 179-192.
Kalechstein, A. D., Newton, T. F., & van Gorp, W. G. (2003). Neurocognitive functioning is associated with employment status: A quantitative review. *Journal of Clinical and Experimental Neuropsychology, 25*(8), 1186-1191.
Kaufman, A. S., & Kaufman, N. L. *Manual: KAIT Kaufman Adolescent & Adult Intelligence Test.*Circle Pines, Minn.: American Guidance Service Inc. 1993.
Kibby, M. Y., Schmitter-Edgecombe, M., & Long, C. J. (1998). Ecological validity of neuropsychological tests: Focus on the California Verbal Learning Test and the Wisconsin Card Sorting Test. *Archives of Clinical Neuropsychology, 13*(6), 523-534.
Kilbourne, A., Reynolds, C. F., Good, C. B., Sereika, S. M., Justice, A. C., & Fine, M. J. (2005).How does depression influence diabetes medication adherence in older patients. *American Journal of Geriatric Psychiatry, 13*(3), 202-210.
Klove, H. (1963). Clinical Neuropsychology. *Medical Clinics of North America, 46,* 1647-1658.
Kurella, M., Chertow, G. M., Luan, J., & Yaffe, K. (2004). Cognitive impairment in chronic kidney disease. *Journal of American Geriatric Society,52,* 1863-1869.
Lafayette Instrument Company (n.d.) *Instructions for the Grooved Pegboard Test,* Lafayette Instrument Company, Lafayette, IN.
Lawton, M.P., & Brody, E. M. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. *Gerontologist, 9,* 179-186.
LeBlanc, J. M., Hayden, M. E., & Paulman, R. G. (2000). A comparison of neuropsychological and situational assessment for predicting employability after closed head injury. *Journal of Head Trauma and Rehabilitation, 15*(4), 1022-1040.
Leventhal, H., Leventhal, E. A., & Contrada, R. J. (1998). Self-regulation, health, and behavior: A perceptual-cognitive approach. *Psychology and Health, 13,* 717-733.
Lewinsohn, P. M., Seeley, J. R., Robert, R. E., & Allen, N. B. (1997). Center for Epidemiologic Studies Depression Scale (CES-D) as a screening instrument for depression among community-residing older adults. *Psychology and Aging, 12*(2), 277-287.
Lezak, M. D. (1995). *Neuropsychological assessment,* 3rd ed. New York: Oxford University Press.
Lin, E. H. B., Katon, W., Von Korff, M., Rutter, C., Simon, G. E., Oliver, M. et al., (2004).Relationship of depression and diabetes self-care, medication adherence, and preventive care. *Diabetes Care, 27*(9), 2154-2160.
Liu, H., Golin, C. E., Miller, L. G., Hays, R. D., Beck, K., Sanandaji, S. et al. (2001). A comparison study of multiple measures of adherence to HIV protease inhibitors. *Archives of Internal Medicine, 134,* 968-977.
Machamer, J., Temkin, N., Fraser, R., Doctor, J. N., & Dikmen, S. (2005). Stability of employment after traumatic brain injury. *Journal of the International Neuropsychological Soceity, 11,* 805-816.
Mackin, R. S., Horner, M. D., Harvy, R. T., & Stevens, L. A. (2005). The relationship between neuropsychological measures and employment problems in outpatients with substance abuse. *Rehabilitation Psychology, 50*(2), 158-163.

MacLaughlin, E. J., Raehl, C. L., Treadway, A., K., Sterling, T. L., Zoller, D. P., & Bond, C. A. (2005). Assessing medication adherence in the elderly: Which tools to use in clinical practice? *Drugs and Aging, 22*(3), 231-255.

MÆland, J. G., & Havik, O. E. (1987). Psychological predictors for return to work after a myocardial infarction. *Journal of Psychosomatic Research, 31*(4), 471-481.

Mannheimer, S. B., Mukherjee, R., Hirschhorn, L. R., Dougherty, J., Celano, S. A., Ciccarone, D. et al. (2006). The CASE adherence index: A novel method for measuring adherence to antiretroviral therapy. *AIDS Care, 18*(7), 853-861.

Marsiske, M., & Margrett, J.A. (2006). Everyday problem solving and decision making.In J.E. Birren & K. W. Schaire (Eds.), *Handbook of the Psychology of Aging* (6th Edition, pp. 315-342). Amsterdam, Netherlands: Elsevier.

Marsiske, M., & Willis, S. L. (1995). Dimensionality of Everyday Problem Solving in Older Adults. *Psychology and Aging, 10(2),* 269-283.

Matas, A. J., Lawson, W., Mchugh, L., Gillingham, K., Payne, W. D., Dunn, D. L. (1996). Employment patterns after successful kidney transplantation. *Transplantation, 61*(5), 729-733.

Mattis, S. (1973). Dementia Rating Scale. Odessa, FL: Psychological Assessment Resources.

McLellan, A., Luborsky, L., O'Brien, C. P., & Woody, G. E. (1980). An improved diagnostic instrument for substance abuse patients: The Addiction Severity Index. *Journal of Nervous and Mental Diseases, 168,* 26-33.

McGurk, S. R., & Mueser, K. T. (2003). Cognitive functioning and employment in severe mental illness. *The Journal of Nervous and Mental Disease, 191*(12), 789-798.

McGurk, S. R., & Mueser, K. T. (2006). Cognitive and clinical predictors of work outcomes in clients with schizophrenia receiving supported employment services: 4-year follow up. *Administration and Policy in Mental Health & Mental Health Services Research, 33*, 598-606.

Meyer, P. S., Bond, G. R., Tunis, S. L., & McCoy, M. L. (2002). Comparison between the effects of atypical and traditional antipsychotics on work status for clients in a psychiatric rehabilitation program. *Journal of Clinical Psychiatry, 63,* 108-116.

Miller, L. G., Honghu, L., Hays, R. D., Golin, C. E., Beck, C K., Asch, S. M. et al. (2002). How well do clinicians estimate patients' adherence to combination antiretroviral therapy? *Journal of General Internal Medicine, 17*(1), 1-11.

Miller, E. N., Satz, P., & Visscher, B. (1991). Computerized and conventional neuropsychological assessment of HIV-1 infected homosexual men. *Neurology, 41,* 1608-1616.

Morisky, D. E., Green, L. W., & Levine, D. M. (1986). Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Care, 24, 67-74.*

Morrissey, P. E., Reinert, S., Yango, A., Gautam, A., Monaco, A., & Gohh, R (2005). Factors contributing to acute rejection in renal transplantation: The role of non-compliance. *Transplantation Proceeding,* 37, 2044-2047.

Murray, M. D., Morrow, D. G., Weiner, M., Clark, D. O., Wanzhu, T., Deer, M. M. et al.

(2004). A conceptual framework to study medication adherence in older adults. *American Journal of Geriatric Pharmacotherapy, 2*(1), 36-43.

Nolin, P., & Heroux, L. (2006). Relations among sociodemographic, neurologic, clinical and neuropsychologic variables, and vocational status following mild traumatic brain injury: A follow-up study. *Journal of Head Trauma Rehabilitation, 21*(6), 514-526.

Overbeck, M., Bartels, O., Decker, J., Harms, J., Hauss, J., & Fangmann, J. (2005). Changes in quality of life after renal transplantation. *Transplantation Proceedings, 37,* 1618-1621.

Park, D. C. & Meade, M. L. (2007). A broad view of medical adherence: Integrating cognitive, social, and contextual factors. In D. C. Park & L. L. Liu (Eds.), *Medical adherence and aging: Social and cognitive perspectives* (pp. 3-21). Washington D. C.: American Psychological Association.

Parsons, J. T., Rosof, E., & Mustanski, B. (2007). Patient-related factors predicting HIV medication adherence among men and women with alcohol problems. *Journal of Health Psychology, 12*(2), 357-370.

Pereira, A. A., Weiner, D. E., Scott, T., & Sarnak, M. J. (2005). Cognitive function in dialysis participants. *American Journal of Kidney Diseases, 45*(3), 448-462.

Phillips, K. D., Moneyham, L., Murdaugh, C., Boyd, M. R., Tavakoli, A., Jackson, K. et al. (2005). Sleep disturbance and depression as barriers to adherence. *Clinical Nursing Research, 14*(3) 273-293.

Pratt, S. I., Mueser, K. T., Driscoll, M., Wolfe, R., & Bartels, S. J. (2006). Medication nonadherence in older people with serious mental illness: Prevalence and correlates. Psychiatric Rehabilitation Journal, *29*(4), 299-310.

Ready, R. E., Stierman, L., & Paulsen, J. S. (2001). Ecological validity of neuropsychological and personality measures of executive functioning. *The Clinical Psychologist, 15*(3), 314-323.

Rabkin, J. G., McElhiney, M., Ferrando, S. J., Van gorp, W., & Lin, S. H. (2004). Predictors of employment of men with HIV/AIDS: A longitudinal study. *Psychosomatic Medicine, 66,* 72-78.

Radloff, L. S. (1977). A self-report depression scale for research in general populations. *Applied Psychological Measurement, 1*, 385-401.

Raiz, L. (1997). The transplant trap: The impact of health policy on employment status following renal transplantation. *Journal of Health Social Policy, 8,* 67-87.

Rand, C. S. (1990). Issues in the measurement of adherence. In. S. A. Shumaker and E. B. Schron, Editors, *The Handbook of Health Behavior Change.* New York: Springer.

Rao, S. M., Leo, G. J., Ellington, M. S., Nauertz, T., Bernardin, L., & Unverazgt, F. (1991).Cognitive dysfunction in multiple sclerosis: Impact on employment and social functioning. *Neurology, 41,* 692-696.

Reger, M., Welsh, R., Razani, J., Martin, D. J., & Boone, K. B. (2002). A meta-analysis of the neuropsychological sequelae of HIV infection. *Journal of the International Neuropsychological Society, 8*(3), 410-424.

Rey, A. (1964). L'examen Clinique en Psychologie. Paris, France: Presses Universitaires de France.

Rieckmann, N., Gerin, W., Kronish, I. M., Burg, M. M., Chaplin, W. F., Kong, G. et al.

(2006). Course of depressive symptoms and medication adherence after acute coronary syndromes. *Journal of the American College of Cardiology, 48*(11), 2218-2222.

Rieckmann, N., Kronish, I. M., Haas, D., Gerin, W., Chaplin, W. F., Burg, M. M. et al. (2006). Persistent depressive symptoms lower aspirin adherence after acute coronary syndromes. *American Heart Journal, 152*(5), 922-927.

Robertson, I H., Ward, T., Ridgeway, V., & Nimmo-Smith, I. (1994). *The Test of Everyday Attention*. Bury St. Edmunds, England: Thames Valley Test Company:

Robinson, D. G., Woerner, M. G., Alvir, J. M. A., Bilder, R. M., Hinrichsen, G. A., & Liberman, J. A. (2002). Predictors of medication discontinuation by patients with first-episode schizophrenia and schizoaffective disorder. *Schizophrenia Research, 57*(2-3), 209-219.

Rosen, M. I., Beauvais, J. E., Rigsby, M. O., Salahi, J. T., Ryan, C. E., Cramer, J. A. (2003). Neuropsychological correlates of suboptimal adherence to metformin. *Journal of Behavioral Medicine, 26*(4), 349-360.

Rosenstock, I. M. (1974a). Historical origins of the health belief model. *Health Education Monographs, 2*(4), 328-335.

Rosenstock, I. M. (1974b). The health belief model and preventive behavior. *Health Education Monographs, 2(4),*354-386.

Rosenstock, I. M., Strecher, V. J., 7 Becker, M. H. (1988). Social learning theory and the health belief model. *Health Education Quarterly, 15*(2), 175-183.

Russell, C. L., Conn, V. S., Ashbaugh, C., Madsen, R., Hayes, K., & Ross, G. (2006). Medication adherence patterns in adult renal transplant recipients. *Research in Nursing & Health, 29*, 521-532.

Sabb, S., Wiese, C., Ibrahim, A. B., Peralta, L., Durazo, F., Han, S., et al. (2007). Employment and quality of life in liver transplant recipients. *Liver Transplantation, 13,* 1330-1338.

Safren, S. A., Duran, P., Yovel, I., Perlman, C. A., & Sprich, S. (2007). Medication adherence in psychopharmacologically treated adults with ADHD. *Journal of Attention Disorders, 10*(3), 257-260.

Sahota, A., Zaghla, H., Adkins, R., Ramji, A., Lewis, S., Moser, J., et al. (2006). Predictors of employment after liver transplantation. *Clinical Transplantation, 20,* 490-495.

Sbordone, R. J. (2001). Limitations of neuropsychological testing to predict the cognitive and behavioral functioning of persons with brain injury in real-world settings. *NeuroRehabilitation, 16,* 199-201.

Sbordone, R. J., & Guilmette, T. J. (1999). Ecological validity: Prediction of everyday and vocational functioning from neuropsychological test data (pp. 227-254). *Forensic Neuropsychology: Fundamental in Practice,* J. J. Sweet, ed. Lisse, the Netherlands: Swets & Zeitling.

Selnes, Ola A. (2002). Neurocognitive aspects of medication adherence in HIV infection. *Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology, 31*(S3), S132-S135.

Selnes, O., A., Jacobson, L., Machado, A. M., & Becker, J. T. (1991). Normative data for a brief neuropsychological screening battery. *Perceptual Motor Skills, 73,* 539-550.

Shallice, T., Burgess, W. F. (1991). Higher-order cognitive impairments and frontal lobe lesions in man. In: Levin, H. S., Eisenberg, H. M., Benton, A. L., eds. *Frontal Lobe Function and Dysfunction.* New York: Oxford University Press.

Shea, S., Misra, D., Ehrlich, M. H., Field, L., & Francis, C. K. (1992). Correlates of nonadherence to hypertension measurement in an inner-city population. *American Journal of Public Health, 82*(12), 1607-1612.

Sherbourne, C. D., Hays, R. D., Ordway, L., DiMatteo, M.R., & Kravitz, R. L. (1992). Antecedents of adherence to medical recommendations: Results from the medical outcomes study. *Journal of Behavioral Medicine, 15*(5), 447-768.

Signoret, J. L. (1991). *BEM-84 Batterie d'Efficience Mnésique réduite,* Editions Scientifiques Elsevier: Paris.

Simmons, R. G., Abress, L., & Anderson, C. R. (1988). Quality of life after kidney transplantation. A prospective, randomized comparison of cyclosporine and conventional immunosuppressive therapy. *Transplantation, 54,* 656-660.

Smith, A. (1982). *Symbol Digit Modalities Test (SDMT) Manual (Revised).* Los Angeles, CA: Western Psychological Association.

Spooner, D. M., & Pachana, N. A. (2006). Ecological validity in neuropsychological assessment: A case for greater consideration in research with neurologically intact populations. *Archives of Clinical Neuropsychology, 21,* 327-337.

Spreen, O., & Strauss, E. (Eds.) A Compendium of Neuropsychological Tests (2nd ed.) New York: Oxford University Press, 1988.

Steiger, J. H., & Fouladi, R. T. (1992). R2: A computer program for interval estimation, power calculations, sample size estimation, and hypothesis testing in multiple regression. *Behavior Research Methods, Instruments, and Computers, 24,* 581-582.

Steiner, J. F., & Prochazka, A. V. (1997). The assessment of refill compliance using pharmacy records: methods, validity, and applications. *Journal Of Clinical Epidemiology, 50* (1), 105-116.

Stilley, C. S., Sereika, S., Muldoon, M. F., Ryan, C. M., & Dunbar-Jacob, J. (2004). Psychological and cognitive function: Predictors of adherence with cholesterol lowering treatment. *Annals of Behavioral Medicine, 27*(2), 117-124.

Strachan, M. W. J., Deary, I. J., Ewing, F. M. E., & Frier, B. M. (1997). Is type II diabetes associated with an increased risk of cognitive dysfunction? *Diabetes Care, 20,* 38–45.

Straka, R. J., Fish, J. T., Benson, S. R., & Suh, J. T. (1997). Patient self-reporting of compliance does not correspond with electronic monitoring: An evaluation using isosorbide dinitrate as a model drug. *Pharmacotherapy, 17*(1), 126-132.

Stuss, D. T., Stethem, L. L., & Pelchat, G. (1988). Three tests of attention and rapid information processing: An extension. *Clinical Neuropsychologist, 2,* 246-250.

Svarstad, B. L., Chewning, B. A., Sleath, B. L., & Claesson, C. (1999). The brief medication questionnaire: A tool for screen patient adherence and barriers to adherence. *Patient Education and Counseling, 37*(2), 113-124.

Tabachnick, B. G., and Fidell, L. S. (2007). *Using multivariate statistics, 5th ed.* Boston, MA: Allyn & Bacon.

Thornton, W. J. L., & Dumke, H. A. (2005). Age differences in everyday problem-

solving and decision-making effectiveness: A meta-analytic review. *Psychology and aging, 20*(1), 85-99.
Thornton, W. L., Shapiro, R. J., Deria, S., Gelb, S., & Hill, A. (2007). Differential impact of age on verbal memory and executive functioning in Chronic Kidney Disease. *Journal of the International Neuropsychological Society, 13*, 344-353.
Thornton, W. J.L., Deria, S., Gelb, S., Shapiro, R. J., & Hill, A. (2007). Neuropsychological mediators of the links between age, chronic illness, and everyday problem solving. *Psychology and Aging, 22*(3), 470-481.
Tiffin, J. (1968). *Purdue Pegboard: Examiner manual.* Chicago: Science Research Associates.
Tucker, J. S., Burnam, M. A., Sherbourne, C. D., Kung, F., & Gifford, A. L. (2003). Substance use and mental health correlates of nonadherence to antiretroviral medications in a sample of patients with human immunodeficiency virus infection. *The American Journal of Medicine, 114*(7), 573-580.
van der Mei, S. F., Krol, B., van Son, W. J., de Jong, P. E., Groothoff, K. W., & van den Heuvel, W. J. A. (2006). Social participation and employment status after kidney transplantation: A systematic review. *Quality of Life Research, 15*, 979-994.
van der Mei, S. F., van Son, W. J., van Sonderen, E. L. P., de Jong, P. E., Groothoff, J. W., & van den Heuvel, W. J. A. (2007). Factors determining social participation in the first year after kidney transplantation: A prospective study. *Transplantation, 84*(6), 729-737.
van Gorp, W. G., Rabkin, J. G., Rerrando, S. J.., Mintz, J., Ryan, E., Borkowski, T., & Mcelhiney, M. (2006). Neuropsychiatric predictors of return to work in HIV/AIDS. *Journal of the International Neuropsychological Society, 13*, 80-89.
Vedhara, K., Wadsworth, E., Norman, P., Searle, A., Mitchell, J., Macrae, N., et al. (2004). Habitual prospective memory in elderly patients with Type 2 diabetes: Implications for medication adherence. *Psychology, Health & Medicine, 9*(1), 17-27.
Verdoux, H., Liraud, F., Assens, F., Abalan, F., & van Os, J. (2002). Social and clinical consequences of cognitive deficits in early psychosis: A two-year follow-up study of first-admitted patients. *Schizophrenia Research, 56*(1-2), 149-159.
Vitolins, M. Z., Rand, C. S., Rapp, S. R., Ribisl, P. M., & Sevick, M. A. (2000). Measuring adherence to behavioral and medical interventions. *Controlled Clinical Trials 21*(5), S188-S194.
Wagner, G. J., Kanouse, D. E., Koegel, P., & Sullivan, G. (2004). Correlates of HIV antiretroviral adherence in persons with serious mental illness. *AID Care, 16*(4), 501-506.
Waldrop-Valverde, D., Ownby, R. L, Wilkie, F. L., Mack, A., Kumar, M., & Metsch, L. (2006). Neurocognitive aspects of medication adherence in HIV-positive injecting drug users. *AIDS and Behavior, 10*(3), 287-297
Waterhouse, D. M., Calzone, K. A., Mele, C., & Brenner, D. E. (1993). Adherence to oral tamoxifen: A comparison of patient self-report, pill counts, and microelectronic monitoring. *Journal of Clinical Oncology, 11*(6), 1189-1197.
Weatherbee, S. R., & Allaire, J. C. (2008). Everyday cognition and mortality: Performance differences and predictive utility of the everyday cognition battery. *Psychology and Aging, 23*(1), 216-221.

Wechsler, D. (1981). *Wechsler Adult Intelligence Scale – Revised.* Psychological Corporation: New York.

Wechsler, D. (1997). *Wechsler adult intelligence scale manual* (3rd ed.). New York: The Psychological Corporation.

Wechsler, D. (1997). *Wechsler Memory Scale – Third Ediction.* San Antonio, TX: The Psychological Corporation – Harcourt Brace.

Wetzels, G. E. C., Nelemans, P. J., Schouten, J. S. A. G., van Wijk, B. L. G., & Prins, M. H. (2006). All that glisters is not gold: A comparison of electronic monitoring versus filled prescriptions – an observational study. *BMC Health Services Research, 6,* 8.

Wetzel, L. & Boll, T. J. (1987). *Short category test, booklet format.* Los Angeles, CA: Western Psychological Services.

Wilcox, R. R. (1995). ANOVA: A paradigm for low power and misleading measures of effect size? *Review of educational research, 65,* 51-77.

Wilkins, F., Bozik, K., & Bennett, K. (2003). The impact of patient education and psychosocial supports on return to normalcy 36 months post-kidney transplant. *Clinical Transplantation,* 17(Suppl. 9), 78-80.

Wilson, B. A., Alderman, N., Burgess, P., Emslie, H., & Evans, J. J. (1996). *Behavioural Assessment of the Dysexecutive Syndrome (BADS)*. Bury St. Edmunds, England: Thames Valley Test Company.

Wilson, B. A., Cockburn, J., & Baddeley, A. (2003). *The Rivermead Behavioural Memory Test (RBMT-II).* London: Harcourt Assessment.

Wood, R. LL., & Rutterford, N. A. (2006). Demographic and cognitive predictors of long-term psychosocial outcome following traumatic brain injury. *Journal of the International Neuropsychological Society, 12,* 350-358.

Ziegelmann, J. P., Griva, K., Hankins, M., Harrison, M., Davenport, A., Thompson, D., et al. (2002). The Transplant Effects Questionnaire (TxEQ): The development of a questionnaire for assessing the multidimensional outcome of organ transplantation – example of end stage renal disease (ESRD). *British Journal of Health Psychology, 7*(4), 393-408.