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Abstract

Depression is common among individuals in primary care. Despite the prevalence of depression in primary care, patients are usually not adequately treated for depression. Often the treatment that is received is generally limited to their specific medical condition and depression is either not treated or is inadequately treated. Self-monitoring is used in research and treatment settings to monitor physical, behavioral, and psychological changes. Previous research has suggested that depression may be reactive to self-monitoring, in that mood, physical activity, and other depressive symptoms often improve when individuals monitor their behaviors and depressive symptoms. Current studies have noted impact on outcomes including improved adherence and symptom improvement based on the type of monitoring. The present study investigated self-monitoring of major depressive disorder symptoms and treatment adherence in a primary care setting. The study was designed to evaluate three main questions. Does computer-based or paper-and-pencil monitoring result in greater compliance with reporting of mood symptoms and adherence to medication in treatment of depression? Do participants who monitor depressive symptoms have better outcomes of depression treatment than those who do not monitor symptoms? Which symptom cluster of depression (cognitive-affective or physical) will improve first during the four-week course of the study? Individuals enrolled in primary care at Walter Reed Army Medical Center, were diagnosed by their primary care provider with depression, and placed on anti-depressant medication

participated in the study (n = 17). Once enrolled, individuals completed self-report measures and interviews of general health status, psychological symptoms, and physical symptoms. Individuals were randomly assigned to one of three groups (control, computer-based, or pencil-and-paper based monitoring). Those in the monitoring conditions maintained daily diaries to track mood, physical activity, medication adherence, and daily stress over the four-week study period. Analysis of daily monitoring data and weekly interviews of depression indicated no significant difference in adherence to daily monitoring of depressive mood symptoms. However, the paper-and-pencil group was more similar across time than the computer-based monitoring condition. No significant group main effects for medication adherence were found between groups. There was a significant effect for time across all groups for improvements in depression symptoms, physical symptoms, and overall general health, regardless of treatment condition. However, there were no significant group main effects. Multiple regression analysis indicates that remission of cognitive-affective symptoms predicts subsequent remission of physical symptoms when controlling for original baseline measures. Results suggest that patients are likely to experience improvements in both cognitive-affective and physical symptoms during the first two weeks of treatment on an antidepressant. Patients with improvements in cognitive-affective symptoms after two-weeks are also likely to develop a reduction in physical symptoms by the end of the fourth week. Theoretical implications as well as questions for future research are discussed.

AMBULATORY ASSESSMENT OF DEPRESSION IN PRIMARY CARE

by

William L. Johnson

Doctoral dissertation submitted to the faculty of the Department of Medical and Clinical Psychology Graduate Program of the Uniformed Services University of the Health Sciences in partial fulfillment for the degree of Doctor of Philosophy.

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Dedication

Dedicated to my grandmother, Elsie Johnson, who passed away while I was in graduate school. She was always there for me when I needed her even when I could not be there for her.

Table of Contents

Section	Page Number
Approval Sheet	i
Copyright Statement	ii
Abstract	iii
Title Page	iv
Acknowledgments	vi
Dedication	vii
Table of Contents	viii
List of Tables	xi
List of Figures	xii
1. Background	1
1.1 Prevalence and Impact of Depression	1
1.2 Somatic and Cognitive-Affective Symptoms of Depression	3
1.3. Depression in Patients with Medical Conditions	6
1.4. Adverse Disease Outcomes Related to Depression	7
2. Effects of Depression Interventions in Patients with Medical Disorders	9
3. Self-Monitoring Theories	12
3.1. Cognitive Mediation Model	14
3.2. Rachlin's Operant Recording Model	15
3.3. Nelson-Hayes's Multiple Cueing Model	16
3.4. Theoretical Integration of Depression and Self-Monitoring	17
4. Self-monitoring and Ambulatory Assessment in Depression	21

4.1. Role of Self-Care and Homework Assignments in Depression Interventions 21

4.2. Ambulatory Assessment of Mood and Physical Symptomatology 23

4.3. Comparison of paper-and-pencil versus computer-based Assessments in Laboratory Settings. 26

4.4. Comparison of paper-and-pencil versus computer-based Assessments in Ambulatory Settings 27

4.5. Ambulatory Monitoring in Depressive/Mood Disorders 30

5. Specific Aims and Hypotheses 34

6. Research Design and Methods 38

6.1. General Overview 38

6.2. Study Participants 38

6.3. Procedures 39

6.3.1. Baseline Study Visit (week 0) 40

6.3.2. Study Phone Call 1 (week 1) 41

6.3.3. Study Visit 2 (week 2) 41

6.3.4. Study Phone Call 2 (week 3) 42

6.3.5. Study Visit 3 (week 4) 42

6.4. Measures Obtained During the Study 43

6.4.1. Assessment of Depression 43

6.4.2. Ambulatory Monitoring of Mood and Symptoms 45

6.4.3. Medication Adherence 48

6.5 Control Variables 49

6.5.1. Health Symptoms 49

6.5.2. Inflammatory Factors and Thyroid Function: Blood Sampling 50

6.5.3. Physical Activity 51

6.5.4 Computer Use 52

6.6. Data Analyses, Sample Size Estimation, and Statistical Power 53

6.6.1 Hypothesis 1 53

6.6.2 Hypothesis 2 56

6.6.3 Hypothesis 3 57

6.6.4 Other Statistical Considerations 58

7. Results 60

8. Discussion 68

8.1 Theoretical Implications 75

9. Limitations 77

9.1 Recruitment 81

10. Conclusions 82

Tables 84

Figures 97

References 103

Appendices 129

List of Tables

Table 1	Variables Affecting the Reactivity of Self-Monitoring
Table 2	Flow Chart of Assessments During Study
Table 3	Late and Non-adherence Summary
Table 4	Baseline Sample Characteristics
Table 5	Hypothesis 1a – Adherence: Percentage and Self-Report
Table 6	Hypothesis 1b – Medication Adherence
Table 7	Hypothesis 1c – Overall Correlations Between Weekly Mood Rating and Final HRD Score (Groups combined)
Table 7a	Correlations of Daily Sad Mood and Weekly HRSD Scores
Table 8	Hypothesis 1c – Mean HRSD Scores from HLM evaluation
Table 9	Hypothesis 1d – Correlation of Adherence and Refill Status
Table 10	Hypothesis 2a – HRSD Changes over the Course of the Study
Table 11	Hypothesis 3 – Predictors of Physical Symptoms by Cognitive-Affective Symptoms
Table 12	Hypothesis 3 – Predictors of Cognitive-Affective Symptoms by Physical Symptoms

List of Figures

Figure 1	Overview of Study Time Points
Figure 2a	Individual Data Computer-Based Monitoring Condition
Figure 2b	Individual Data Paper-and-Pencil Monitoring Condition
Figure 2c	Daily Sad Mood Weekly Totals by Group
Figure 3	Hypothesis 3 – PHQ Data
Figure 4	Hypothesis 3 – CESD Data

1. Background

1.1. Prevalence and Impact of Depression

Major depressive disorder is a common condition with estimated prevalence rates in the United States of 2-4% (Kessler et al., 1994). The World Health Organization has estimated that the lifetime incidence rate of major depression is 17% (WHO International Consortium in Psychiatric Epidemiology, 2000). Major depressive disorder has negative effects on quality of life, such as perceived health, increased disability days, and higher rates of health care utilization (Spitzer et al., 1994; Ormel et al., 1994; Ormel et al., 1994). It is also one of the most disabling conditions in industrialized countries causing increased disability above and beyond physical disability and negatively affecting role functioning (Murray & Lopez, 1996; Ormel et al., 1994).

Major Depressive Disorder is defined by the American Psychiatric Association as the presence of either (a) depressed mood, and/or (b) loss of interest in normally pleasurable activities (anhedonia) for over 2 weeks, plus at least four of the following symptoms: changes in sleep, changes in appetite or weight, fatigue, change in psychomotor activity (increase or decrease), feelings of guilt or worthlessness, difficulty thinking or concentrating, or recurrent thoughts of death and/or suicidal plans or attempts (American Psychiatric Association, 2000).

Specific to this study, depression is more prevalent among patients with medical disorders compared to healthy individuals (Ormel et al., 1994). Rowe and colleagues (1995) surveyed 1898 patients attending a variety of primary care clinics and reported that 21.7% of women and 12.7% of men met criteria for major depression (DSM-III-R; American Psychiatric Association, 1987) during the previous 30 days. Lifetime estimates ranged from 36.1% for women to 23.3% for men (Rowe, Fleming, Barry, Manwell, & Kropp, 1995). Other studies have estimated the prevalence of major depression in primary care outpatients in the range of 20% (Schulberg & Burns, 1988; Barrett, Barrett, Oxman, & Gerber, 1988) to 30% (Kamerow, 1988). McQuaid and colleagues (1999) screened 511 family practice patients with a medical illness using a variety of screening measures for depression and anxiety. Screening resulted in 169 patients meeting initial criteria on at least one measure of major depression. These individuals were then followed up with a telephone delivered structured diagnostic interview (CIDI; Kessler et al., 1994) . Additionally, 44 patients not meeting criteria for screening were interviewed as a control group (total N=213). A total of 62/213 (29.1%) patients met criteria for a major depressive episode. When combined with the originally screened group, the results provide a conservative estimate of 12% of the original 511 patients meeting criteria for a major depressive episode. The findings of McQuaid and colleagues (1999) suggest that the prevalence rates found in other studies may be somewhat inflated (Coyne, Fechner-Bates, & Schwenk, 1994; Spitzer et al., 1994; Spitzer et al., 1994).

A recent review provides insight into the factors that may account for varying estimates of major depressive disorder in primary and general medical settings. Waraich and colleagues (2004) conducted a review of all depression related prevalence studies published between 1980 and 2000. Their findings suggest that the lifetime prevalence rate of depression in the general population is 6.7% (95% CI 4.2%-10.1%) and the 1-year prevalence rate is 4.1% (95% CI 2.4%-6.2%). Depression prevalence was higher in primary care settings with rates ranging from 2.2% (Barrett et al., 1988) to 13.5% (Tiemens, Ormel, & Simon, 1996; Coyne et al., 1994). However, in their review of primary care studies, prevalence estimates were complicated by methodological variations between studies, a variety of screening methods and measures, and unclear definitions in each study for point and period prevalence rates (Waraich et al., 2004). These methodological variations and disparate definitions may explain the variance in prevalence estimates in primary care, which are nonetheless consistently higher than prevalence rates found in the general population.

1.2 Somatic and Cognitive-Affective Symptoms of Depression

In primary care settings there are two primary symptom components of depression, somatic and cognitive-affective symptoms. Somatic symptoms of depression normally encompass loss of energy, sleep, change in appetite, poor concentration, and fatigue. The cognitive-affective symptoms of depression refer to sadness, sense of failure, loss of pleasure, guilt, punishment, self-dislike, self-

criticalness, suicidal thoughts, crying, agitation, loss of interest, indecisiveness, worthlessness, and irritability (van Diest & Appels, 1991; Whisman, Perez, & Ramel, 2000).

In primary care patients, depression often overlaps with somatic symptoms, particularly fatigue, sleep disturbances, and weight change. These somatic symptoms may reflect atypical features of depression (e.g., hypersomnia, hyperphagia), typical depressive symptoms (reduced sleep, lack of appetite and weight loss), or symptoms of a variety of medical conditions (e.g., diabetes, cardiovascular disease, etc). Thus, the elevated prevalence of depression in patients with medical disorders could partially reflect these overlapping somatic symptoms rather than an actual increase in depression rates within primary care.

Several studies suggest, however, that this increased prevalence is not a simple artifact of overlapping symptoms. Approximately 50% to 70% of patients with medically unexplained symptoms have a depressive disorder (Kroenke et al., 1994). The risk of depression rises as the number of physical symptoms increases (Jackson, O'Malley, & Kroenke, 1998). Wilson et al. (1983) found various physical symptoms such as pain are the initial presenting symptoms of patients who are subsequently diagnosed with depression in a family practice clinic. Somatic symptoms of depression, particularly fatigue, have been shown to predict the development of affective symptoms (notably sadness and guilt) in a non-clinical population (Berlin, 2006). In a review of the World Health Organization study on Psychological Problems in General Health Care (Sartorius

et al., 1993), Barkow et al. (2004) used regression analysis to evaluate the contribution of somatic symptoms to the detection of depression. The authors concluded that general practitioners should carefully evaluate medically unexplained physical symptoms. These symptoms included back pain, feelings of bodily heaviness or lightness, bodily weakness, seizures/convulsions, permanent tiredness, exhaustion after a minimum of effort and, to a smaller extent, diverse anxiety symptoms (e.g. feelings of anxiousness/nervousness, feelings of tension, difficulties relaxing). The authors noted that these symptoms can be used to enhance the detection of depressive disorders (Barkow et al., 2004). These findings suggest that medically unexplained physical symptoms, beyond those used for diagnosis of depression (fatigue, sleep disturbances and weight loss), may be particularly relevant in identifying depression within a primary care setting.

While the evaluation of physical symptoms may help in diagnosing depression, the impact of depression treatment on unexplained physical symptoms is still unclear. Greco and colleagues (2004) followed 573 patients over 9 months of anti-depressant therapy. The patients' physical symptoms were evaluated using the 15 items Patient Health Questionnaire (PHQ-15; Kroenke, Spitzer, & Williams, 2002). During one month of treatment for depression, the prevalence of physical symptoms, such as stomach pain, headaches, sleep problems, etc., dropped substantially. Over the remaining 8 months of treatment only minimal improvement in these symptoms occurred, with pain symptoms showing the least improvement. Affective symptoms also displayed substantial

improvement after one month of treatment. In contrast to the physical symptoms, the affective symptoms continued to improve during the remaining 8 months of treatment. The authors concluded that the physical symptoms are a partially separate entity from depression. The study also highlights the importance of primary care physicians counseling patients in that cognitive-affective and somatic symptoms frequently improve during the first month of antidepressant treatment for many patients (Greco et al., 2004).

1.3. Depression in Patients with Medical Conditions

Depression also adversely affects clinical outcomes of co-morbid medical conditions (Spitzer et al., 1994; Coulehan et al., 1997). Simon and collegeues (2000) and McQuaid (1999) reported that depression and co-morbid medical conditions resulted in increased health care costs. Several authors have reported increased referrals to subspecialties (O'Malley, Wong, Kroenke, Roy, & Wong, 1998; O'Malley et al., 1998; Ekstrand, O'Malley, Labutta, & Jackson, 2004). Hays (1995) and Wells (1989) found greater impairments in quality of life related to comorbid depression. Eckstrand (2004) and others (Williams et al., 2004) reported that depression often results in adverse progression of co-morbid diseases. These negative health effects suggest that the treatment of depression within medical settings may aid in improving medical outcomes.

Despite these negative consequences of depression in primary care and other medical settings, patients are usually not adequately treated for

depression, and treatment that is received is generally limited to their specific medical condition. Multiple reasons may account for the under-diagnosis and under-treatment of depression, including: (1) physicians' perception that the depression is an understandable or expected phenomenon based on the patient's medical condition; (2) physician underestimation of adverse effects of depression on medical condition; (3) the atypical nature of depression in medical patients; (4) time constraints associated with assessment in the primary care setting; (5) an attempt to avoid the social stigma associated with a diagnosis of depression; and (6) a lack of awareness of treatment options (Coulehan et al., 1997; Kop & Ader, 2001)

1.4. Adverse Disease Outcomes Related to Depression

Numerous studies indicate depression and comorbid medical illness can result in increased negative impact on disease outcomes. Ormel and colleagues (1994) noted that these comorbid diseases resulted in greater impairment of daily functioning. Poorer quality of life was found by Spitzer (1994) and Coulehan (1997). Additionally Spitzer (1994) and Ormel (1994) noted greater disability and/or lost productivity because of illness than non-depressed patients with identical illnesses. Furthermore, depression is associated with an increased risk of morbidity and mortality in patients with coronary artery disease (Kop et al., 2001; Lesperance, Frasure-Smith, Talajic, & Bourassa, 2002), heart failure (Ramasubbu & Patten, 2003), renal failure (Lopes et al., 2002; Kimmel et al.,

2000), and cancer (Valente & Saunders, 1997). Depressed patients with diabetes mellitus have poorer glycemic control and elevated rates of diabetic complications compared to diabetic patients without depression (de Groot, Anderson, Freedland, Clouse, & Lustman, 2001; Lustman et al., 2000). Thus, depression is not only more prevalent among patients with medical conditions, but also predicts adverse progression of these conditions.

Both biological and behavioral pathways have been suggested to explain the predictive value of depression on adverse health outcomes. Depression is related to neurohormonal dysregulation as well as altered autonomic nervous system activity. Major depressive disorder is associated with hypothalamic-pituitary-adrenal (HPA) axis dysregulation, elevated plasma and urinary catecholamines, and increased cortisol levels. Autonomic nervous system changes related to depression include increased sympathetic nervous system activity and vagal withdrawal. The central nervous system-related changes in neurohormonal and autonomic nervous system activity associated with both major and minor depression may promote various disease processes by affecting immune system parameters (Thase & Howland, 1995; Petito, Revicki, & Hartemink, 2001), promoting procoagulant and proinflammatory processes, such as C-reactive protein, fibrinogen, IL-6, TNFα, and IL-10 (Kiecolt-Glaser & Glaser, 2002), among other biological factors involved in chronic and acute medical conditions (Carney, Freedland, Miller, & Jaffe, 2002). These biological pathways may clarify why unexplained physical symptoms are commonly associated and

predictive of depression in primary care (Jackson et al., 1998; Wilson et al., 1983; Barkow et al., 2004).

Depression is also associated with adverse health behaviors such as smoking (Covey, Glassman, & Stetner, 1998), decreased exercise levels (Ciechanowski, Katon, & Russo, 2000; Stilley, Sereika, Muldoon, Ryan, & Dunbar-Jacob, 2004), and poor compliance with medication regimen (Valente et al., 1997). The biological factors and adverse health behaviors associated with depression are interrelated. However, more research is needed to fully understand the biobehavioral processes involved in the relationship between depression and adverse health outcomes in patients with medical conditions.

2. Effects of Depression Interventions in Patients with Medical Disorders

Treating depression in primary care settings greatly improves depressive symptoms, health-related functioning, and quality of life (Jackson, DeZee, & Berbano, 2004). However, studies examining the effectiveness of treating depression on clinical progression of comorbid medical disorders are equivocal at best (Ekstrand et al., 2004; Williams et al., 2004). Williams and colleagues (Williams et al., 2004) conducted a subgroup analysis of diabetes-related outcomes in a study in which patients were randomly assigned to receive either usual care or the treatment arm, which consisted of psychoeducation, meeting with a depression clinical specialist, and also allowed the patient to choose either antidepressant medication or psychotherapy. Depression treatment improved

affective depressive symptoms shortly after initiation of the intervention. Mental and physical functioning also improved, but at a slower rate than affective symptoms. In spite of these findings, the intervention group only improved in increasing exercise days at 12 month follows up. There were no differences on the other self-care behaviors such as diet, medication adherence, or the mean number of glucose testing or foot inspections. One notable limitation of the study is that both groups reported excellent adherence to the diabetes self-care regimens at study entry. Previous studies with diabetics have indicated that depression treatment may improve glycemic control but the effects on self-care behaviors have not been adequately evaluated (Williams et al., 2004).

Coulehan and colleagues (1997) examined the relationship between depression severity and functional status of medical comorbidity in 276 primary care patients. Patients were randomly assigned to Interpersonal Therapy (IPT), nortriptyline, or usual care. The intent to treat analysis revealed that both treatment arms resulted in significant improvements in all outcome measures except those assessing general health and pain. When treatment completers were compared, however, both treatment groups showed greater improvements in general health and pain than the usual care treatment completers. There was no relationship between burden of medical comorbidity and severity of depression. Coulehan and colleagues (1997) conclude that mental and social functioning may improve with low-level treatment for depression, whereas pain and overall physical functioning may require more intensive depression-specific therapy.

A depression management program versus usual care was evaluated in treating high utilizers of medical treatment in primary care (Katzelnick et al., 2000). The treatment program included providing educational materials and training for physicians and patients, specific antidepressant treatment recommendations, and ongoing support for patients via monitoring, feedback and specialty consultation. Depression management resulted in increased antidepressant treatment to adequate levels and decreased depressive symptom severity. After 12 months follow-up, the treatment group also reported improved social functioning and general health perception. However, there was no significant improvement in physical functioning, role functioning, or pain perception.

Koike and colleagues (2002) examined the impact of depression treatment on patients with and without a comorbid medical disorders. The active treatment was a quality improvement program that included screening, assessment, patient education, and a nurse depression specialist who served as a case manager for either 6 or 12 months. Additionally, patients in the quality improvement condition were allowed to choose treatment with antidepressant medication, psychotherapy, or no treatment. At 6 and 12-month follow-up, patients with comorbid medical illness were still at increased risk of having a depressive disorder. Even with this increased risk, the, rates of successful depression treatment were similar in patients with and without a medical illness. These findings suggest that depression can be effectively treated in primary care.

The evidence suggests that overall physical, mental, and social functioning all improve with depression treatment. Yet, the impact on specific medical illness outcomes has been equivocal. According to Jackson (2004) and others (Coulehan et al., 1997) one possible explanation for the disparity may be that treating depression requires sustained treatment beyond the acute-phase to show benefit for medical symptoms.

Certain physical symptoms may be more amenable to treatment (such as symptoms other than pain) but still evidence a plateau effect (Greco et al., 2004). Evidence from Greco and colleagues (2004) and Williams et al., (2004) suggest that affective symptoms will remit faster than somatic symptoms within primary care. These studies, as well as others, are somewhat limited because the short-term sequelae of symptom remission are not assessed. Most clinical treatment studies often use follow-up periods of 1-3 months after treatment commences, rather than examining what occurs within the first month of treatment. By examining the first month more closely, a better understanding of immediate symptom responses to treatment can be documented. These short-term responses are important for providers when counseling patients about the expected course of treatment and symptom relief.

3. Self-Monitoring Theories

Self-monitoring, self-recording, and self-observation are common terms used to describe a process of client's or patient's recording behaviors, feelings, and thoughts. Thoresen and Mahoney define self-monitoring as a two-step

process: (1) the patient first discriminates the occurrence of the behavior and then (2) systematically records the observation (Thoresen & Mahoney, 1974).

Self-monitoring is not a new concept; Thoreson and Mahoeny (1974) describe a procedure used by Benjamin Franklin in his attempts to increase the development of 13 virtues. In psychology the use of self-monitoring can be traced to historical origins in classical psychophysics (Guilford, 1936) and to structuralism, which employed a specific form of self-observation – introspection (Chaplin & Krawiec, 1960). More recently, self-monitoring has been incorporated as the basis for behavioral treatments of various psychological disorders (Korotitsch & Nelson-Gray, 1999) and self-monitoring is used as homework to monitor thoughts and emotions in cognitive-behavioral therapies (Beck, 1995).

Research on self-monitoring has focused on assessment and reactive therapeutic consequences. Assessment functions include identifying baseline measures to compare with later treatment effects. Reactive therapeutic functions refer to the psychological changes associated with monitoring including behaviors, thoughts, and feelings. These psychological changes occur in the desired treatment direction such that positive behaviors increase (e.g. pleasant activities, positive mood, and social interactions) and negative behaviors decrease (e.g. negative mood, ruminative thinking, suicidal ideation) and are thus considered therapeutic (Korotitsch et al., 1999). The theories of self-monitoring and how it results in reactivity are presented to provide an understanding of why reactivity may occur and how self-monitoring may be utilized in the treatment of depression in a primary care setting.

Previous research has shown that the “reactive effects of self-monitoring” can have an impact on a diverse range of behaviors including hallucinations (Rutner & Bugle, 1969), paranoid ideation (Williams, 1976), ruminative thinking (Frederiksen, 1975), insomnia (Jason, 1975), and suicidal ideation (Clum & Curtin, 1993). The unique effects of self-monitoring have been demonstrated in some studies but the overall early results have been mixed (see (Kazdin, 1974) for a review). However, support for the use of self-monitoring in depression is abundant in the CBT-depression literature. Additionally, two studies have utilized self-monitoring as a specific treatment component. In both of these studies self-monitoring increased pleasant activities {Harmon, 1980 183 /id;Hunter, 2003 278 /id}. Three theories have been developed to explain reactivity in self-monitoring.

3.1. Cognitive Mediation Model

One of the earliest theories of reactivity is the cognitive-mediation model of Frederick Kanfer (1975; Kanfer, 1972; Kanfer, 1970). In Kanfer’s theory, control over one’s behavior includes three components; self-monitoring, self-evaluation, and self-reinforcement. These three components occur in a sequence of events triggered by the preceding component to allow the person to self-regulate behavior. The sequence begins when an individual observes and records some personal behavior (self-monitoring). The person reacts to the results of self-monitoring by comparing the behavior to specific performance criteria (self-evaluation). If the performance is equal to or exceeds the

established criteria the result is positive self-reinforcement for the behavior. Alternatively, if the performance is lower than expected then negative self-reinforcement may result in increased behavior to reach performance goals (Mace & Krotochwill, 1985). In the case of depression, patients would track pleasant activities, for example, and if such activities were to meet a desired goal during the monitoring period the success of meeting the desired goal would provide internal positive-reinforcement resulting in an increase in pleasant activities and subsequent improvement in depression (Lewinsohn et al., 1973; Zeiss, Lewinsohn, & Munoz, 1979).

3.2. Rachlin's Operant Recording Model

Howard Rachlin's theory of reactivity to self-monitoring focuses on environmental cues (Rachlin, 1974) as opposed to the internal, cognitive, focus of the aforementioned Kanfer's model (Kanfer, 1975). Specifically the tracking of events and positive and negative reinforcement are mechanisms to increase salience of a relationship between one's behavior and the external (or environmental) consequences of that behavior. This theory emphasizes producing reactive effects through the act of self-recording. The act of self-recording triggers increased awareness of the behavior, strengthening the relationship between the individual's behavior and the external consequences of that behavior (Rachlin, 1974). As a result, the individual is more aware of the targeted behavior and may subsequently engage in that behavior according to

the established behavioral goals. For example, in an effort to engage in more pleasant activities, an individual will increase the number of pleasant activities because of the recording of the actual number of pleasant activities that are engaged in during a specific time frame. These positive behaviors will then be reinforced via external factors such as a therapist social contingencies or the enjoyment of the activity resulting in continuing to increase pleasant activities.

3.3. Nelson-Hayes's Multiple Cueing Model

Rosemery Nelson and Steven Hayes (Nelson & Hayes, 1981) expanded Rachlin's (1974) model by implicating the entire self-recording process as the key to link awareness of behaviors with external consequences of the behaviors. Their model suggest that the process of self-recording is only part of the mechanism of change. They maintain that the self-recording response is not solely responsible for the association with external consequences that develops but initiates a reactivity chain. The reactivity chain that leads to behavior change includes: self-monitoring instructions, training in self-monitoring, the self-monitoring device, feedback from others, and the self-recording process itself. In addition, self-evaluation and self-administered consequences are also acknowledged as cues to the individual signaling environmental contingencies that can then be used to control one's behavior. This reactive chain and other cues may serve to increase the salience of the association between the individual's behaviors and the environmental consequences (Mace et al., 1985).

Thus, in the depressive paradigm the instructions to monitor activity, the act of monitoring, the monitoring device, and the feedback received all serve to strengthen the relationship between the pleasant activity and the external reinforcements (i.e. therapist praise, improved mood, etc.).

Insert Table 1 about here.

3.4. Theoretical Integration of Depression and Self-Monitoring

Research indicates that self-monitoring of either mood and/or pleasant activities in depressed patients results in improved mood and an increase in positive activities {Harmon, 1980 183 /id;Hunter, 2003 278 /id}. The three theories of reactivity described earlier provide a behavioral view of reactivity, and primarily are related to the cognitive and behavioral theories of depression.

The intervention of self-monitoring is a powerful behavioral mechanism for change, however, examining this mechanism through only the behavioral perspective may limit its utility because depression is multifaceted and several theoretical accounts of depression are not based in behavioral theory. One component of psychotherapy that is consistent regardless of the theoretical orientation is the basic fundamental process of educating an individual with depression. All forms of psychotherapy include an educational component but the education is accomplished in different ways and at different points in therapy. For example, in psychoanalytic therapy, education is provided by allowing the individual to experience corrective emotional experience through helping with

confrontation of avoided intrapsychic fears such as guilt or anger towards another person or object. This education often occurs later rather than sooner in treatment, although in the newer short-term dynamic model the early establishment of a termination date helps to increase anxiety. This increased anxiety results in the patient acknowledging that therapy will not last and helps to speed the confrontation with the previously avoided intrapsychic fears (Nielsen & Barth, 1991).

The behavioral models of depression are based on operant conditioning. Operant conditioning is based on the principles that behavior has an effect on the environment and begins with an antecedent. An antecedent is a particular event that occurs before the behavior, such as a seeing one's spouse. The individual then responds to the antecedent, for instance talking with one's spouse, as opposed to ignoring the spouse. The behavior is then positively reinforced if the spouse responds approvingly and the behavior continues or increases. If the spouse does not respond then negative punishment occurs and the behavior is likely to cease or decrease (see Schwartz et al., 1993 for a more complete review).

While the three theories of reactivity to self-monitoring differ on the specifics the general view is that of operant conditioning. The individual, who is self-monitoring, identifies a target behavior occurring and then records the action. In the Rachlin and the Nelson-Hayes models recording serves to increase the individual's awareness of the behavior and resulting consequences (either negative or positive), leading to the appropriate therapeutic response. Individuals

with depression often overemphasize the negative aspects of life; by monitoring actual daily moods individuals may learn that certain aspects of life provide positive reinforcement, resulting in improvement of mood. These situations that result in more positive moods can then be repeated, increased, or expanded upon to continue the reinforcement of the individual's mood, thereby aiding in decreasing depressive symptoms. The individual is able to learn what behaviors result in positive reinforcement and subsequent improvement in mood and engage in those behaviors. Additionally those negative behaviors that result in depressed mood can be avoided or decreased.

Kanfer's cognitive model (1972) serves as a bridge between the behavioral and cognitive theories of depression. However, it is very useful in understanding how self-monitoring may be used in Seligman's theory of depression (Seligman, 1975) and the updated version of this theory (Abramson et al., 1989). As the patient monitors the target behavior, a comparison against a given standard occurs, such as number of pleasant or success activities completed in one day. The standard may be internal, established by the individual, or external, given by a treatment provider. The individual then compares the monitored behavior against the standard, internal positive reinforcement then occurs if the standard is met, or negative reinforcement if it is not. In Kanfer's model (1972), reinforcement may take cognitive forms, such as self talk. As monitoring continues and increased success in meeting the standards is met, the individual may improve from learning to have control over

the environment, as well as from the self-reinforcement received for increasing the target behavior.

Reinforcement from these educational goals comes from both therapist and the patient as the patient experiences changes from the education gained in therapy. In monitoring behavior, mood, and thoughts, individuals may also attain education and understanding of their own reactions to various situations. In essence, self-monitoring is a self-educational process that functions similar to the educational process that occurs in various types of therapy. The above hypotheses regarding the educational aspects of self-monitoring are largely speculative.

To date only one study has examined the three reactivity theories and the results were mixed as to the best explanation of why reactivity works (Mace et al., 1985). This study found support for various aspects of all three theories, although of note was the utility of experimenter instructions that served to improve the efficiency of the behavioral-change paradigm. Limited support for any of the models regarding goal setting and its effects on either external or internal (self) reinforcement was found. The authors noted that the limited support might be the result of a reinforcement strategy that was not powerful enough to yield a large enough effect. Further studies of self-monitoring and reactivity will be necessary to determine the most useful theory explaining the processes involved as well as the reasons why ambulatory monitoring may have positive effects on depression.

4. Self-monitoring and Ambulatory Assessments in Depression

4.1. Role of Self-Care and Homework Assignments in Depression Interventions

A common feature in all treatment methods is the requirement of patients to participate in various methods of self-care. In the case of pharmacological treatment, self-care involves adherence to the medication regimen (Pampallona et al., 2004; Rand, 1999). In psychological therapies, self-care is often referred to as “homework”, with the goals of generalizing the learning that takes place in the therapy session to the patient’s daily life and assisting the patient in understanding their behavior in a given situation (Young, Weinbrger, & Beck, 2001; Gillies, 2001) .

Homework assignments are a central component of Cognitive Behavioral Therapy (CBT;Young et al., 2001) and Behavioral Therapy (Shelton & Levy, 1981) for depression. Typically these assignments involve self-monitoring of activities (Coyne et al., 1994), interpersonal interactions (Kamerow, 1988), negative cognitions (Spitzer et al., 1994), or a combination of these events (Spitzer et al., 1994). Occurring outside of the therapeutic setting, homework serves as the major method of data collection in CBT, providing information to both the therapist and the patient. Such assignments are also used to track and, after training, evaluate the accuracy of and challenge negative thoughts. Finally, homework assignments enable patients to independently practice what has been

learned in therapy. Patients are able to practice dealing with problems (Garland & Scott, 2002) and acquire specific cognitive-behavioral skills that can be used post-treatment to prevent relapse (Primakoff, Epstein, & Covi, 1986).

Studies that have examined effects of homework assignments and/or adherence to homework assignments consistently demonstrate that adequate completion of assignments is significantly associated with improved depressive symptoms. In a recent meta-analysis of CBT Homework studies over the past 20 years (1980-2000), Kazantzis and colleagues (2000) evaluated the effects of homework assignments on therapy outcome and the relationship between homework compliance and therapy outcome. The authors reported a moderate effect size for homework in depression treatment studies of 0.38 (95% CI 0.38-0.38; as reported by the authors - only two studies were used to determine this CI). However, the effect size was moderated by the method used to measure adherence. When the patient provided the assessment of compliance the overall effect size was 0.43 (95% CI 0.32-0.54). When the therapist provided the assessment of compliance the effect size was 0.38 (95% CI 0.38-0.38; three studies were used to determine this CI and the authors reported no variance in effect size of the studies). When an objective measure was used, the effect size was 0.29 (95% CI 0.29-0.29; one study was used to determine the CI). However, the actual objective measures used in the various studies were not well specified as the authors only report that some form of electronic marker was incorporated into audiotape equipment. In conclusion the results support the use of homework

assignments in the psychological treatment of depression and indicate that greater patient adherence with assignments will result in better outcomes.

4.2. Ambulatory assessment of Mood and Physical Symptomatology

Ambulatory assessment refers to the collection of psychological or physiological data in a natural setting based on explicit research criteria (Fahrenberg, 1996). This methodology allows the use of paper-and-pencil and, more recently, electronic computer-assisted techniques, to acquire self ratings of mood changes, symptoms, coping strategies, and behavior (Fahrenberg, 1996). With ambulatory assessment, patients are able to self-monitor a variety of disease-related data to document symptom changes over time. Different domains of ambulatory assessment modules exist, including: (1) Physiological and biological parameters such as blood pressure, heart rate, salivary cortisol, and blood glucose that can be obtained by the patient at home; (2) Self-reported physical symptoms that are directly related to the patient's disease, such as pain; and (3) Self-reported symptoms not necessarily related to the patient's disease such as general well being, mood, cognitions, or situational factors (Schandry & Leopold, 1996).

Training patients to self-monitor their health status is not solely related to ambulatory assessment in research settings. Health care providers often assist patients in learning to perceive their symptoms. Examples include patients with prominent disease symptoms such as bronchial asthma, patients who are

required to learn awareness of airway obstruction and take appropriate countermeasures (Kotses et al., 1991), and depressed patients undergoing CBT learning to identify and challenge negative cognitions (Beck, 1995). In diseases without prominent symptoms, such as hypertension, medical regimen compliance is often poor because of the absence of cues to indicate the severity of the illness (Schandry et al., 1996).

Until recently, almost all self-reporting was accomplished using paper-and-pencil diaries or retrospective reports that occur days, weeks, or months after the phenomena being investigated. The use of diaries was intended to avoid inaccuracies and biases that affect the retrospective reporting of data, by obtaining the self-report closer to the actual event (Hufford, Stone, Shiffman, Schwartz, & Broderick, 2002; Stone, Shiffman, Schwartz, Broderick, & Hufford, 2003).

Paper-and-pencil diaries have several advantages but also many disadvantages (Stone, Shiffman, Schwartz, Broderick, & Hufford, 2002). The advantages of paper-and-pencil diaries include: reproduced at relatively little expense, easy to handle by the patient, and provide visual feedback to the patient regarding adherence. Yet, paper-and-pencil methods have limitations, primarily related to the accuracy of the timing of the self-report. Entries are normally desired at predetermined time frames, such as upon awakening or based on the occurrence of an event, such as a migraine headache. paper-and-pencil diaries do not allow verification of the accuracy of the entry time and research indicates that participants often complete the entries in batches well

after the fact (Hufford et al., 2002; Stone et al., 2003). The completion of diary data retrospectively, also called “parking lot compliance”, interferes with data quality and results in a continuation of potential recall biases that ambulatory monitoring is designed to overcome (Hufford, Shiffman, Paty, & Stone, 2001; Hufford et al., 2001).

Inaccuracy of ambulatory assessments is not limited to paper-and-pencil self-report assessments. Objective measurements such as blood glucose are also dependent on correct adherence at a set point in time. Access to past data may help a patient observe progress, but may also influence subsequent self-reports, which is not always desirable (i.e., access to information from past entries may inadvertently alter subsequent reports). Finally, in research there is a need to transfer data from the paper-and-pencil entries to an electronic medium for further calculations and statistical analyses, which is time consuming and associated with increased expense and chance for error (Schandry et al., 1996).

Many of the limitations of paper-and-pencil diaries can be overcome with the use of electronic devices such as hand held computers. These devices can be programmed with a clock driven signal as a reminder to complete the diary, thereby reducing the probability of neglecting an entry. To document compliance with reporting instructions, the exact time of data entry can be annotated. Participants cannot change entries at a later time or date. The diary can be designed so that reviewing previous entries is not possible and will not influence later reporting. The data can also be easily transmitted from the handheld device to a desktop computer to aid in data processing (Schandry et al., 1996).

4.3. Comparison of Paper-and-Pencil versus computer-based Assessments in Laboratory Settings.

Switching from traditional paper-and-pencil to a computer monitoring methodology may introduce challenges for clinical use. The equivalence of these two methods requires validation, and the acceptability for respondents is also relevant. Most of the research in this area has been conducted to examine equivalency of ability research regarding test administration with these two methods in a clinical or laboratory setting, whereas less is known about paper-and-pencil versus computer-based assessments during ambulatory assessment (Hank & Schwenkmezger, 1996).

Several studies have examined the equivalency of paper-and-pencil versus computer-based measures. Honaker (1988) reviewed the evidence regarding computerized administration of the Minnesota Multiphasic Personality Inventory (MMPI). Significant differences in mean MMPI scores were found across several studies, but no consistent bias towards level or direction of the scores was observed (Honaker, 1988). Schwenkmezger and Hank (1993) analyzed the State-Trait-Anxiety Inventory (STAI; Spielberger, 1999) and the State-Trait-Anger-Expression Inventory (STAXI; Spielberger, 1999), which revealed that item statistics, dispersion measures, and measures of reliability were all equivalent, but the two methodologies resulted in different mean scores. When answering on the computerized version, participants reported more state

anger and anxiety as well as increases on several aspects of the trait scales. The increased state anger and anxiety levels among individuals using computer-based assessments are not readily interpretable because no controls were used to adjust for computer-related anxiety levels or prior experience with computers.

Johnson and colleagues (2001) conducted the only systematic comparison between paper-and-pencil versus computer-based assessments using a qualitative instrument: the Loevinger Sentence Completion Test for Ego Development. In the study there were no differences in ego levels regardless of administration format. However, responses on the computer were significantly more elaborate than those obtained on paper-and-pencil as measured by word count. Generalizability of the study is limited because the sample consisted of college students with considerable computer experience. In summary, computer administered testing can be used in lieu of paper-and-pencil testing; but for each test, specific research is required to establish normative data for the new test medium and assessments regarding computer experience and computer anxiety are necessary.

4.4. Comparison of Paper-and-Pencil versus computer-based Assessments in Ambulatory Settings

Ambulatory paper-and-pencil versus computerized monitoring assessments have been evaluated by Hank and Schwenkmezger (1996). Counterbalanced assessments were made in 80 individuals (mean age

37.7±11.2 years) examining paper-and-pencil or computer monitoring. Self-monitoring was conducted six times daily, two days per week, for a recording period of two months. The self–monitoring items included current activity levels, location of activity, interactions with others (i.e. alone or with others), psychological meaning of the activity, and mood state at the time of monitoring. The results showed that 7 of 10 mood ratings measured on paper-and-pencil diaries had higher means and standard deviations, which indicated greater experiential variability than computer administration. paper-and-pencil self-monitoring resulted in almost perfect self-reported compliance, whereas the computer monitoring response rate was 75%. However, over-estimation of compliance with the paper-and-pencil measure is probable since there was no control on the actual date or time of completion, whereas computer assessment compliance may have been under-estimated because participants were to immediately report symptoms and not delay longer than 10 minutes before responding.

In an attempt to assess compliance with paper-and-pencil diaries Stone and colleagues (Hufford et al., 2002; Stone et al., 2003) used a novel approach. The study used a photosensor built into a paper diary that triggered an electronic record of the date and time of each diary opening and closing. The paper diary compliance rates were compared to a second group of chronic pain patients who used an electronic diary on a handheld computer. Two types of compliance were analyzed: 1) reported compliance based on the time and date written on the completed paper diary cards and 2) actual compliance based on automatic

recording by the photosensor in the paper diary. The electronic diaries allowed entries to be made within a ±15 minute window around a scheduled assessment time. Reported compliance with the paper diary was 90%, however, the objective measure revealed actual compliance averaged only 11% (95% CI: 8%-14%). In contrast the electronic diary patients completed each pain report within the required 30-minute window with an actual compliance rate of 94% (95% CI: 91%-96%).

In contrast to Stone and colleagues findings (Hufford et al., 2002; Stone et al., 2003), Green and colleagues (Green, et al., 2006) found many similarities between pencil-and-paper and computer-based monitoring. They reviewed the results of two previous studies and found similar psychometric and statistical equivalence between the two methods. Notably, in a study that required 10 paper diary entries per day they found that compliance was 66%. Further, when they adjusted for early morning responses, when many participants were still asleep, compliance rates rose to 75%. The authors noted that given the amount of responses each day it was unlikely that participants would be able to keep track of the exact time they were notified by electronic signal to complete the diary entries, making “parking lot compliance” less likely. The second study reviewed by the authors more directly compared the two monitoring methods. In this study participants completed diaries every three hours after waking related to their positive and negative moods and circadian rhythms. The results suggested that psychometrically the two methods were very similar in compliance rates and data equivalence. Notable differences cited by the authors included fewer participants

providing at least three diaries per day and greater within-person variance for the paper-and-pencil diary. The authors noted that the instructions and question format for the two methods were slightly different for the two conditions, which may account for the differences in variability. Finally, the authors conducted their own study in a once a day study. They asked married couples to complete either a paper-and-pencil or computer-based diary and the end of each day for one week and then utilized the other method for the second week. As in their review of the second study psychometrically they found no differences in either compliance or data equivalence with either method. They did note that checklists that were presented individually in the computer-based diary condition showed increased variability than the paper diary. This was likely due to the individual presentation of the question in contrast to the list format in the paper diary. Green and colleagues (Green, et al., 2006) findings suggest that psychometric equivalence between paper-and-pencil and electronic diaries is dependent on the study question, participant population, and goal of monitoring.

4.5. Ambulatory Monitoring in Depressive Mood Disorders

To date there have been no studies of ambulatory monitoring in depressed patients with co-morbid medical illnesses. However, several studies have monitored mood or depressive symptoms within a variety of affective disorders. Lewinsohn and colleagues (1972; 1973) conducted pivotal research in this area. In two of these studies, subjects were divided into three groups

(depressed patients, psychiatric controls, and normal controls). The patients monitored mood, pleasant activities, and depressive symptoms each day for 30 days. The participants in these two studies monitored daily activities that were generated from responses on the Pleasant Events Schedule (MacPhillamy & Lewinsohn, 1971). In the first study (Lewinsohn et al., 1972), college students were used as participants, and in the follow-up study a wider variety of participants was recruited to better generalize the outcomes (Lewinsohn et al., 1973). The results of both studies indicated that depressed individuals engaged in significantly fewer pleasant activities. Additionally, the results suggest that increasing events or activities that an individual considers "pleasant" could be beneficial in the treatment of depression.

In a subsequent treatment study, Grosscup and Lewinsohn (1980) conducted daily monitoring assessing both pleasant and aversive events as well as daily mood. All participants were treated with a standardized treatment protocol ("Increase Pleasant Activities"; Zeiss et al., 1979). The goal of treatment was to increase the patients' rate of engagement in pleasant activities. Strong support was found for the association between the daily rate of unpleasant events and depressed mood. Importantly, improvement of depression was first characterized by a decrease in the level of aversiveness of experienced events.

Stamenkovic and colleagues (2001) examined the use of daily monitoring among 22 patients treated with fluoxetine for recurrent brief depressive (RBD) episodes. The dairy consisted of reporting the frequency, duration, and severity of 18 psychopathological symptoms of major depression according to DSM-IV

depressive criteria and was administered for 54 days. Additionally, diary observations of nine patients continued for 140 days after the end of the study (196 days of total observations). Of the 17 patients who completed the 56-day treatment, all showed significant improvements in depressive symptoms including the reported symptoms in their daily dairy. For those patients who continued treatment and dairy monitoring beyond the initial 56-day trial, continued improvements in depressive symptoms were observed.

In continuing the work of Lewinsohn and colleagues (Grosscup et al., 1980; Lewinsohn et al., 1972; Lewinsohn et al., 1973), Hopko and colleagues examined the relationship between mood, activities, and anticipated reward value of activities (Hopko, Armento, Cantu, & Lejuez, 2003). The study compared normal participants to mildly depressed patients (minor depression), and individuals with major depressive disorder. Participants were monitored daily for seven days using activity monitoring forms that included questions about how rewarding or pleasurable a particular activity was, and also how likely the participants believed the behavior would lead to future rewards. In contrast to earlier findings by Lewinsohn and colleagues (Grosscup et al., 1980; Lewinsohn et al., 1972; Lewinsohn et al., 1973), this study did not pre-identify pleasant activities but instead evaluated normal day-to-day activities. Additionally, each participant completed the Positive and Negative Affect Scales (PANAS; Watson, Clark, & Tellegen, 1988), which includes two 10-item scales measuring positive and negative emotions. The findings were in support of previous research by Lewinsohn and colleagues (Grosscup et al., 1980; Lewinsohn et al., 1972;

Lewinsohn et al., 1973), indicating that self-reported depressive symptoms (and daily negative affect ratings) were inversely related to general activity levels and the amount of reward or pleasure that participants obtained through activities. Findings also indicated that mildly depressed individuals reported a lower expectation that current behaviors would result in future rewards than controls.

Harmon and colleagues {Harmon, 1980 183 /id} used a counterbalanced design to study self-monitoring of mood and activity. Six patients were assigned to the experimental condition and two patients served as the control group. Patients in the experimental condition were monitored for mood or activity based on an ABAC design. Patients were examined in three conditions: (A) baseline (no hourly monitoring; (B) hourly monitoring of mood; (C) monitoring of activity levels, counterbalanced for sequence. During baseline, patients and control group patients completed the Depression Adjective Check List (DACL; Lubin, 1965) and the Pleasant Event Schedule (PES; MacPhillamy et al., 1971) every evening. During the experimental periods, these forms were completed and the patients either monitored their mood or activity on a 1-hour variable-interval schedule triggered by a portable timer. Additionally, all patients, including controls, attended one-hour group treatment sessions each week. Results indicated that overall self-monitoring of mood or activity resulted in improved mood compared to the control group and the baseline condition (A) among patients. This study provides evidence that reactivity occurs to monitoring of mood and behavior in depressed patients. Harmon and colleagues {Harmon, 1980 183 /id} also showed

that mood is reactive to monitoring when conducted over several periods throughout the day.

In summary, prior research has shown that daily monitoring of symptoms is associated with improved adherence (Schandry et al., 1996) and self-reported depressive symptoms {Harmon, 1980 183 /id;Harmon, 1980 183 /id}. However, reliability of ambulatory self-reports has been variable (Stone et al., 2002; Stone et al., 2003), and is determined by the difficulty and invasiveness of the monitoring procedure, as well as patient characteristics (Kazantzis et al., 2000). Thus, computer-based techniques have been developed to improve the accuracy of ambulatory self-reports of physical symptoms and mood (Stone et al., 2002; Stone et al., 2003; Schandry et al., 1996). To examine the role of ambulatory monitoring techniques in the treatment of major depressive disorder in a primary care setting, the present investigation was designed to test the following specific aims:

5. Specific Aims and Hypotheses

The aims of this investigation involved the evaluation of ambulatory assessment tools (computer-based and paper-and-pencil) in the assessment of depressive mood symptoms and adherence to monitoring and anti-depressive medication regimen. Specific Aim 1 addressed the accuracy of ambulatory depressive mood symptom reports against standardized structured clinical interview techniques. Reliability of ambulatory-assessed medication use was

evaluated against refills of medication. Specific Aim 2 addressed the effects of computer-based versus paper-and-pencil monitoring on the clinical course of standardized depression assessments based on structured clinical interview, which is the "gold standard" for the evaluation of depression. Specific Aim 3 examines which symptoms of depression (somatic vs cognitive-affective) will improve first during the follow-up period. The following Specific Aims and hypotheses were examined:

Specific Aim 1 was to investigate whether computer-based ambulatory assessments resulted in more accurate (timing and completeness) self-reports of depressive mood symptoms and medication adherence as compared to traditional paper-and-pencil methodology. It was hypothesized that:

(a) computer-based monitoring will be associated with better adherence to daily monitoring of depressive mood symptoms, based on timing and completeness of responses, compared with the paper-and-pencil techniques.

(b) computer-based monitoring will be associated with better adherence to medication regimen, based on refill of medication, compared with the paper-and-pencil monitoring techniques.

(c) The correspondence between retrospective assessment of depression based on structured clinical interview with ambulatory computer-based self-report of depressive mood symptoms over the same observation period, will be higher than the correspondence between retrospective and ambulatory paper-and-pencil assessments.

(d) The correspondence between refill of medication with ambulatory computer-based self-report of medication use over the same observation period, will be higher than the correspondence between refill of medication and ambulatory paper-and-pencil assessments of medication use.

Specific Aim 2 was to investigate whether improved symptom reports and medication adherence (Specific Aim 1) in the computer-based monitoring group versus the paper-and-pencil group were associated with better outcomes of depression at 4-week follow-up, and that both monitoring techniques will be associated with less depression at follow-up than patients who were not monitored daily. It was hypothesized that:

(a) computer-based monitoring will be associated with less depression than paper-and-pencil monitoring based on structured clinical interview at 4-week follow up.

(b) Ambulatory monitoring by either computer-based techniques or paper-and-pencil techniques will be associated with less depression as documented by structured clinical interview at 4 week follow-up as compared to a control condition without ambulatory monitoring

Specific Aim 3 was to document the trajectory of depression symptom remission in the clinical course of depression among primary care patients. It was hypothesized that:

(a) Symptoms of depressed affect will remit prior to somatic symptoms of depression during the course of 4-weeks ambulatory monitoring.

6. Research Design and Methods

6.1. General Overview

Psychological and physiological measures were assessed in 16 participants randomly assigned to a daily monitoring condition using computer-based electronic diaries, paper-and-pencil diaries, or a control condition. As shown in Figure 1, participants were evaluated weekly throughout the protocol: (1) at baseline; (2) via phone during week 1 and 3; (3) in person at week 2 and 4.

Insert Figure 1 about here

6.2. Study Participants

Participants were eligible patients from the Walter Reed Army Medical Center (WRAMC) internal medicine primary care clinic. Twenty-five individuals were diagnosed with depression and referred for enrollment in the study by their primary care provider. Seventeen patients enrolled in the present study and were randomly assigned to one of the three study groups. Six patients completed daily monitoring using a hand held computer (Group 1 – computer-based), 6 participants completed daily monitoring using structured paper-and-pencil diaries (Group 2 – paper-and-pencil), and 5 participants did not complete daily monitoring (Group 3 – control). Of the nine patients not enrolling 4 did not meet

eligibility requirements by not taking anti-depressants or having been on them for an extended period of time, 2 declined to enroll, and 3 could not be contacted. Inclusion criteria were: (1) Current diagnosis of depression as evaluated by the patient's primary care provider; (2) Referred for and currently taking antidepressant pharmacotherapy; and (3) Not treated for depression (either pharmacotherapy or psychotherapy) within the last 2 years.

Exclusion criteria: (1) Age <18; (2) history of bi-polar disorder or psychosis; (3) currently under the treatment of a psychiatrist or psychologist for a mental disorder *other* than depression; (4) visual or cognitive impairment interfering with completion of the questionnaires and ambulatory diary. These impairments include, but are not limited to, blindness or partial blindness that interferes with reading ability, illiteracy, or other deficits that interfere with completion of a practice diary during the initial session; (5) active suicidal ideation as determined by the primary care physician or a positive response to question three on the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960; Hamilton, 1967). (No active suicidal ideation was reported by study participants); (6) refusal to informed consent.

6.3. Procedures

Participants were referred to the study by their primary care providers. Participants were then contacted by study personal and briefed on the study. Following informed consent, participants were randomly assigned to one of three

group conditions (computer-based, paper-and-pencil, or control) and were followed for 4 weeks. Ambulatory assessments of depressive mood symptoms and medication use were obtained daily (Aim 1), except in the control group. Assessments of depression was obtained by interview using the Hamilton Rating Scale for Depression (HRSD; (Hamilton, 1960; Hamilton, 1967) at baseline (week 0), and after 2 and 4 weeks (Simon et al., 2000) (Specific Aim 2). Additional assessments with the HRSD and Patient Health Questionnaire-15 (PHQ-15) were obtained via telephone interview at week 1 and 3. (See Table 2) Interviews were administered by a trained technician and evaluated by a licensed clinical psychologist (Dr. Jennifer Francis).

Covariates that may affect symptom report and/or the clinical course of depression were assessed throughout the study and included: health symptoms (SF-12), general anxiety (BAI), computer experience and anxiety (CTS), inflammatory factors and thyroid function, and physical activity.

Insert Table 2 about here

6.3.1. Baseline Study Visit (week 0)

After providing written informed consent, participants were randomly assigned to one of the three groups (computer-based, paper-and-pencil, or control). A structured interview to evaluate depressive symptoms (Appendix A) and a set of questionnaires related to general health status, physical symptoms,

and comfort level with handheld computers (Appendix B) were then completed. A practice diary entry was completed for those assigned to the computer-based and paper-and-pencil groups. The training ensured that patients understood how the daily questionnaire operated and provided patients an opportunity to ask questions about daily monitoring. The following information was also obtained to rule out potential confounding variables including: age, height, weight, marital status, military status (i.e. active duty, retiree, or family member), race/ethnicity, current medications, and general health status including comorbid medical diagnoses. One blood sample (20 mL) was collected at the Department of Medicine, WRAMC for analysis of inflammation and thyroid function markers, however these samples were not analyzed as part of this study.

6.3.2. Study Phone Call 1 (week 1)

Participants were contacted via telephone to assess current depression based on the HRSD (Potts, 1991; Simon, Revicki, & VonKorff, 1994). The HRSD was used, because prior studies have validated this instrument as a telephone-based assessment tool for depression. Participant questions related to the self-monitoring assessments were also addressed. The script for this phone call is included as Appendix C.

6.3.3. Study Visit 2 (week 2)

Two weeks following study entry, participants returned to the clinic. For the paper-and-pencil group, self-monitoring assessments were collected and new diaries provided for the subsequent two monitoring weeks. For participants in the computer-based group, data was downloaded in coded fashion and the program reset for the subsequent 2-weeks of data collection. The three groups completed measures as shown in Table 2 and the HRSD interview was conducted to assess current depression status. Feedback was also provided regarding each patient's adherence to completing the monitoring assessments.

6.3.4. Study Phone Call 2 (week 3)

Consistent with study phone call 1 at week 1, participants were contacted via telephone to assess depression and physical symptoms in call 2, 3 weeks after enrollment. As in the first phone interview, participants also had an opportunity to ask questions regarding the self-monitoring assessments.

6.3.5. Study Visit 3 (week 4)

Four weeks after enrollment, participants returned for the final evaluation. This visit included assessment of depression using the HRSD interview, as well as all other measures used at baseline (MFI and PHQ-15). A measure of self-reported adherence to the ambulatory self-monitoring assessments was also obtained to investigate differences between self-reported adherence versus

study-based criteria for adherence. For participants in the monitoring conditions an additional questionnaire regarding the ease of use and acceptability of the medium of monitoring was administered.

6.4. Measures Obtained during the Study

Repeated assessments of depression were obtained to assess the effects of the type of monitoring technique (computer-based versus paper-and-pencil; Aim 2). General health-related symptoms, which have been shown to be highly correlated with depression (Jackson et al., 1998; Kroenke et al., 1994), and adherence were examined weekly. A blood sample was obtained at study entry to account for inflammatory processes and thyroid dysfunction as potential contributing factors to depression. Appendix A includes the interview assessment. Appendix B includes the other questionnaires, and Appendix D contains instructions provided to individuals in the computer-based monitoring condition and Appendix E includes the ambulatory assessment questions used by both the computer-based and paper-and-pencil monitoring conditions.

6.4.1. Assessment of Depression

A standardized measure was used to assess depressive symptoms. The Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960; Hamilton, 1967) was used as the primary diagnostic tool for depression. The advantage of the

HRSD over other structured interviews is that it enables evaluation of *severity* of depression (see below for details). The Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977) was also used to evaluate depression. The CES-D was included to allow comparisons with the ambulatory monitoring techniques (because the HRSD format is not readily transferable into an ambulatory format). The use of two depression inventories is also consistent with previous research, indicating that the combination of instruments increases the reliability and convergent validity of depression assessments (Kelner, 1994).

The Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960; Hamilton, 1967) is a 21-item interview assessing behavioral and somatic symptoms of depression. The HRSD was used as the primary diagnostic tool for assessment of depression. Overall inter-rater agreement is high, commonly exceeding 0.84 (Hedlund & Virmani, 1979). Total scores range from 0 to 52, with scores from 7-17 reflecting mild depression and scores above 17 indicating clinical depression (Hamilton, 1960; Hamilton, 1967).

The Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977) is a 20-item self-report inventory using a 4-point rating scale (0-3). The CES-D evaluates four main areas of depression: dysphoria, well-being, interpersonal difficulties, and somatic complaints (Cronbach's α=0.85). The cut off score for the CES-D is normally set at 16 (Dozois & Dobson, 2002).

Atypical forms of depression are often common in medical patients (Kop et al., 2001; Lesperance & Frasure-Smith, 2000) and were assessed using the Multidimensional Fatigue Inventory (Smets, Garssen, Bonke, & De Haes, 1995)

and specific components of the HRSD (hypersomnia and hyperphagia; Matza et al., 2003). The Multidimensional Fatigue Inventory (MFI) is a 20-item self-report instrument designed to measure fatigue. It covers the following dimensions: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation and Reduced Activity (Cronbach's α=0.84).

The questionnaires and interview were completed at all three visits, and took approximately 45 minutes per visit. The participants completed the questionnaires and data was stored in coded fashion without identifying information.

6.4.2. Ambulatory Monitoring of Mood and Symptoms

Participants in the monitoring groups were asked to complete a series of 22 questions at the beginning of each day and 29 questions each evening during the 4-week study. The daily diary questions are presented in Appendix D, and include assessments of mood (including feeling happy, alert, frustrated, anxious/tense, sad, angry, energetic, depressed/blue, stressed), physical activity, physical symptoms, sleep, and use of medications. Patients in Group 3 (controls) did not complete ambulatory assessments.

There are several factors that have been identified as variables that can influence reactivity to self-monitoring. (e.g. Kopp, 1988; Korotitsch et al., 1999). These factors and how they impact reactivity are presented in Table 1 (Korotitsch et al., 1999). Two of these variables, valence and self-recording device will be

the primary focus in the current study. Negative and positive moods, which are hypothesized to have a negative and positive valence, will be monitored, as will pleasant activities. The positive valence of these pleasant activities will be based on the patient's definition of pleasant and success activities. This method is similar to that utilized by (Grosscup & Lewinsohn, 1980) who allowed the participants in their study to identify if the activities engaged in each day were positive or negative. For self-recording device either a handheld computer diary or a paper-and-pencil diary will be utilized. Previous studies {Harmon, 1980 183 /id;Hunter, 2003 278 /id} have utilized paper-and-pencil diaries. It is hypothesized based on the results of previous studies (Korotitsch et al., 1999), that the more obtrusive nature of the handheld computer, including alarm reminders, will result in both increased reactivity and adherence to the diary.

Patients chose preferred times of diary completion at the two phases of the day (morning and evening) and were required to complete the diary within a 30 minute time-frame of these preset entry times.

Measures of adherence with ambulatory monitoring. Patients in the paper-and-pencil group were instructed to document the exact time that the monitoring was completed regardless of whether documentation was within the prescribed timeframe or not. Adherence was measured based on number of entries completed at the designated times (±15 minutes; Hufford et al., 2002) for both paper-and-pencil and computer-based monitoring groups. Of the total entries the paper-and-pencil group did not complete within the timelines 58 times in

comparison to the computer-based group, which was earlier or later than the designated time 134 times. See table 3 for overall percentages.

A second measure of adherence to the paper-and-pencil condition was the percentage of complete responses; as a cut-off for satisfactory adherence we used 80% completion of diary entries over the 2-week periods (Hufford et al., 2002; Stone et al., 2002; Stone et al., 2003). In the current study there were no partially completed computer or paper diaries. Computer-based monitoring by default results in complete responses because the program does not allow patients to not complete an assessment once begun (as stated above, patients can provide entries at a later point in time, which will be used as a measure of non-adherence). Thus, blank responses in the paper-and-pencil or computer-based condition will be considered as non-adherent entries. Those in the computer-based condition missed 134 opportunities to complete their bi-daily diary entries, while the paper-and-pencil group failed to make 81 dairy entries. For participants using computer-based monitoring, five consecutive entries using the default were considered as non-adherent. In the current study no participants provided default settings for five successive entries. Finally self-reports of compliance were obtained during debriefs of patients in both groups, which have been shown to elicit truthful responses from non-compliant participants (Stone & Shifford, 2002). See table 3 for a breakdown of percentages of non-adherence to the daily dairies.

Insert table 3 about here

6.4.3. Medication Adherence

Medication adherence was assessed using refill of prescriptions. This technique provides a reliable objective measure to compare with daily self-assessments (Choo et al., 1999; Grymonpre, Didur, Montgomery.P.R., & Sitar, 1998). Verification of refills does not allow assessment of day-to-day and actual timing of medication use, which is a potential limitation of the adherence assessment. Daily medication monitoring has been shown to provide high concordance with prescription refills (Garber, Nau, Erickson, Aikens, & Lawrence, 2004). Medication adherence will be defined as refilling of medication at least once after initial prescription (Thompson, Peveler, Stephenson, & McKendrick, 2000) as verified by prescription records vice patient self report. Medication refills normally occurred 4-6 weeks after initial prescription, depending on the amount of medication prescribed. However, several patients (N=5) received initial prescriptions for 60-90 days and four of these individuals obtained their prescriptions after the 90-day period, which was beyond the scope of the current study of thirty days. These five individuals were not included in the overall analysis for medication adherence.

This investigation documented ambulatory measures during 4 weeks only and no providers changed the medicine regimen for any participants during the study (American Psychiatric Association, 2004).

6.5. Control Variables

Because depression has multifactorial origins, particularly in primary care patients (Barkow et al., 2004; Cassano et al., 2002), this study carefully assessed variables that may importantly affect the clinical course of depression, including health-related physical symptoms, anxiety, and physical activity levels. In addition, experience and anxiety related to computer use may adversely affect outcomes in the computer-based monitoring group, and this variable will be assessed, and statistically adjusted for if necessary.

6.5.1. Health Symptoms

Because ambulatory depressive mood symptoms are likely correlated with physical symptoms, we measured common physical symptoms in primary care patients as potential effect-modifying covariates (e.g., pain, and fatigue). The Patient Health Questionnaire (PHQ-15; Kroenke et al., 2002), is the self administered portion of the Primary Care Evaluation of Mental Disorders (PRIME-MD; Spitzer et al., 1994). This measure includes 15 common medical symptoms, including: gastrointestinal complaints, musculoskeletal pain, fatigue, sleep disturbances, and common anxiety-related physical symptoms such as pounding or racing heart, and fainting spells. These symptoms were monitored daily, as well as during the weekly follow-up evaluations. Physical symptoms are related to depression and previous research suggest a differential effect based

on type of presentation to primary care (physical versus psychological presenters; Keeley et al., 2004), This measure allowed for the evaluation of differential effects based on type of presentation and will serve as a covariate if there is a significant effect.

The Medical Outcomes Study 12-Item Short-Form Health Survey was used as a general measure of functioning (Ware, Kosinski, & Keller, 1996). This questionnaire provides a physical component scale (PCS-12) and a mental component scale (MCS-12) with eight additional subscales. This measure has been designed with a short-term version to provide information regarding the previous week, which will allow for weekly follow up with this instrument.

Anxiety has been shown to highly overlap with depression (Joiner, 1999). The Beck Anxiety Inventory (BAI; Beck & Steer, 1993) is a 21-item self-report measure that addresses the frequency of anxiety related symptoms over the previous week. The BAI has been reported to have less overlap with depression than other measures of depression (Campbell & Brown, 2002). The BAI was used to assess anxiety levels and serve as a covariate.

6.5.2. Inflammatory Factors and Thyroid Function: Blood Sampling

Thyroid function and inflammatory processes may importantly contribute to depressive symptoms in primary care patients. To rule out the possibility that changes in depression during the course of 4 weeks are related to initial thyroid or inflammatory parameters we obtained blood samples at study entry. It is

additionally important to assess inflammatory parameters in this project, because prior research indicates that the level of pro-inflammatory markers at the onset of pharmacotherapy is predictive of subsequent treatment outcomes (Lanquillon et al., 2000; Tuglu et al., 2003). However, the role of these markers in primary care has not been evaluated. A 19-gauge needle was used to collect 20 mL blood at study entry (Visit 1)). Samples were snap-frozen and stored at –70 C until assay. Analysis of thyroid functioning included a measure of free T4 (FT4) to rule out hypothyroidism, which can mimic depressive symptoms (Aikens et al., 1998). Markers of low-grade inflammation (C-reactive protein, fibrinogen, IL-6, TNFα, and IL-10) will be obtained using commercially available methods (Cushman, Cornell, Howard, Bovill, & Tracy, 1995; Kop et al., 2002). A trained technician at WRAMC blood laboratory conducted the blood draws. Assessment of inflammatory markers is not routinely conducted as part of usual medical care in depression, and was obtained to determine the role of inflammatory processes in the course of depression in primary care patients. The inflammatory markers will not be analyzed as part of this dissertation.

6.5.3. Physical Activity

In order to examine possible effects of physical activity on ambulatory depressive mood symptoms and depression at the time of clinic and telephone-based assessment, both objective ambulatory assessments of physical activity, as well as self-reported activity were evaluated. For the first two weeks of the

study (14 days), participants in the two monitoring conditions wore an activity monitor (Actiwatch; Mini Mitter Co., Inc, Bend, OR). An Actiwatch is the size and weight of an ordinary wristwatch and is used to measure activity level by a free-moving electrical transducer (piezo-electrode) that detects movement changes in more than one direction. Signals are stored digitally and downloaded on computer for off-line analyses. This device has been validated to differentiate levels of ambulatory activity (Patterson et al., 1993). Actigraphy was used to document the extent to which participant's diary report of activity coincides with an objective measure of physical activity.

6.5.4. Computer use

The Computer Thoughts Survey (CTS; Rosen & Weil, 1992) is a 20-item self-report measure designed to assess specific thoughts and cognitions related to computer use. Examples of question include: "I am going to make a mistake"; "I enjoy learning about this"; "people will notice if I make a mistake". The three subscales include; negative computer cognitions (Cronbach's α =0.93), positive computer learning cognitions (Cronbach's α =0.74), and computer enjoyment (Cronbach's α =0.69). The subscales were used to conduct post-hoc analyses evaluating determinants of adherence to the computer-based monitoring (Group 1).

6.6 Data Analyses, Sample Size Estimation, and Statistical Power

Previous findings reported in the literature were used to estimate effect sizes of ambulatory monitoring {Lewinsohn, 1973 163 /id;Lewinsohn, 1972 129 /id;Stamenkovic, 2001 165 /id;Hopko, 2003 160 /id;Harmon, 1980 183 /id;Greco, 2004 207 /id} and computer-based versus paper-and-pencil based monitoring (Hufford et al., 2002; Stone et al., 2002; Stone et al., 2003). The sample size of 25 participants will be sufficient to examine all hypotheses at a power >80% ($\beta<0.20$) with a Type I error (α) set at 0.05 (two-tailed), with a 25% attrition rate. No corrections of the α-level were made to correct for multiple statistical tests, to enhance the power of the study, and because larger sample sizes were not feasible. To test the hypotheses of the current proposal (see “Specific Aims” section 5), statistical analysis and power for each of the three main hypotheses will be addressed separately.

The overall aim was to examine the use of ambulatory monitoring techniques to evaluate the clinical course of depression in primary care patients; Table 2 provides the study outline. All power analyses were performed with the nQuery Advisory power calculation software package and all statistical analyses were conducted using SPSS.

6.6.1. Hypothesis 1:

H.1.a. Computer-based monitoring will be associated with better adherence to daily monitoring of depressive mood symptoms compared with the paper-and-pencil techniques.

H.1.b. Computer-based monitoring will be associated with better adherence to medication regimen compared with the paper-and-pencil monitoring techniques.

H1.c. Computer-based monitoring will be associated with higher correspondence between retrospective assessment of depression based on structured clinical interview versus ambulatory self-report of depressive mood symptoms over the same observation period, as compared to the correspondence between retrospective and ambulatory paper-and-pencil assessments.

H.1.d. Computer-based monitoring will be associated with higher correspondence between medication adherence and refills, as compared to the correspondence between adherence and refills with ambulatory paper-and-pencil assessments of medication use.

Statistical Analysis Hypothesis 1:

The dependent variables will be the accuracy of timing and completeness of ambulatory symptom reports (hypothesis 1.a.) as previously defined. The independent variable will be the monitoring condition (computer-based versus paper-and-pencil).

Mixed model analyses of variance will be conducted with group status (computer-based versus paper-and-pencil ambulatory monitoring) as between

subjects factor, and the repeated measure adherence (week 0 till week 4) as within subjects factor. Significant main and interaction effects will be further examined using independent and paired t-tests.

Hypothesis 1.b. Use of logistic regression with the prescription refill status as the outcome variable with modality of monitoring condition (computer-based versus paper-and-pencil) as the predictor variable.

Hypothesis 1.c. Addresses correspondence between ambulatory versus retrospective self-report monitoring, and postulates that the correspondence will be higher in participants in the computer-based condition compared with the paper-and-pencil condition. The predictor variables will be ambulatory-assessed depressive mood symptoms, which will be correlated with retrospective measures of depression (assessed by the HRSD). Specifically hypothesis 1.c. will be evaluated using residual scores from the linear regression week 4 HRSD total scores and weekly average ambulatory depressive mood symptoms. The absolute values of the residual scores will then be used to conduct a one-way ANOVA between the paper-and-pencil diary group versus the computer-based diary group.

Hypothesis 1.d. Logistical regression was used to examine the relationship between ambulatory reported medication use (days reporting medication compliance/total number of days) and monitoring conditions with refill status as the outcome variable.

Power Computation Hypothesis 1: Power analyses for hypotheses 1.a. 1.b. and 1.d. are based on the between subjects' t-tests for group differences at the end of follow-up (4 weeks). Based on previous research {Harmon, 1980 183 /id}, a one standard deviation difference between the groups is anticipated. Using the procedures of power estimation described by Cohen (Cohen, 1988), this effect size will require 17 subjects per group to detect between-group differences of 1 standard deviation at an alpha level of 0.05 and a power of 0.80. For within-group analyses over time (from week 0 to week 4), 17 patients will allow detection of 0.72 s.d. at a power of 80%. Twenty-five patients per group will be enrolled to allow for a 25% attrition rate.

Power analysis for hypothesis 1.c. are based on the proposed residual scores between groups at the end of follow-up (4 weeks), and an effect size of one standard deviation difference between computer-based versus paper-and-pencil ambulatory monitoring measures of accuracy (as described above). Seventeen participants will enable detection of a one standard deviation effect size at α=0.05 with 80% power.

6.6.2. Hypothesis 2:

H.2.a. computer-based monitoring will be associated with less depression than paper-and-pencil monitoring based on structured clinical interview at 4-week follow up.

H.2.b. Ambulatory monitoring by either computer-based techniques or paper-and-pencil techniques will be associated with less depression as

documented by structured clinical interview at 4 week follow-up as compared to a control condition without ambulatory monitoring

Statistical Analysis Hypothesis 2:

The analyses are designed to examine whether computer-based monitoring will be associated with less depressive symptoms at 4 weeks follow-up compared with patients monitoring with the paper-and-pencil techniques (hypothesis 2.a.). In order to examine this hypothesis, a mixed model analysis of variance will be conducted as in the analyses for hypotheses 1.a. and 1.b. We further will document whether ambulatory monitoring per se (irrespective of computer or paper-and-pencil technique) will result in better outcomes of depression at 4 weeks follow-up (hypothesis 2.b.). A 3 level between subjects factor (computer-based, paper-and-pencil, and control) will be used, and planned comparison ANOVAs will be conducted by combining the ambulatory computer-based and paper-and-pencil groups for analysis related to hypothesis 2.b.

Power Computation Hypothesis 2:

Power analysis for hypothesis 2.a. is based on the between subjects t-tests for group differences on the Hamilton Depression Rating Scale scores at the end of follow-up (4 weeks). Based on previous research, a difference of one standard deviation between groups is anticipated. Seventeen participants per group are needed to detect this between-group difference at α=0.05 and a power of 0.80.

6.6.3. Hypothesis 3:

(a) Symptoms of depressed affect will remit prior to somatic symptoms of depression during the course of 4-weeks ambulatory monitoring.

Statistical analysis:

Mixed model analysis of variance was used to examine at which time during the 4 week follow up period specific changes in depressive symptoms occurred and whether these changes differ by monitoring technique. We further conducted exploratory time series analyses to examine which symptoms change first and whether these early symptom changes can be used to predict depression status at 4-week follow-up. Because of the exploratory nature of this objective, no formal a priori power analysis was conducted. The proposed sample size of N=75 allows for a detection of an auto-correlation coefficient of 0.31, which is consistent with the aforementioned effect-sizes of this project.

6.6.4. Other Statistical Considerations:

Because gender is a potential effect-modifying factor, the groups will be matched for gender. Analysis of covariance will be used to explore potential confounds including; age, race, season of assessment, physical symptom severity (PHQ15), general anxiety, and computer experience/anxiety,

In an effort to increase power a post hoc decision was made to utilize hierarchical linear modeling (HLM) to analyze the daily diary data. The basic idea underlying HLM is that there are separate analyses for each individual, and the results of

these analyses become the dependent variables for analyses at the group level (Bryk & Raudenbush, 1992; Osborne, 2000). HLM allows for the use of all repeated-measures data rather than average the weekly diary data. As a consequence of substantial delays in study enrollment we were able to enroll 17 of 75 participants (see limitations section in the discussion). This has resulted in reduced power of the proposed statistical tests. However, we have used Hierarchical Linear Modeling, using all available data points to circumvent this unanticipated limitation. As described in the results section, over 250 ambulatory data entry points were available for analysis, which positively affects the statistical power of this investigation.

7. RESULTS

Demographic Characteristics

The sample was 50% female (a mean age of 54.2±12.9 years, 68.8% Caucasian, 18.8% African-American, 6.3% Asian-American, and 6.3% Latino). As a military treatment facility, participants' military status was also obtained and the sample included 25% active duty members, 31.3% spouses, 37.5% retirees, and 6.3% dependent children (over 18 years old). Zoloft was the most common anti-depressant prescribed to participants (37.5%; Paxil 18.8%: Prozac, Celexa, and Wellbutrin 12.5%; and Effexor 6.3%). Additionally 9 of the 17 participants (52%) were involved in psychotherapy, which was described as interpersonal. Categorical demographic variables were analyzed across the three groups using Chi-square analyses. No differences between the groups were found based on medication prescribed, marital status, education level, military status or race. One-way Analyses of Variance (ANOVA) assessing group differences on quantitative variables revealed no significant group differences on age, anxiety, perceived social support, physical symptoms, or depression level at study entry. See Table 4.

Insert table 4 about here

Hypothesis 1a: Analysis of Adherence to Daily Monitoring of Depressed Mood Symptoms

A mixed model analysis of variance was conducted on adherence as defined previously based on accuracy of timing and completeness of ambulatory symptom reports (Daily monitoring completed/Total days in study). This analyses revealed no significant main effect for time ($F_{time}(1,9)=1.61$; $\rho=0.24$) or treatment group ($F_{condition}(1,9)=0.49$; $\rho=0.50$). (Table 5) Data were lost during four 2-week periods by computer-based users (participant did not recharge computer; recharger broke) and two 2-week periods for a paper diary user (the participants did not return the diaries at the end of the study). These periods were counted as non-compliant based on the original study plan (Table 3). No significant group difference was observed, however, the observed effect size based on type of diary ($\eta^2 = 0.05$) was low, consequently post hoc power for the analysis was low (0.10).

Self reported adherence to daily monitoring revealed no significant group by period interaction or main effect for group condition ($F_{condition}(1,9)=0.004$; $\rho=0.95$). However, there was a significant main effect of time ($F_{time}(1,9)=6.01$; $\rho=0.04$). Participants reported being significantly more compliant with monitoring during the first period compared to the second half of the study (mean diff=1.37; sd=.56; $\rho=0.04$). Effect size between computer-based and paper-and-pencil diaries revealed no treatment effect based on self report (η^2, 0.01). (see Table 5 and Figure 2)

Insert table 5 about here

Insert Figure 2 about here

Hypothesis 1b: Analysis of Adherence to Medication Use

In order to predict refill status based on treatment condition, logistical regression analysis was performed. The model regressed group membership and depressive symptoms throughout treatment on refill status. To control for possible confounding variables, weekly percentages of side effects were included in the model first, prior to the group status. After adjusting for the aforementioned control variables, group membership did not significantly predict refill status (Wald 1.134, df=2, p=0.51).

Insert table 6 about here

Hypothesis 1c: Analysis of correspondence between ambulatory and retrospective mood

Weekly average ambulatory depressive mood symptoms were correlated with week 4 HRSD total scores to obtain residual scores. The absolute values of the residuals scores were then used to conduct a one-way ANOVA between the paper-and-pencil diary group and the computer-based diary group. There were no significant differences for type of monitoring and correspondence between ambulatory and retrospective self-report monitoring ($F_{condition}(1,5)=0.03$; $\rho=0.87$). However, the observed effect size was small ($\eta^2 = 0.01$) as was post-hoc power (0.052). See table 7 for overall correlations between weekly self reported mood and final HRSD score.

Insert Table 7 about here

In an effort to increase power a post hoc decision was made to utilize hierarchical linear modeling (HLM) to analyze the data. The results of HLM analysis indicated no significant effect for monitoring condition ($F_{condition}(1,388)=0.28$; $\rho=0.60$) for type of monitoring and depression (HRSD). However, further analysis indicated a significant correlation between weekly mood scores and the weekly HRSD scores for the computer-based group ($R=0.79$; $\rho=0.01$), but the relationship was not as strong in the paper-and-pencil group ($R=0.16$; $\rho=0.48$).

Insert Table 7a and 8 about here

Insert figure 2a and 2b about here

Hypothesis 1.d. Logistical regression with refill status as the predictor variable was not significant based on group membership (Wald 0.09, df=1, p=0.76). When adherence, based on actual daily reported adherence (see Table 9) was included the model was also unable to accurately predict group membership (Wald 0.00, df=1, p=1.00). There was some partial support for this hypothesis as refill status was significantly correlated with medication adherence during the first two weeks for the computer-based group. However, this same relationship was not found during the second two-week period. Additionally, there was no correlation between the paper-based condition during either period of the study. (See table 9).

Insert table 9 about here

Hypothesis 2a: Impact of Type of Monitoring on Depression

A mixed model analysis of variance was conducted on depression levels as defined by HRSD scores at each of the weekly interviews. This analyses revealed a significant main effect for time ($F_{time}(4,56)=3.76$; $\rho=0.01$). This analyses revealed no significant main effect for group by period interaction ($F_{interaction}$ $(8,56)=0.73$; $\rho=0.67$) or group condition ($F_{condition}(2,14)=0.86$; $\rho=0.44$). Post hoc power analysis for group by time interaction was 0.30, and 0.17 for treatment condition. The effect size for group by time was medium to large ($\eta^2 = 0.09$) and a large effect for treatment group ($\eta^2 = 0.11$). Post hoc testing indicated a significant change in HRSD scores from week 0 to week 2 (Mean diff=3.97 std. error=1.14; $\rho<0.01$) and from week 0 to week 4 (Mean diff=3.00; std. error=0.81; $\rho<0.01$), but not from week 2 to week 4 (Mean diff=-0.72; std. error=1.22; $p=0.56$)

Insert Table 10 about here

Hypothesis 2b: Impact of Monitoring on Depression

Mixed model analysis of variance was used to examine HRSD-based depression in both monitoring conditions combined versus the control group. Similar to the hypothesis 2a results, there was a significant main effect for time ($F_{time}(4,60)=3.67$; $\rho=0.01$). This analyses revealed no significant main effect for group condition ($F_{condition}(1,15)=0.25$; $\rho=0.63$) or group by period interaction ($F_{interaction}$ $(4,60)=1.07$; $\rho=0.38$). Effect size for group by period interaction was

large ($\eta^2 = 0.19$) and a small effect for monitoring condition ($\eta^2 = 0.02$). The post hoc power analysis was 0.42 for group by period interaction and 0.08 for group condition. As in hypothesis 2a significant differences were identified between week 0 and week 2 (Mean diff=4.33 std. error=1.20; $\rho<0.01$) and week 0 and week 4 (Mean diff=3.50; std. error=0.90; $\rho<0.01$). Additionally, a significant difference was found between baseline (week 0) and week 1 (Mean diff=2.20; std. error=0.94; $\rho=0.03$).

Similar results were obtained with the SF12 in that there was significant change across time. From baseline to week 2, all three groups displayed significant improvements in overall quality of life during the first two weeks (baseline to week 2; mean diff=22.55; std. error=2.17; $\rho<0.00$). However, there was significantly less change from week 2 to week 4 (Mean diff=1.12; std. error=1.62; $\rho=0.50$).

Hypothesis 3: Remission of Depressed Affect and Somatic Symptoms of Depression

The PHQ and CESD were evaluated to provide a further clarification of type of symptoms – somatic and affective, respectively. Based on analysis of the somatic and cognitive-affective components of the PHQ and CESD, a significant effect was observed with changes in somatic and cognitive-affective symptoms over time ($F_{timePHQ}$ (2,28)=11.04; $\rho<0.01$ and $F_{timeCESD}(2,28)=6.51;\rho=0.01$, respectively). The PHQ displayed significant change from baseline to week 2 ($F_{PHQ1\text{-}2}(1,14)=11.24;\rho=0.01$) but not from week 2 to week 4 ($F_{PHQ2\text{-}}$

$_3$(1,14)=1.67;ρ=0.22). The CESD was also significantly different from baseline to week 2 ($F_{CESD1-2}$(1,14)=6.49;ρ=0.02), but not from baseline to week 4 ($F_{cesd2-3}$(1,14)=2.85;ρ=0.11). While these results did not suggest differential effects on outcome, previous research has suggested that affective symptoms are likely to predict physical symptoms of depression.

Insert Figure 3 about here

In order to evaluate the differential progression of depressive symptoms, hierarchical regression analysis was performed examining the assessments of somatic and affective symptoms at each of the study visits. The regression model regressed week 4 PHQ scores as the dependent variable on cognitive-affective symptoms at visit 2 (the primary predictor variable). To control for possible confounding variables, two covariates (baseline somatic symptoms, baseline cognitive-affective symptoms) were included in the model first, prior to the inclusion of cognitive-affective symptoms and physical symptoms at visit 2. After adjusting for the aforementioned control variables, the cognitive-affective symptoms at visit 2 (week 2) were predictive of physical symptoms at visit 3 (week 4) (R^2 change=0.07; F Change 10.134, p<0.01) (see Table 11). Adding the physical symptoms at visit 2 did not significantly add to the model (R^2 change<0.06; F Change 0.60, p=0.46). Therefore, remission of cognitive-affective symptoms predicted subsequent remission of physical symptoms. (See Table 11)

Insert Figure 4 about here

Further exploratory analyses were conducted to examine whether physical symptoms at visit 2 were predictive of subsequent physical symptoms at week 4, which was not supported by the present data (R^2 change=0.17; F Change 4.64, p=0.05). (See table 12)

The potential of multicolinearity was considered by examining the tolerance and variance inflation factor (VIF) of each of the predictor variables. The VIF is the inverse of tolerance, defined as $(1/(1-R_i^2)$. As the VIF increases, so does the variance of the regression coefficient. Biases resulting from multicolinearity are expected to be unlikely because of the overall moderate intercorrelations between the predictor variables, and the moderate correlation between each independent variable with the dependent variable (Table 11).

Insert Table 11 about here

Insert Table 12 about here

8. Discussion

On the basis of prior research indicating that depressive symptoms are reactive to self-monitoring the present study was conducted to answer the following questions: 1) Does computer-based monitoring result in better adherence to ambulatory monitoring compared to paper-and-pencil techniques; 2) Does computer-based monitoring result in less depressive symptoms than paper-and-pencil monitoring techniques; and 3) Do symptoms of depressive affect remit prior to somatic symptoms of depression during the course of 4-weeks ambulatory monitoring.

Hypothesis 1.a. Computer-based monitoring will be associated with better adherence to daily monitoring of depressive mood symptoms, based on timing and completeness of responses, compared with the paper-and-pencil techniques.

This hypothesis was not confirmed, as there were no significant differences in adherence levels between types of monitoring condition. Consistent with prior research there was a difference in self-reported adherence to monitoring as both groups reported significant reductions in their monitoring adherence during the second monitoring period. However, in contrast to prior studies the paper and pencil monitoring remained at adherence levels consistent with the computer monitoring condition. Based on research by Stone (Stone et al., 2002) it is possible that the self-reporting of adherence on the paper diaries may have been exaggerated. If subjects did exaggerate at the time, but not when

reporting adherence at the end of the study that may partially explain the difference in adherence over time. The low power and effect size also limits further examination of causal factors associated with differences in monitoring conditions.

Hypothesis 1.b. Computer-based monitoring will be associated with better adherence to medication regimen, based on refill of medication, compared with the paper-and-pencil monitoring techniques.

During the initial two weeks of the study computer-based monitoring was correlated with medication refill status. However, this relationship was not displayed during the second week of the study or in the paper-based monitoring group. This may suggest that greater adherence to medication regimen early in treatment is likely to be associated with long-term adherence. Since this association was not seen with the paper-based monitoring condition though further research would be required to clarify this relationship.

Hypothesis 1.c. Computer-based monitoring will be associated with higher correspondence between weekly assessment of depression based on structured clinical interview and ambulatory self-report of depressive mood symptoms over the same observation period than ambulatory paper-and-pencil assessments.

The planned statistical analysis revealed no significant differences in correspondence between retrospective assessments of depression based on the week 4 HRSD scores. When the data was analyzed using HLM that incorporates

prediction of HRSD scores at the end of each week based on weekly monitoring of depression, as opposed to the final HRSD scores, similar results were obtained with no differences between the two groups. Correspondence between weekly scores and end of each week HRSD scores however, were significant for the computer-based monitoring conditions but not the paper-based condition. Stone (Stone et al., 2002) and other researchers have suggested that individuals often complete paper diaries immediately prior to returning them, so called "parking lot compliance." Then the lower correspondence between symptoms and HRSD scores with the paper diaries would be consistent with such an explanation. However, if this were the case in the current study then the data would likely have showed a differential effect based on reporting period. Since diaries were only turned in during week 2 and week 4 these weeks should have reflected higher correspondence than week 1 and 3. Less correspondence at week 1 and 3 when the diaries where not turned in and thus not completed in the "parking lot" was not observed in the current study. This may result from the limited number of subjects and subsequently low power to detect overall differences.

It may also suggest that there are differential effects related to the type of monitoring condition that were not included in the current study. As noted in previous research (Green, et al., 2006) found psychometric equivalence between both methods. However, the authors did not evaluate convergent validity, which is the correlation of one measure of a construct with another measure of the same construct. The differences in the current study may reflect greater

convergent validity for depressed mood symptoms when monitored by computer in contrast to paper-and-pencil monitoring. Future studies comparing monitoring methods should include measures of convergent validity.

A further possibility is that the paper diaries provide continual feedback to the patient – allowing review of the previous day's information and obtain reinforcement based on their performance. In the current study the hand-held computers were not programmed to provide this feedback. Future research should examine the possibility of enhancing reactivity based on feedback. With the current programmability of computers this would be a relatively straightforward process of programming the monitoring device to either provide or not provide feedback on a regular schedule.

Hypothesis 1.d. As with Hypothesis 1.b. self-reported adherence levels did not differentiate refill status. While previous research has shown that self-reported adherence is a reliable and accurate indicator of medication compliance (Choo et al., 1999; Grymonpre et al., 1998). However, studies of medication compliance have not traditionally specified the method of monitoring used and how the method used may impact the study outcome.

Specific Aim 2 was to investigate whether improved symptom reports and medication adherence (Specific Aim 1) in the computer-based monitoring group versus the paper-and-pencil group are associated with better outcomes of depression at 4-week follow-up, and that both monitoring techniques will be

associated with less depression than follow-up of patients who were not monitored daily.

This hypothesis was not confirmed, there was a significant reduction in depressive symptoms, but there were no significant differences based on monitoring condition. There were statistically significant changes from baseline to week two and from baseline to week 4. The mean changes in HRSD scores were 3.97 (sd=1.14) and 3.00 (sd=0.81), which are likely not clinically significant changes. While the predicted hypothesis was not supported the small sample size resulted in insufficient power to detect a difference. However, the effect size of 0.11 is notable as this is considered a large effect size in behavioral research and indicates that with a larger sample size a statistically significant, and possible clinically significant, differences may be revealed (Cohen, 1988). Additionally, the level of change observed in the SF-12 results suggests a clinically significant change during the first two weeks of treatment. While not conclusive, these results suggest that future studies should examine possible improvements prior to the traditional 4-6 weeks commonly referred to in both clinical practice and previous research.

Monitoring with either paper-and-pencil or computer-based techniques did not result in a statistically significant reduction in symptoms compared to no monitoring. However, hypothesized group by period interactions were not observed, suggesting that all subjects experienced proportionate decreases in depressive symptoms during the course of the study.

The failure to observe an impact for monitoring condition may indicate true null findings. The findings may also reflect the limited sample size or the lack of additional therapeutic treatment incorporated into the current study. Previous research that has shown reactivity to monitoring in depression has generally been conducted in the context of psychotherapy treatment {Harmon, 1980}. Pharmacotherapy monitoring studies, in contrast, have focused on adherence to the medication regimen. Additionally, in the study by Harmon {Harmon, 1980}, slightly better results were observed when participants monitored activity levels as opposed to mood. In the present study the main focus was on monitoring of mood rather than activity. Increasing the focus on monitoring activity levels may also have resulted in improved outcomes regarding depression at follow-up.

Alternatively it may be related to 8 patients in the current study who scored below the threshold score of 17 on the HRSD21. This was possible because inclusion criteria required physician-based diagnosis of depression and did not set a cut-off point based on HRSD score. This finding would suggest that some primary care providers may, at times, treat subclinical depression. This subclinical depression may be more appropriately diagnosed as an adjustment disorder or depressive disorder not otherwise specified, in contrast to major depressive disorder. However, further research would be required to explore this hypothesis as it contradicts most research of diagnosis of depression in primary care, which indicates that depression is under diagnosed in primary care settings.

Specific Aim 3 was to document the trajectory of depression symptom remission in the clinical course of depression among primary care patients. It was hypothesized that symptoms of depressed affect will remit prior to somatic symptoms of depression during the course of 4-weeks ambulatory monitoring.

This hypothesis was confirmed and is consistent with previous research. It also reflects two different factors. First, patients are likely to experience improvements in both cognitive-affective symptoms and physical symptoms during the first two weeks of treatment on an antidepressant. Second, those with greater improvements in cognitive-affective symptoms after two weeks of treatment on an antidepressant are also more likely to develop a significant reduction in physical symptoms by the fourth week of follow-up.

While these improvements may not meet the definitions required for clinically significant change, they may be salient enough for patients to be aware of them during this initial treatment period. It may also imply that future research should begin to evaluate those that do not respond within the first 2-4 weeks and consider alternative or other adjunctive methods of treatment sooner than the American Psychiatric Association guidelines of 4-6 weeks before changing or adjusting anti-depressant medications.

The main focus of this hypothesis was on the cognitive-affective symptoms predicting physical changes by the fourth week of follow-up. The opposite has been found in exercise withdrawal paradigms in that somatic symptoms predict cognitive-affective symptoms at the onset of depression over a two week course of exercise withdrawal (Berlin, 2004). It is also important to note

that there was no parallel predictive value of physical symptoms on cognitive-affective symptoms during this same period. Greco (Greco et al., 2004) and others (Jackson et al., 2004) have noted that affective and physical symptoms both remit during the first 4 weeks of treatment for depression. However, physical symptoms appear to reach a plateau after the first four weeks unlike the affective symptoms, which continue to improve after the initial month of treatment. It is beyond the scope of this dissertation to examine the possible reasons for this differential treatment effect. Future research should continue to explore if physical symptoms eventually remit or possibly are more treatment resistant in some patients and require other adjunctive treatment options.

8.1. Theoretical Implications

Although larger studies, replication, and further research are necessary, several findings from the current study may have significant theoretical implications for primary care treatment of depression and future monitoring studies. The use of HLM data analysis use all data points may be potentially useful in future diary studies. In the current study this method provided statistical power to examine the correspondence between daily monitoring and retrospective recall at the end of each week. The data suggested a potential method to examine “parking lot compliance.” To date, few studies have utilized this statistical method for diary and/or monitoring studies. This method can also be employed in evaluating theories of monitoring that have not been studied in any in-depth manner since a review of the original studies (Kopp, 1988).

The failure to detect a significant difference between the monitoring conditions may reflect a true null finding. If this were an accurate finding then future studies could use paper and pencil monitoring or computer based monitoring with no expected differences on adherence or clinical course of depression. However, it is unlikely that these two methods have no true differences based on previous research and the null findings associated with this study are more likely related to the limited statistical power as a consequence of the small sample size.

Based on the literature review conducted for this study it does not appear that the compliance evaluated in diary studies have been utilized in psychotherapy homework studies. Specifically, psychotherapy homework studies have focused exclusively on compliance as the homework being completed at the next session, not when it was completed (daily vs immediately before coming to the clinic). In contrast, diary studies have begun to examine when, during the course of the study, participants completed the diary. It would be useful in future research to examine the effect of timeframe of diary completion on treatment outcomes in future studies of psychotherapy homework. This information would be useful for researchers or clinicians that would prefer to use computer-based diaries in research and treatment.

This study found outcomes consistent with previous research that suggests cognitive-affective and physical symptoms of depression can improve over the first month of treatment. This is in contrast to most information provided to patients that suggest symptoms are not likely to begin to improve until 4-6

weeks after treatment initiation. Additionally, previous research (Berlin A, 2004; Greco et al., 2004) has suggested that physical and cognitive-affective symptoms of depression may have a differential course over time. The current study also found differences in outcome, specifically cognitive-affective symptoms at week two predicted physical symptoms at week four. Further studies may examine if these differential outcomes can be used to predict differential treatment outcomes of depressed patients. These outcomes could include such factors as response to specific type of antidepressant medication or need for adjunctive treatment options such as changing or increasing medication or referring to specialty care.

9. Limitations

The primary limitation of the current investigation is the limited sample size. While failure to detect significant differences may have been a true null finding, it is likely that the limited power resulting from small sample size has reduced the ability to detect true differences. As a result, the majority of the analyses had insufficient power to detect differences that may have existed between the groups. Effect sizes for many of these variables were moderate to large, suggesting that a larger sample size would have addressed this lack of power and possibly resulted in statistically significant differences between the groups.

Not unrelated to sample size are concerns regarding the loss of data, both computer based and paper and pencil. There were no significant differences in participant comparisons to predict data loss. This level of data loss is slightly above other computer monitoring studies and it is unclear if newer hand-held computers may have limited data loss. Several of the newer hand-held computers use standard power cables such as those found on cellular phones and portable speaker systems. The current study utilized an older version of the Palm M130 hand-held computer that requires a power cable that was reported as difficult to use and several broke during the study when patients unplugged them, resulting in depleted battery charges and subsequent loss of data.

Potential confounds, such as health symptoms, computer experience and anxiety, inflammatory factors and thyroid function, and physical activity, were carefully evaluated. However, as a result of the limited sample size they were not statistically adjusted for in the current investigation. It was not feasible, however, to measure all the possible confounds involved in depression within a primary care setting. Examples of potential confounds not specifically addressed in the current study include different referral sources (some PCMs were more amenable to referring participants than others), medication used for depression, specific medical diagnosis, multiple medical diagnoses, and major depression criteria as the diagnosis of depression was based on the primary care provider's diagnosis as opposed to a standardized measure of depression. As a consequence of the randomization procedure, such potentially confounding factors are expected to be evenly distributed across the computer-based and

paper-and-pencil monitoring groups. Thus minimizing chances of major biases related to unevaluated parameters.

The measure of paper-and-pencil-based adherence, self-report, may also serve as a limitation. Previous studies have shown that self-reported adherence is often quite high, often reaching 100% (Hank et al., 1996; Hufford et al., 2002; Stone et al., 2003). To address this issue, three methods were used. The first is outlined in Section 7.5.1, using the residual scores to evaluate concordance of self-reported mood with retrospective mood at weekly assessment. It was anticipated that if patients were completing paper-and-pencil diaries haphazardly there would be less relationship between these two variables. In contrast, if "parking lot compliance" were more prevalent then the relationship of these two variables will be significantly greater in the paper-and-pencil group than the computer-based group (Hufford et al., 2001; Hufford et al., 2001). The data in the current study was contradictory as the data as a whole suggested "parking lot compliance." However, when evaluated on a week-to-week basis, specifically for weeks 1 and 3 when the concordance between diary and HRSD scores should be lower in the paper-and-pencil group, this contrast was not found. This contradictory result suggest that examining just the relationship between weekly self-report of depression and weekly depression may be insufficient to thoroughly evaluate the impact of adherence to monitoring on depression. Secondly, as recommended by Stone and Shiffman (2002) patients in the paper-and-pencil group were thoroughly debriefed and subjects in the current study did not readily admit to faking time of reports. Finally, adherence to monitoring that was

anticipated in the computer-based group did not result in a reactivity effect, and subsequent decline in depressive symptoms at study completion (Hypothesis 2.a.). While the participants did experience a decline over time in depressive symptoms this decline occurred across all groups, not just the monitoring condition or more specifically the computer-based group. These findings may be, as previously noted, related to the focus on mood or lack of a psychotherapy treatment component. It is also possible that the amount of "attention" provided all three treatment conditions resulted in a "Hawthorne" effect (Roethlisberger & Dickson, 1939). This is the phenomena that people will change behavior when they are aware that they are being observed by others. In the current study participants were aware they were being evaluated weekly and were aware of the nature of the study including the three possible conditions and which treatment group they were assigned.

The use of prescription refills for measuring adherence is a potential limitation. Several studies have identified the Medication Event Monitoring System (MEMS) container to be the current standard for medication adherence monitoring (Grymonpre et al., 1998; Choo et al., 1999). However, this method is limited for many studies as a consequence of the expense associated with the system. Previous research also has indictated that the use of retrospective self-report (72% sensitivity with compliance at 80%) and pharmacy data provide the most useful alternatives. In individuals diagnosed with depression, blood concentrations provided the least satisfactory method of assessing compliance for patients on TCAs (George et al., 2000). The present study supports previous

findings that self-report and pharmacy records can be useful methods to determine compliance. However, future research examing the impact of the type of monitoring on depression should include the MEMS system to accurately evaluate the self-report compliance with the gold standard. This would allow for a more comprehensive understanding of the impact of monitoring type on adherence.

9.1 Recruitment

The initial study plan was to obtain 75 participants with 25 per group. However, several factors resulted in lower recruitment than planned and the study was switched to a timeline for completion as opposed to a specific number of participants. The main factor that apparently contributed to low recruitment was relying on the primary care providers (PCP to refer participants in to the study. While several PCPs provided referrals on a regular basis the majority did not. One of the incentives was for the research assistant to provide weekly feedback to the PCPs regarding the depression levels based on the weekly HRSD scores. It was learned late in the study that this had not been completed on a consistent basis and resulted in reduced referrals by several PCPs. The reason for the lack of feedback may have resulted from switching research assistants during the study. In an effort to increase participation a request was made to add psychiatry to the protocol. However, the length of time it took for this addition to be approved was beyond the ending date of the study. This delay in approval processing resulted from having to find a psychiatrist to serve as a

representative and then obtaining Institutional Review Board (IRB) approval. Finally the initial study was approved for the three internal medicine primary care clinics at Walter Reed Army Medical Center. The study had the full support of the service chief in charge of these clinics during the initial proposal processing. Unfortunately early in the study he was reassigned to a new clinic and the new service chief provided less than optimum support for the research proposal.

10. Conclusion

The present findings indicate that there are likely to be important uses for daily monitoring in both depression studies and primary care research. In spite of the limitations in the current study, the results point to important differences in monitoring methods and differential changes in the remission of cognitive-affective and physical symptoms of depression. Importantly anti-depressants may begin to provide some improvements during the first two weeks in contrast to the normal 4-6 weeks that most providers brief their patients to expect to experience symptom reduction. It also highlighted the problems with using computer based monitoring that can include data loss due to computer errors or problems with battery life as well as the positive aspects such as ease of data transfer, ability to adjust questions based on response, and that they may be easier to use in public than a large paper diary. Alternatively paper diaries are easier to incorrectly assess the time of data entry, although there is less chance for data loss and paper diaries may be easier to complete for some participants. Specifically, research should examine the pros and cons of both types of

monitoring to determine the method best suited to their research and clinical needs.

Table 1. Variables Affecting the Reactivity of Self Monitoring

Variables affecting reactivity	Optimal conditions for enhanced reactivity
Target behavior valence	Positively valenced behaviors increase in frequency while negatively valenced behaviors decrease in frequency.
Motivation	The client is highly motivated to change the target behavior.
Topography of the target behavior	The target behavior is overt–motoric.
Schedule of recording	Each occurrence of the target behavior is self-monitored.
Concurrent response requirements	A single target behavior is self-monitored.
Timing of recording	Recordings are made just before the occurrence of the target response.
Goal setting, feedback, and reinforcement	Goals for changes in the target behavior are clearly specified, and reinforcement contingent on behavior change is provided.
Nature of the self-recording device	Some studies have indicated that an obtrusive recording device enhances reactivity.

(Korotitsch et al., 1999)

Table 2. Flow Chart of Assessments During Study

Study Phase	**Procedures**	**Measures**	**Completion time**
Visit 1 - Baseline	Questionnaires and Interview Blood draw	Depression (HRSD, CES-D, MFI) Health symptoms (PHQ-15, SF-12) Computer familiarity (CTS) Anxiety (BAI) Thyroid function, inflammation	45 Minutes
Phone 1 - Week 1	Phone contact	Depresion (HRSD) Health symptoms (PHQ-15) Diary adherence	10 minutes
Visit 2 - Week 2	Questionnaires and interview	Depression (HRSD, CES-D, MFI) Health symptoms (PHQ-15, SF-12) Computer familiarity (CTS) Anxiety (BAI)	45 minutes
Phone 2 - Week 3	Phone contact	Depression (HRSD) Health symptoms (PHQ-15) Diary adherence	10 minutes
Visit 3 - Week 4	Questionnaires and interview	Depression (HRSD, CES-D, MFI) Health symptoms (PHQ-15, SF-12)	45 minutes
Daily (For monitoring groups only)	Self-monitoring questions	Depressed mood, medication adherence, physical symptoms, activity level	10-15 minutes

Table 3. Late and Non-adherence Summary

Group		Late Percentage	No data percentage	Actual monitored percentage	Actual monitored - controlled (note 3)
computer-based					
	End of Week 2	7%	31%	63%	63%
	End of Week 4	9%	57%	33%	56%
paper-and-pencil					
	End of Week 2	16%	25%	58%	70%
	End of Week 4	19%	22%	59%	70%

Note 1 – All data are based on the number of late or non-compliance in relation to total possible responses.
Note 2 – First three columns may not be exactly 100% due to rounding errors
Note 3 – This column controlled for lost data (computer and paper). This is the percentage based on excluding the missing data from individuals in the percentage.

Table 4. Baseline Sample Characteristics

	control (N=5)	computer-based (N=6)	paper-and-pencil (N=6)
Female	3	2	3
Age years (SD)	40 (15.1)	57 (11.5)	52 (16.6)
Caucasian	2	4	5
African-American	3	0	0
Initial HRSD (SD)	19.4 (5.2)	17.83(5.7)	12.17 (7.0)
Initial PHQ (SD)	9.2 (4.4)	8.0 (5.8)	10.33 (4.9)
Total days in study (SD)	33 (5.8)	30.5 (3.1)	29.5 (4.5)
Initial Rx length (SD)	36.6 (32.06)	66 (32.86)	53.5 (31.2)
Other medical illnesses			
None	40% (n=2)	50% (n=3)	17% (n=1)
Diabetes	0	0	17% (n=1)
Cardiovascular	0	17% (n=1)	33%(n=2)
Gastro-intestinal	0	17% (n=1)	0
Sleep Apnea	20% (n=1)	0	17% (n=1)
Other *	40% (n=2)	17% (n=1)	17% (n=1)

* Other included Cerebral Palsy, Pituitary tumor, and high cholesterol

Table 5. Hypothesis 1a. – Adherence: Percentage and Self-Report

	Week 2 Adherence *	Week 4 Adherence *
Computer group (n=5)	62.75 (sd=30.90)	33.38 (sd=31.07)
Paper group (n=6)	58.37 (sd=32.47)	58.68 (sd=29.91)

* Based on actual percentage of adherence based on study definition

Self Reported measure of adherence

	Week 2 Self Report *	Week 4 Self Report *
Computer group (n=5)	2.40 (sd=1.52)	1.0 (sd=1.00)
Computer group (n=6)	2.33 (sd=1.37)	1.0 (sd=1.26)

* Based on a 5 point likert scale of adherence (0=low adherence, 4=high adherence)

Table 6. Hypothesis 1b – Medication Adherence

Weekly Self-reported adherence

	Week 2 Adherence *	Week 4 Adherence *
Computer group (n=5)	52% (sd=0.37)	27% (sd=0.37)
Paper group (n=6)	58%(sd=0.32)	59% (sd=0.30)

Refill Adherence

	Percent Refilled
Computer group (n=5)	40%
Paper group (n=6)	50%
control Group (n=6)	50%

Table 7. Overall Correlations Between Weekly Mood Rating and Final HRSD score (Groups combined)

	Week 1	Week 2	Week 3	Week 4	HRSD Week 4
Week 1	1.0				
Week 2	0.99 **	1.00			
Week 3	0.94 **	0.92 **	1.00		
Week 4	0.99 **	0.98 **	0.98 **	1.00	
HRSD Week 4	0.37	0.36	0.67	0.55	1.00

computer-based Monitoring Correlations between Weekly Mood Rating and Final HRSD Score

	Week 1	Week 2	Week 3	Week 4	HRSD Week 4
Week 1	1.0				
Week 2	0.99 **	1.00			
Week 3	1.00 **	0.88	1.00		
Week 4	1.00 **	0.97	0.97	1.00	
HRSD Week 4	0.99 **	0.52	0.84	0.68	1.00

paper-and-pencil based Monitoring Correlations between Weekly Mood Rating and Final HRSD Score

	Week 1	Week 2	Week 3	Week 4	HRSD Week 4
Week 1	1.0				
Week 2	0.89 **	1.00			
Week 3	0.84	0.99 **	1.00		
Week 4	0.88	0.97 **	0.96 **	1.00	
HRSD Week 4	0.69	0.81	0.75	0.88	1.00

** Significant at .01 level

Table 7a. Correlations of Daily Sad Mood and Weekly HRSD Scores

Overall	r	p	N
Palm	0.78	p<0.01	136
Paper	0.16	p=0.05	146
Week 1			
Palm	0.81	p<0.01	42
Paper	-0.16	p=0.34	36
Week 2			
Palm	0.88	p<0.01	42
Paper	-0.36	p<0.05	32
Week 3			
Palm	0.80	p<0.01	24
Paper	0.51	p<0.01	41
Week 4			
Palm	0.70	p<0.01	28
Paper	0.40	p<0.05	32

Table 8. Hypothesis 1c – Mean HRSD Scores from HLM evaluation

	Mean HRSD scores (sd)	95% Confidence Interval	
		Lower Bound	Upper Bound
computer-based (df=196.54)	15.92 (sd=0.67)	14.59	17.23
paper-and-pencil (df=154.86)	13.31 (sd=0.69)	11.93	14.67

Table 9, Hypothesis 1d – Correlation of Adherence and Refill Status

		Week 2 Medication Adherence	Week 4 Medication Adherence	Refill
computer-based monitoring				
	Week 2 Medication Adherence	1.0		
	Week 4 Medication Adherence	-0.59	1.0	
	Refill	0.83 *	-0.29	1.0
Paper-based monitoring				
	Week 2 Medication Adherence	1.0		
	Week 4 Medication Adherence	0.91 *	1.0	
	Refill	-0.59	-0.33	1

* Significant at $p<0.05$ level.

Table 10. Hypothesis 2a – HRSD Changes over the Course of the Study

	HRSD Week 0	HRSD Week 1	HRSD Week 2	HRSD Week 3	HRSD Week 4
control (n=5)	19.40 (sd=5.18)	14.00 (sd=6.78)	11.50 (sd=5.32)	15.75 (sd=8.10)	14.40 (sd=7.54)
Computer group (n=6)	17.83 (sd=5.74)	17.00 (sd=8.32)	16.20 (sd=10.43)	17.50 (sd=10.39)	14.67 (sd=8.69)
Paper group (n=6)	14.60 (sd=4.04)	11.00 (sd=6.26)	8.83 (sd=5.15)	13.67 (sd=9.40)	11.33 (sd=5.75)
Total	17.31 (sd=5.15)	14.00 (sd=7.25)	12.00 (sd=7.57)	15.63 (sd=9.02)	13.41 (sd=7.12)

Table 11. Hypothesis 3 – Predictors of Physical Symptoms by Cognitive-Affective Symptoms

Predictor	B	Standard Error	Beta	T	ρ	Zero-order r	Partial r	Tolerance	VIF
Constant	-2.03	1.27	.	-1.60	0.14				
Physical symptoms at Baseline (Week 0)	0.64	0.32	0.68	1.99	0.75	0.92	0.53	0.06	16.90
Affective-cognitive symptoms at Baseline (week 0)	-0.09	0.06	-0.22	-1.49	0.17	0.43	-0.43	0.31	3.27
Physical symptoms at Week 2 (Week 2)	0.28	0.36	0.25	0.77	0.46	0.94	0.24	0.06	15.57
Affective-cognitive symptoms at Week 2 (Week 2)	0.16	0.08	0.27	2.05	0.07	0.61	0.54	0.40	2.51

Table 12. Hypothesis 3 – Predictors of Cognitive-Affective Symptoms by Physical Symptoms

Predictor	B	Standard Error	Beta	T	ρ	Zero-order r	Partial r	Tolerance	VIF
Constant	-4.02	3.78	.	-1.06	0.31				
Physical symptoms at Baseline (Week 0)	0.71	0.96	0.36	0.74	0.48	0.64	0.23	0.06	16.90
Affective-cognitive symptoms at Baseline (week 0)	-0.34	0.19	-0.40	-1.84	0.10	0.34	-0.50	0.31	3.27
Affective-cognitive symptoms at Week 2 (Week 2)	1.00	0.23	0.82	4.34	0.01	0.83	0.81	0.40	2.51
Physical symptoms at Week 2 (Week 2)	0.23	1.07	0.10	0.22	0.83	0.74	0.07	0.06	15.57

Figure 1. Overview of Study Time Points

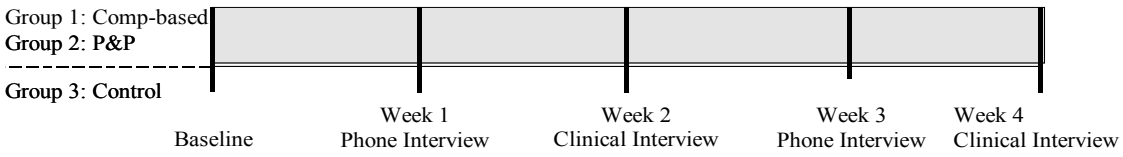
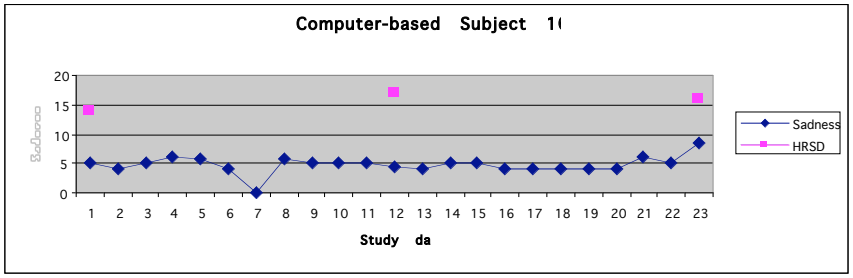
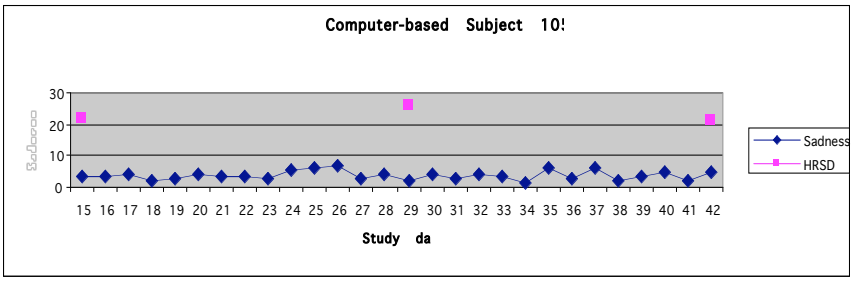
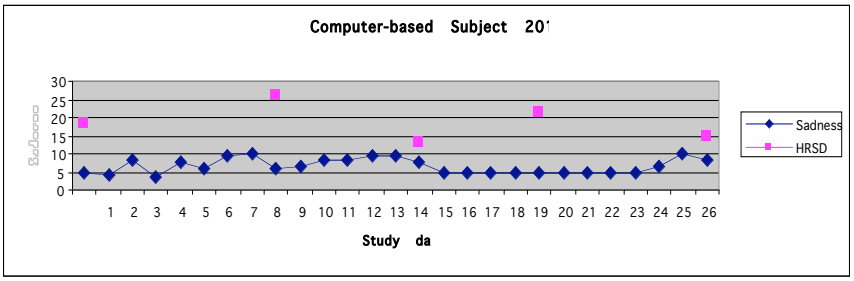
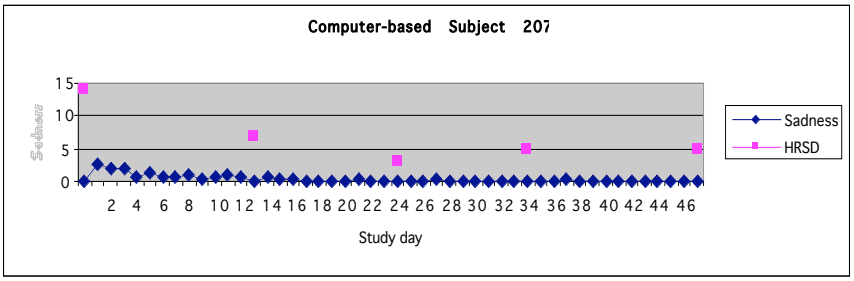


Figure 2a. Individual Data computer-based Monitoring Condition









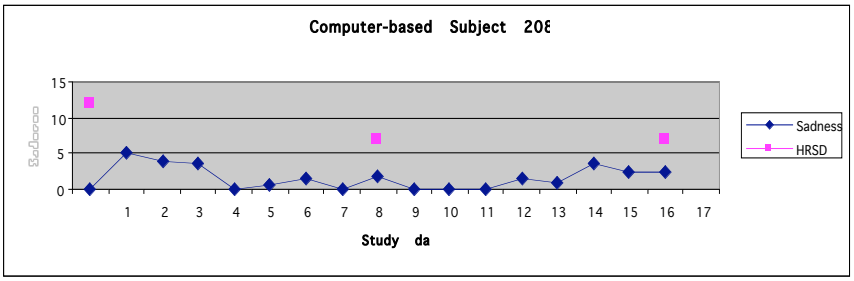
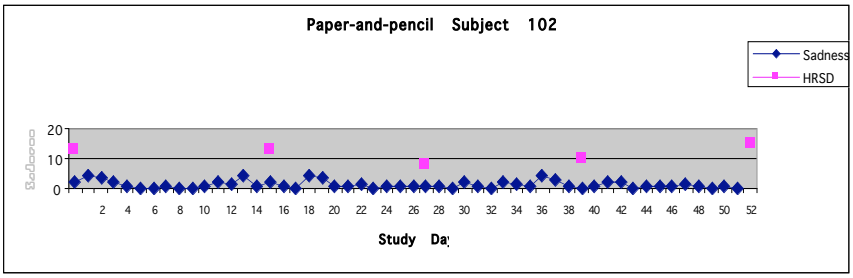
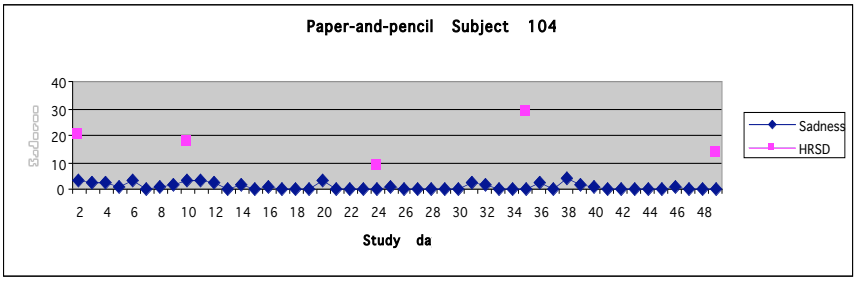
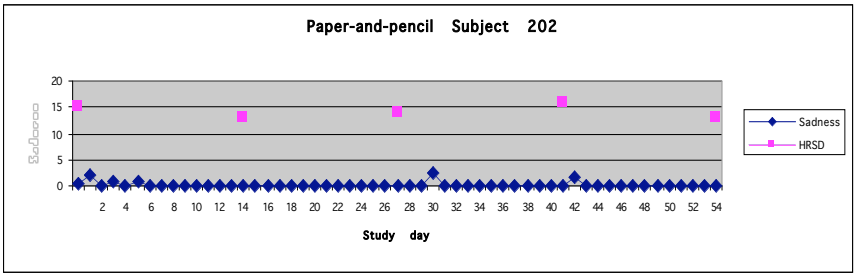
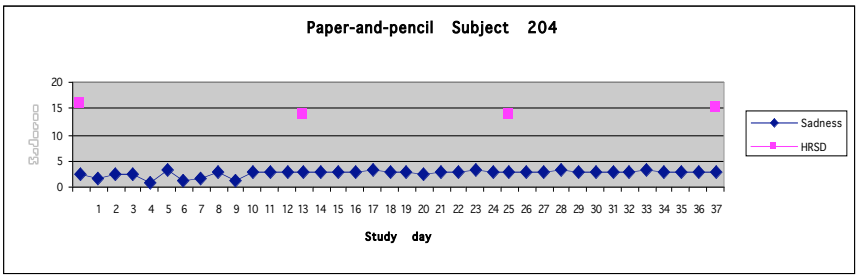


Figure 2b. Individual Data paper-and-pencil Monitoring Condition









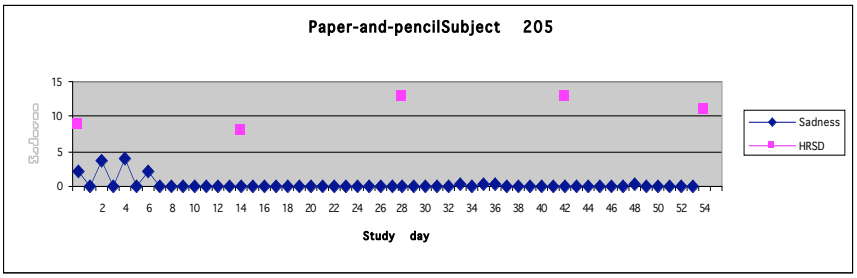
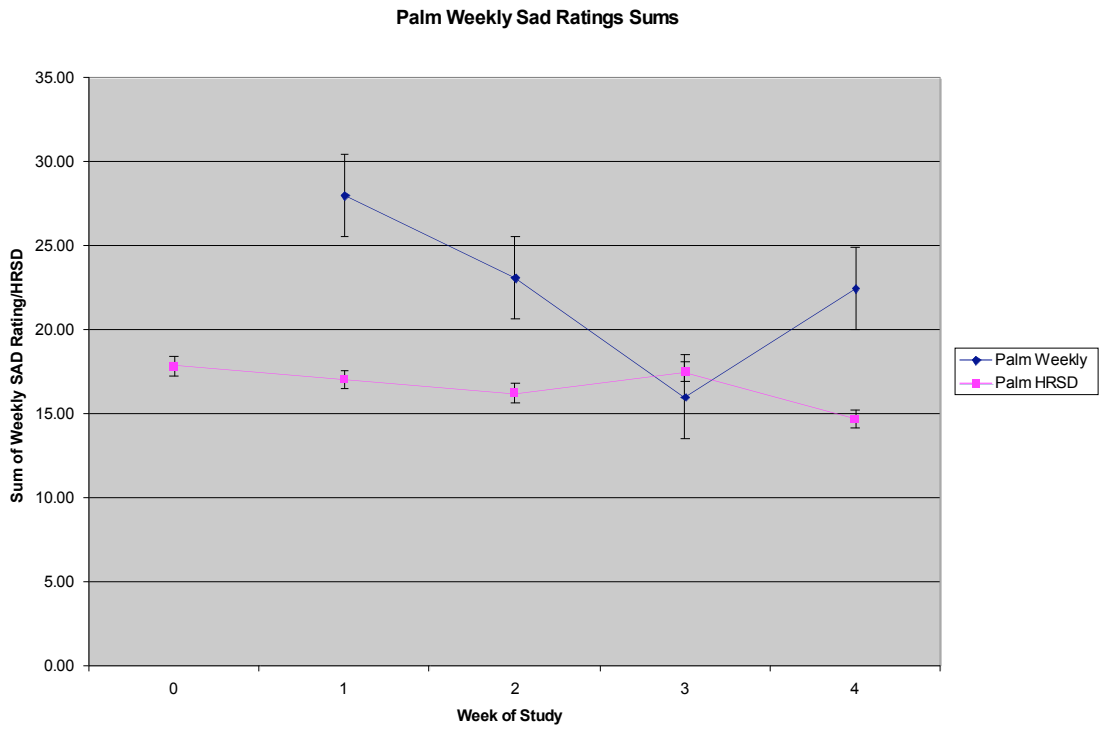


Figure 2c. Daily Sad Mood Weekly Totals by Group



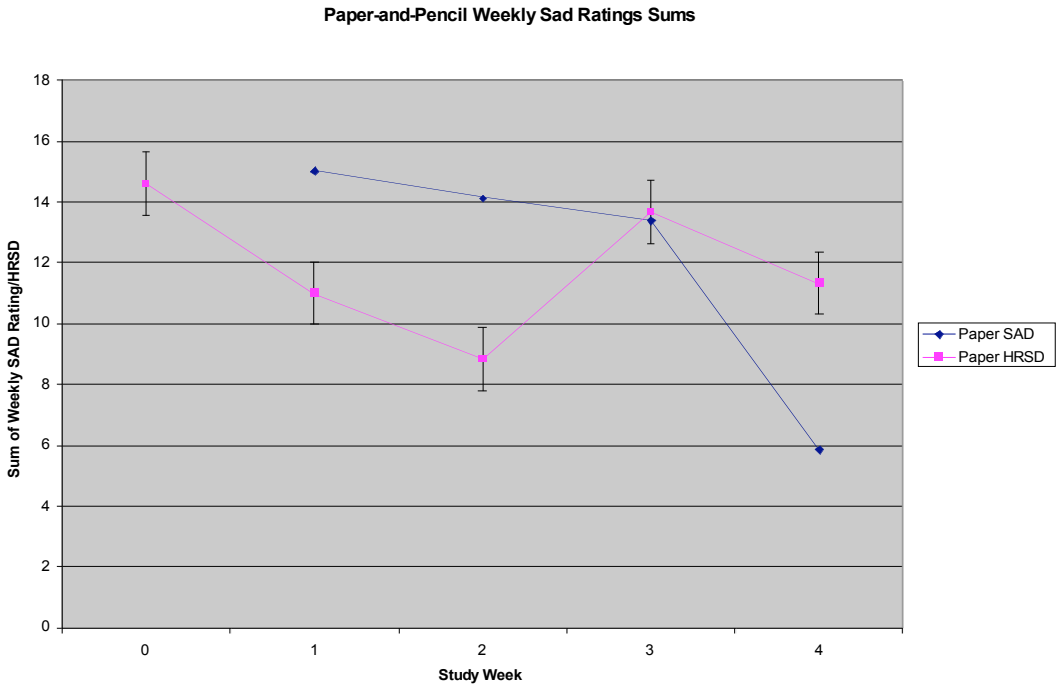
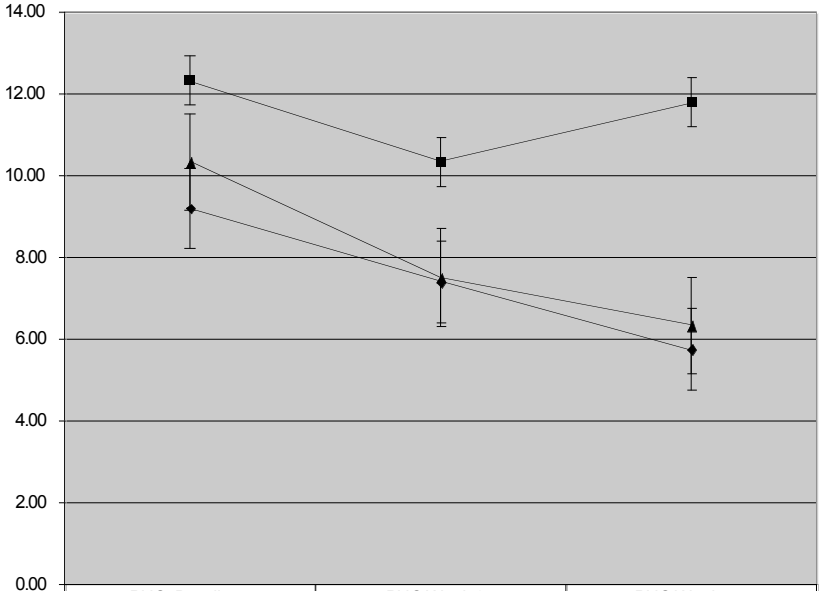
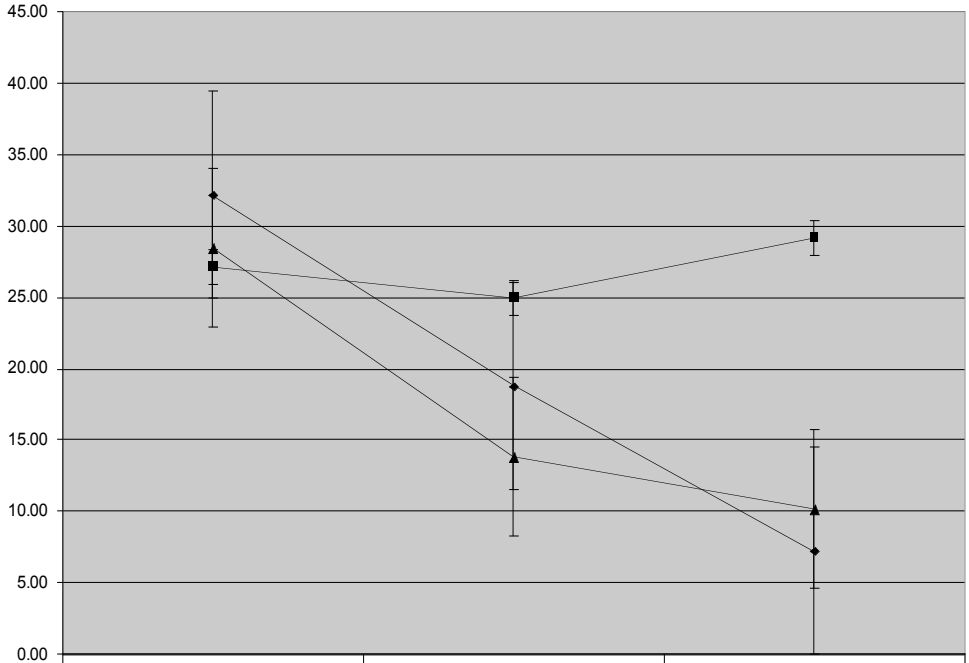


Figure 3. Hypothesis 3 PHQ Data



	PHQ_Baseline	PHQ Week 2	PHQ Week 4
Control	9.20	7.40	5.75
Computer-based	12.33	10.33	11.80
Paper-and-pencil	10.33	7.50	6.33

Figure 4. Hypothesis 3 CESD Data



	CESD Baseline	CESD Week 2	CESD Week 4
Control	32.20	18.80	7.25
Computer-based	27.17	25.00	29.20
Paper-and-pencil	28.50	13.83	10.17

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Appendix A – Hamilton Rating Scale for Depression (HRSD)

Structured Interview for the Hamilton Depression Rating Scale

ID _____

Interviewer _____

Date _____

OVERVIEW: I'd like to ask you some questions about the past week, since last (DAY OF WEEK). How have you been feeling since then?

1. H1 (HAM 1)

What's your mood been like this past week (sadness, compared to when you feel OK)? Hopeless, helpless, worthless):

Have you been feeling down or depressed?

Sad? Hopeless? Helpless? Worthless?

In the last week, how often have you felt (OWN EQUIVALENT)? Every day? All day?

Have you been crying at all?

DEPRESSED MOOD

0 = absent
1 = indicated only on questioning
2 = spontaneously reported verbally
3 = communicated non-verbally, i.e. facial expression, posture, voice, tendency to weep
4 = Pt reports virtually only these feeling states in spontaneous verbal and non-verbal communication

IF SCORED 1-4 ABOVE, ASK: How long have you been feeling this way?

2. H2 (HAM 7) IF OUTPATIENT:

Have you been working this week (in or out of the home)?
IF NOT: Why not?

IF WORKING: Have you been able to get as much (work) done as you usually do (when you're feeling OK)?

How have you been spending your time this past week (when not at work)?

Have you felt interested in doing (THOSE THINGS), or do you feel you have to push yourself to do them?

Have you stopped doing anything you used

WORK AND ACTIVITIES: (ANHEDONIA)

0 = no difficulty
1 = thoughts and feelings of incapacity, fatigue or weakness related to activities, work or hobbies
2 = loss of interest in activity, hobbies or work – by direct report of the patient or indirect in listlessness, indecision And vacillation (feels he has to push self to do work or activities)
3 = decrease in actual time spent in activities or decrease in productivity. ***In hospital***, *patient spends less than 3 hours/day in activities (hospital job*

to do? IF YES: Why? ***or hobbies) exclusive of ward chores***

Is there anything you look forward to?

4 = stopped working because of present illness. ***In hospital***, *no activities except ward chores, or fails to perform ward chores unassisted*

3. A1. (Not_HAM)

In the last week, have you been as social as when you feel well?

IF NO: Tell me which fits you best. (READ DOWN ANCHOR DESCRIPTIONS AND RATE ACCORDINGLY.)

*SOCIAL WITHDRAWAL:

0 = interacts with other people as usual
1 = less interested in socializing with others but continues to do so
2 = interacting less with other people in social (optional) situations
3 = interacting less with other people in work or family situations (i.e., where it is necessary)
4 = marked withdrawal from others in family or work situations

4. H3. (HAM 14)

This week, how has your interest in sex been? (I'm not asking about actual sexual activity, but about your interest in sex – how much you think about it.)

Has there been any change in your interest in sex (from when you were not depressed)?

Is it something you've thought much about?
IF NO: Is that unusual for you compared to when you feel well? (Is it a little less or a lot less?)

GENITAL SYMPTOMS (such as loss of libido, menstrual disturbances):

0 = absent
1 = mild
2 = severe

5. H4 (HAM 12)

. How has your appetite been this past week? (What about compared to your usual appetite?)

Have you had to force yourself to eat?

Have other people had to urge you to eat? (Have you skipped meals?)

SOMATIC SYMPTOMS: GASTROINTESTINAL

0 = none
1 = loss of appetite but eating without encouragement
2 = difficulty eating without urging from others. Marked reduction of appetite and food intake

6. H5 (HAM 16).

Have you lost any weight since you started feeling depressed or down? IF YES: Did you lose any weight this last week? (Was it because of feeling depressed?) How much did you lose?

IF NOT SURE: Do you think your clothes are any looser on you?

LOSS OF WEIGHT (Rate either A or B):

A. When rating by history:
0 = no weight loss
1 = probable weight loss due to current depression
2 = definite (according to patient) weight loss due to depression
NA = not assessed

B. When actual weight changes are measured:
0 = less than 1 pound loss in week
1 = greater than 1 pound loss in week
2 = greater than 2 pounds loss in week
NA = not assessed

7. A2 (Not_HAM). *Omit if lost weight*

Have you gained any weight in the last week? IF YES: Was it because of feeling depressed or down? How much did you gain?

***WEIGHT GAIN:**

0 = no weight gain
1 = probable weight gain due to current depression
2 = definite (according to patient) weight gain due to depression

8. A3 (Not_HAM). *Omit if lost weight*

In the past week, has your appetite been greater than when you feel well or OK? IF YES: Do you want to eat a little more, somewhat more, or much

*APPETITE CHANGE:

0 = no increase in appetite
1 = wants to eat a little more than usual, more than when you feel well or OK?
2 = wants to eat somewhat more than normal
3 = wants to eat much more than usual

9. A4 (Not_HAM).

In the past week, have you actually been eating more than when you feel well or OK? IF YES: A little more, somewhat more, or much more than when you feel well or OK?

*INCREASED EATING

0 = is not eating more than usual
1 = is eating a little more than normal
2 = is eating somewhat more than usual
3 = is eating much more than usual

10 – NOT USED FOR MODS STUDY. A5 (Not_HAM).

In the last week, have you been craving or eating more starches or sugars?

IF YES: Have you been eating or craving starches or sugars more than when you feel well or OK, much more, or has it been irresistible?

*CARBOHYDRATE CRAVING OR EATING (in relation to total amount of food desired or eaten)

0 = no change in food preference or consumption
1 = craving or eating more carbohydrates (starches or sugars) than before
2 = craving or eating much more carbohydrates than before
3 = irresistible craving or eating of sweets or starches

Has it been mainly starches or mainly sweets? Which specific foods have you been craving?
LIST:

CIRCLE ONE OR BOTH: Mainly starches / Mainly sweets / Both

Have you actually been eating more starches or sweets, or just craving them?

CIRCLE ONE OR BOTH: Craving / Eating / Both

Has the (CRAVING OR EATING) occurred at any particular time of day? (_____o'clock)

USUAL TIME OF CRAVING OR EATING:

0 = it comes and goes at various times
1 = usually morning
2 = usually afternoon or evening
3 = virtually all the time

RATER NOTE: IF BOTH CRAVING AND EATING, RATE TIME OF EATING. DO NOT COUNT ABOVE SCORE IN TOTALS.

11. H6 (HAM4).

I'd like to ask you now about your sleeping during the past week.

Have you had any trouble falling asleep at the beginning of the night? (Right after you go to bed, how long has it been taking you to fall asleep?)

How many nights this week have you had trouble falling asleep?

INSOMNIA EARLY (INITIAL INSOMNIA):

0 = no difficulty falling asleep
1 = complains of occasional difficulty falling asleep – i.e., more than ½ hour
2 = complains of nightly difficulty falling asleep

12. H7 (HAM 5).

During the past week, have you been waking up in the middle of the night?
IF YES: Do you get out of bed? What do you do? (Only go to the bathroom?)

When you get back in bed, are you able able to fall right back asleep?

Have you felt your sleeping has been restless or disturbed some nights?

INSOMNIA MIDDLE:

0 = no difficulty
1 = complains of being restless and disturbed during the night
2 = waking during the night – any getting out of bed (except to void)

13. H8 (HAM 6).

What time have you been waking up in the morning for the last time, this past week?

IF EARLY: Is that with an alarm clock, or do you just wake up yourself?

What time do you usually wake up (that is, when you feel well)?

INSOMNIA LATE (TERMINAL INSOMNIA):
0 = no difficulty
1 = waking in early hours of morning but goes back to sleep
2 = unable to fall asleep again after getting up

14. A6 (Not_HAM).

Have you been sleeping more than usual this past week?
IF YES: How much more?
IF NO: What about weekends?

(What time have you been falling asleep? Have you been taking naps? That means you've been sleeping about ___ hours a day altogether? How much time do you usually sleep when you feel well?)

*HYPERSOMNIA

0 = no increase in sleep length
1 = at least 1 hour increase in sleep length
2 = 2-hour increase
3 = 3-hour increase
4 = 4-hour increase

Sleep length used (circle one):

Usual # of hours of sleep: _____

15. H9 (HAM 13).

a. How has your energy been this past week?

IF LOW ENERGY: Have you felt tired? (How much of the time? How bad has it been?)

SOMATIC SYMPTOMS GENERAL:
A.
0 = none
1 = Vague loss of energy and fatigability.
2 = any clear-cut symptom of loss of energy/fatigue

b. This week, have you had any aches or pains? (What about backaches, headaches, or muscle aches?

B.
0 = none
1= Vague aches or pains
2 = any clear cut aches or pain

c. Have you felt any heaviness in your limbs, back or head?

C.
0 = none
1= vague heaviness in limbs, back or head
2 = any clear-cut heaviness in limbs

Final Hamilton Score #15
Take highest of A,B and C

Final Score:
0 = none
1 = heaviness in limbs, back or head. Backaches, headaches, muscle aches. Loss of energy and fatigability
2 = any clear cut symptom

16. A7 (Not_HAM).

IF ACKNOWLEDGED FEELING TIRED ON PREVIOUS ITEM: How much of the time have you felt tired? (Every day? How much of each day?)

Very tired, or just a little?

*FATIGABILITY (or low energy, or feelings of being heavy, leaden, weighed down);

0 = does not feel more fatigued than usual
1 = feels more fatigued than usual but this has not impaired function significantly; less frequent than in (2)
2 = more fatigued than usual; at least one hour a day; at least three days a week
3 = fatigued much of the time most days
4 = fatigued almost all the time

17. H10 (HAM 2).

Have you been putting yourself down, this past week, feeling you've done things wrong, or let others down?
If Yes: What have your thoughts been?

Have you been feeling guilty about anything that you've done or not done? What about things that happened a long time ago?

Have you thought that you've brought (THIS DEPRESSION) on yourself in same way?

FEELINGS OF GUILT:

0 = absent
1 = self-reproach, feels he/she has let people down
2 = ideas of guilt or rumination over past errors or sinful deeds
3 = present illness is a punishment: delusions of guilt
4 = hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

Do you feel your being sick is a punishment?

18. H11 (HAM 3).

This past week, have you had any thoughts that life is not worth living? IF YES: What about thinking you'd be better off dead? Have you had thoughts of hurting or killing yourself?

IF YES: What have you thought about? Have you actually done anything to hurt yourself?

SUICIDE:

0 = absent
1 = feels life is not worth living
2 = wishes he were dead or any thoughts of possible death to self
3 = suicidal ideas or gesture
4 = attempts at suicide

19. H12 (HAM 10).

Have you been feeling especially tense or irritable this past week? IF YES: Is this more than when you are not depressed or down?

Have you been unusually argumentative or impatient?

Have you been worrying a lot about little things, things you don't ordinarily worry about? IF YES: Like what, for example?

ANXIETY PSYCHOLOGICAL:

0 = no difficulty
1 = subjective tension and irritability
2 = worrying about minor matters
3 = apprehensive attitude apparent in face or speech
4 = fears expressed without questioning

20. H13 (HAM 11).

In this past week, have you had any of the following physical symptoms? (READ LIST, PAUSING AFTER EACH SX FOR REPLY. CIRCLE POSITIVE SXS.)

Have you had these only while you've been feeling depressed or down? IF YES: How much have these things been bothering you this past week? (How bad have they gotten? How much of the time, or how often, have you had them?)

Do you have any physical illness or are you taking any medication that could be causing these symptoms?

(IF YES, RECORD PHYSICAL ILLNESS OR MEDICATION, BUT RATE SYMPTOMS ANYWAY:_____)

ANXIETY SOMATIC -physiologic
Concomitants of anxiety, such as:
GI – dry mouth, indigestion, gas diarrhea, stomach cramps, belching
C-V – heart palpitations, headaches
Resp – hyperventilating, sighing, having to urinate frequently sweating:

0 = absent
1 = mild
2 = moderate
3 = severe
4 = incapacitating

21. H14 (HAM 15).

In the last week, how much have your thoughts been focused on your physical health or how your body is working (compared to your normal thinking)? (Have you worried a lot about being or becoming physically ill? Have you really been preoccupied with this?)

Do you complain much about how you feel physically?

Have you found yourself asking for help with things you could really do yourself but can't b/c due to physical health?
IF YES: Like what, for example? How often has that happened?

HYPOCHONDRIASIS:

0 = not present
1 = self-absorption (bodily)
2 = preoccupation with health
3 = frequent complaints, requests for help, etc.
4 = hypochondriacal delusions

22. H15 (HAM 17).

RATING BASED ON OBSERVATION DURING INTERVIEW.

INSIGHT:

0 = acknowledges being depressed and ill
1 = acknowledges illness but attributes cause to bad food, overwork, virus, need for rest, etc.
2 = denies being ill at all

23. H16 (HAM 8).

RATING BASED ON OBSERVATION DURING INTERVIEW

IF TELEPHONE INTERVIEW: Do you feel that your speech or physical movements are sluggish? Has anyone actually commented on this?

RETARDATION (slowness of thought and speech; impaired ability to concentrate; decreased motor activity):

0 = normal speech and thought
1 = slight retardation at interview
2 = obvious retardation at interview
3 = interview difficult
4 = complete stupor

24. H17 (HAM 9).

RATING BASED ON OBSERVATION INTERVIEW.

IF TELEPHONE INTERVIEW: As we talk, are you fidgeting at all, or having trouble sitting still? For instance, are you doing anything like playing with your hands or your hair, or tapping your foot? Do others notice that you are restless?

AGITATION:

0 = none
1 = fidgetiness
2 = playing with hands, hair, etc.
3 = moving about, can't sit still
4 = hand- wringing, nail biting, hair-pulling, biting of lips

17-ITEM TOTAL SCORE HAMILTON DEPRESSION _____

25. H18 (HAM 18a).

Over the past week, in the first few hours after waking up have you been feeling better or worse or no different from before you go to sleep?

DIURNAL VARIATION TYPE A:

A. Note whether symptoms are worse after awakening or before sleeping. If NO diurnal variation, mark none:
0 = no variation OR not currently depressed
1 = worse after awakening
2 = worse in evening

RATER NOTE: DO NOT COUNT ABOVE SCORE IN SCALE TOTALS.

26. H18 (HAM 18b).

IF VARIATION: How much worse do you feel in the (MORNING OR EVENING)? IF UNSURE: A little bit worse or a lot worse?

B. When present, mark the severity of the variation:
0 = none
1 = mild
2 = severe

27. A8 (Not_HAM).

This week, have you regularly had a slump in your mood or energy in the afternoon or evening?

IF YES: Is it mostly in your mood or your energy? Does it occur every day? At what time has the slump usually begun? (_____o'clock). When has it ended? Has that been at least an hour before you go to sleep? How big a slump do you have – would you say it's generally mild, moderate, or severe?

*DIURNAL VARIATION TYPE B:

0 = no
1 = yes, of mild intensity
2 = yes, of moderate intensity
3 = yes, of severe intensity

CIRCLE ONE OR BOTH:	Mood Slump	Energy Slump

NOTE: RATE ONLY SLUMPS THAT ARE FOLLOWED BY AT LEAST AN HOUR OF RECOVERED MOOD OR ENERGY BEFORE SLEEP.

28. H19 (HAM 19).

In the past week, have you ever suddenly had the sensation that everything is unreal, or you're in a dream, or cut off from people in some strange way?

IF YES: Tell me about it. How bad has that been? How often this week has that happened?

DEPERSONALIZATION AND DEREALIZATION
(such as feelings of unreality and from other Nihilistic ideas):

0 = absent
1 = mild
2 = moderate
3 = severe
4 = incapacitating

29. H20 (HAM 20).

This past week, have you thought that anyone was trying to give you a hard time or hurt you?

What about talking about you behind your back?

IF YES: Tell me about that.

PARANOID SYMPTOMS:

0 = none
1 = suspicious
2 = ideas of reference
3 = delusions of reference and persecution

30. H21 (HAM 21).

In the past week, have there been things you've had to do over and over again, like checking the locks on the doors several times, or washing your hands? IF YES: Can you give me an example?

Have you had any thoughts that don't make any sense to you, but that keep running over and over in your mind? IF YES: Can you give me an example?

OBSESSIONAL AND COMPULSIVE SYMPTOMS:

0 = absent
1 = mild
2 = severe

21-ITEM TOTAL SCORE HAMILTON DEPRESSION (without starred items): _____ _____

TOTAL 8-ITEM ATYPICAL SCORE (starred items only): _____ _____

TOTAL 29-ITEM SIGH-SAD SCORE _____ _____

ATYPICAL BALANCE SCORE (total 8-item atypical score divided by total 29-item SIGH-SAD score, multiplied by 100): _____ _____ . _____

NOTE for seasonal affective study: If patient is not depressed and score is derived primarily from symptoms of hypomania (e.g., items H4, H5, H6, H7, H8, H12, H17), administer HIGH-SAD and report both scores.

Modified from Kelly Rohan's SAD study (2002-2005)

HAM = original Hamilton item #
* = not part of original Hamilton Depression scale

Appendix B –Questionnaires Used in Study

Demographics Ambulatory Monitoring Study

ID Number: _____

Date _____

Group: CB PP Ctr

Gender M F

Marital status: 1. Married
2. Divorced/Separated
3. Single
4. Widowed

children living in household _____
Lives with partner y n

Height: _____ (Ft,In)

Weight: _____ (Lbs)

Status: AD FM Ret Other

Race African Am
Asian Am
Caucasian Am
Native American
Pacific Islander
Other _____

Ethnicity Latino/Hispanic Yes No

Medical Condition(s): _____
_____
_____
_____

Current Medication(s): _____
_____
_____
_____

Center for Epidemiological Studies Depression Scale, Revised

Below is a list of the ways you might have felt or behaved. Please check the boxes to tell me how often you have felt this way in the past week or so.

	A. Last Week				
	Not at all or less than 1 day	1 to 2 days	3 to 4 days	5 to 7 days	Nearly every day for 1 week
My appetite was poor.	☐	☐	☐	☐	☐
I could not shake off the "blues."	☐	☐	☐	☐	☐
I had trouble keeping my mind on what I was doing.	☐	☐	☐	☐	☐
I felt depressed.	☐	☐	☐	☐	☐
My sleep was restless.	☐	☐	☐	☐	☐
I felt sad.	☐	☐	☐	☐	☐
I could not get going.	☐	☐	☐	☐	☐
Nothing made me happy.	☐	☐	☐	☐	☐
I felt like a bad person.	☐	☐	☐	☐	☐
I lost interest in my usual activities.	☐	☐	☐	☐	☐
I slept much more than usual.	☐	☐	☐	☐	☐
I felt like I was moving too slowly.	☐	☐	☐	☐	☐
I felt fidgety.	☐	☐	☐	☐	☐
I wished I were dead.	☐	☐	☐	☐	☐
I wanted to hurt myself.	☐	☐	☐	☐	☐
I was tired all the time.	☐	☐	☐	☐	☐
I did not like myself.	☐	☐	☐	☐	☐
I lost a lot of weight without trying to.	☐	☐	☐	☐	☐
I had a lot of trouble getting to sleep.	☐	☐	☐	☐	☐

I could not focus on the important things. ☐ ☐ ☐ ☐ ☐

MFI-20

Instructions: We would like to get an idea of how you have been feeling lately using the following statements. Take, for example, the statement "I feel relaxed." If you think that this is entirely true, that indeed you have been feeling relaxed lately, please place an X to the extreme left, like this:

Yes, that is true. *No, that is not true.*

The more you disagree with a statement, the further you can place an X in the direction of "No, that is not true." Please do not skip any statements, and place an X next to each one.

1. I feel fit.

Yes, that is true. *No, that is not true.*

2. Physically, I feel only able to do a little.

Yes, that is true. *No, that is not true.*

3. I feel very active.

Yes, that is true. *No, that is not true.*

4. I feel like doing all sorts of nice things.

Yes, that is true. *No, that is not true.*

5. I feel tired.

Yes, that is true. *No, that is not true.*

6. I think I do a lot in a day.

Yes, that is true. *No, that is not true.*

7. When I am doing something, I can keep my thoughts on it.

Yes, that is true. *No, that is not true.*

8. Physically, I can take on a lot.

Yes, that is true. *No, that is not true.*

9. I dread having to do things.

Yes, that is true. *No, that is not true.*

10. I think I do very little in a day.

Yes, that is true. *No, that is not true.*

11. I can concentrate well.

Yes, that is true. *No, that is not true.*

12. I am rested.

Yes, that is true. *No, that is not true.*

13. It takes a lot of effort to concentrate on things

Yes, that is true. *No, that is not true.*

14. Physically, I feel I am in bad condition

Yes, that is true. *No, that is not true.*

15. I have a lot of plans.

Yes, that is true. *No, that is not true.*

16. I tire easily.

Yes, that is true. *No, that is not true.*

17. I get little done

Yes, that is true. *No, that is not true.*

18. I don't feel like doing anything.

Yes, that is true. *No, that is not true.*

19. My thoughts easily wander.

Yes, that is true. *No, that is not true.*

20. Physically, I feel I am in excellent condition.

Yes, that is true. *No, that is not true.*

Please indicate on the line below how tired you have been feeling lately. The more tired you have been feeling, the further to the right you should place the X.

21. Lately, I have been feeling... *Not at all tired.* *Extremely tired*

PHQ-15

1. **During the last week, how much have you been bothered by any of the following problems?**	**Not bothered**	**Bothered a little**	**Bothered a lot**
a. Stomach pain	☐	☐	☐
b. Back pain	☐	☐	☐
c. Pain in your arms, legs, or joints (knees, hips, etc.)	☐	☐	☐
d. Menstrual cramps or other problems with your periods	☐	☐	☐
e. Pain or problems during sexual intercourse	☐	☐	☐
f. Headaches	☐	☐	☐
g. Chest pain	☐	☐	☐
h. Dizziness	☐	☐	☐
i. Fainting spells	☐	☐	☐
j. Feeling your heart pound or race	☐	☐	☐
k. Shortness of breath	☐	☐	☐
l. Constipation, loose bowels, or diarrhea	☐	☐	☐
m. Nausea, gas, or indigestion	☐	☐	☐

SF-12 Health Survey

Instructions: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Please answer every question by marking one box. If you are unsure about how to answer, please give the best answer you can.

1. In general, would you say your health is:

Excellent	Very Good	Good	Fair	Poor
☐	☐	☐	☐	☐

The following items are about activities you might do during a typical day. Does <u>your health now limit you</u> in the activities? If so, how much?

	Yes, Limited A Lot	**Yes, Limited A Little**	**No, Not Limited At All**
2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
3. Climbing several flights of stairs	☐	☐	☐

During the <u>past week,</u> have you had any of the following problems with your work or other regular daily activities <u>as a result of your physical health?</u>

	Yes	**No**
4. Accomplished less than you would like	☐	☐
5. Were limited in the kind of work or other activities	☐	☐

During the <u>past week</u>, have you had any of the following problems with your work or other regular daily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious?

	Yes	**No**
6. Accomplished less than you would like	☐	☐
7. Were limited in the kind of work or other activities	☐	☐

8. During the <u>past 4 weeks</u>, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely

☐ ☐ ☐ ☐ ☐

These questions are about how you feel and how things have been with you <u>during the past week.</u> For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the <u>past week:</u>

	All of the Time	**Most of the Time**	**A Good Bit of the Time**	**Some of the Time**	**A little of the Time**	**None of the Time**
9. Have you felt calm and peaceful?	☐	☐	☐	☐	☐	☐
10. Did you have a lot of energy?	☐	☐	☐	☐	☐	☐
11. Have you felt downhearted and blue?	☐	☐	☐	☐	☐	☐

12. During the <u>past week</u>, how much of the time has you <u>physical health or emotional problems</u> interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

COMPUTER THOUGHTS SURVEY
Please check the box that indicates how often you currently have each of the following thoughts **when you use a computer or think about using a computer.**

Not included due to Copyright restrictions

Beck Anxiety Inventory

Not included due to Copyright restrictions

Follow-up Diary Questionnaire

	Not at all	Somewhat	Moderately	Very Much	Extremely
Was the Paper and Pencil Diary easy to use?	1	2	3	4	5
Was the text easy to read?	1	2	3	4	5
Were the interviews easy to complete?	1	2	3	4	5
How clear was the Paper and Pencil Diary training?	1	2	3	4	5
We originally asked you to make regular diary entries every 12 hours. How successful do you think you were at doing this?	1	2	3	4	5

Appendix C Week 1 and 3 Phone Script

Palm patients:
Did you have any complications or problems with the diary and completing entries each day?
If yes – What were they and attempt to solve or mail new Palm pilot if necessary.
If no – thank patient for continuing to be involved in the study, encourage them with the diary completion process.

Paper and pencil diary patients:
Did you have any complications or problems with the diary and completing entries each day?
If yes – What were they and attempt to solve or mail new paper diary if necessary.
If no – thank patient for continuing to be involved in the study, encourage them with the diary completion process.

Thank you very much for your time.

I would like to schedule you for your follow up appointment next week. Would _____ or _____ be better? What time on _____ would be best for you we have _____ or _____ available.

Time/Date end call. _____

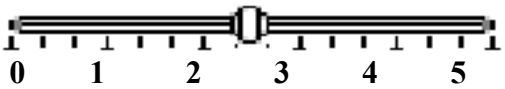
Appendix D – Instructions to Palm Pilot Users

Important things to highlight to participants

Before you begin, there are a few important things that I need to point out to you:

- When you are beeped and are ready to take the survey, tap "OK" and then anywhere on the screen.

- Many question will require you to answer on a sliding scale that looks like this:



  To answer, tap the bar in the middle, and drag it to the appropriate number (0 = "Not at all" to 5 = "The most ever").

- On most screens you will need to tap "Okay", "Next", or "Done" at the bottom to bring you to the next screen.

- In the morning and evening surveys, there will be questions that ask about the how you're feeling now and how you've felt for the whole day. Make sure you read the instructions and respond about the correct time period.

- There will be some questions that ask about certain negative or positive thoughts that you've had *(explain negative and positive thoughts)*.

- You don't need to take the Palm Pilot with you when you leave the house. Just put it someplace where you get to it easily at the times we've set to take the survey. If you do have the Palm with you you're driving or doing something where it would be dangerous to take the survey, please do not!

- Question inquiring about the "most stressful event" since last being beeped. What's a stressful event? Anything at all that bothers you can count as stressful, even if it's something that happened to someone else. If *absolutely nothing* has happened, just respond with "0" for all of the questions about the event.

- The program is very sensitive, so it's important that you don't do anything else with the Palm Pilots.

- These Palm Pilots are USUHS property. It's very important that you return them in a timely manner. If you don't do so, we'll contact you by any of the means with which you've provided us on the contact sheet, until we get the Palm back.

II. Quick directions for participants

- Palm Pilot will beep you two times a day for two weeks, once in the morning, and once in the evening.

- When you are beeped and are ready to take the survey, tap "OK" and then tap anywhere on the screen.

- Take the survey. Try to answer each question within a minute, or the survey will "sleep" and you won't be able to answer any more questions unless you go back to the beginning.

- At the end of the survey, just leave the Palm. It will turn itself off and be ready for the next time – you don't have to do anything.

- Try to take the survey within 20 minutes of being beeped, but definitely within one hour.

Trouble-shooting:

- If you accidentally hit something and are brought back to the main screen, you can tap on the "iESP" icon on the main menu to get back into the survey (you can always get to the main menu by tapping the picture of the house right below the screen on the left). If this happens, you'll have to start they survey over again from the beginning.

- If you miss a few alarms, the next time you go to take the survey, you may see a screen that lists the survey times you missed. Just tap OK, and you will be taken to the survey.

- If the Palm Pilot has turned itself off, you can press the black button between the Palm symbol and the "m130" symbol at the top and you will be brought back to the same point in the survey where you left off.

- Any questions, call (301) 346-9223 or email wjohnson@usuhs.mil

Thanks for participating!

We will be contacting you by phone on: _____

See you in two weeks (this appointment date will be coordinated at the time of the phone call follow up and is scheduled for: _____

Appendix E – Ambulatory Monitoring Questions

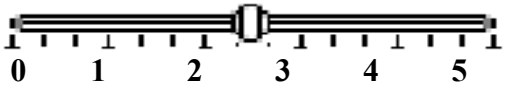
III. Morning Questions

Begin Date: _____ Time: _____

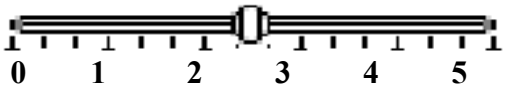
On these questions please rate how you have felt since awakening this morning.

We will use a rating scale from "0-Not at all" to "5-The most ever"

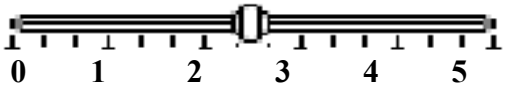
How ALERT have you felt since you woke up this morning?



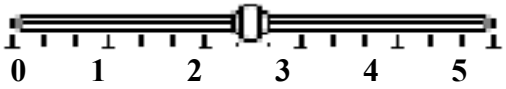
How FRUSTRATED have you felt since you woke up this morning?



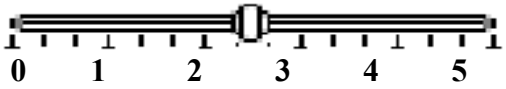
How ENERGETIC have you felt since you woke up this morning?



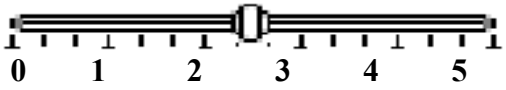
How ANXIOUS have you felt since you woke up this morning?



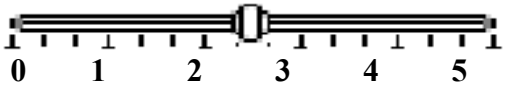
How HAPPY have you felt since you woke up this morning?



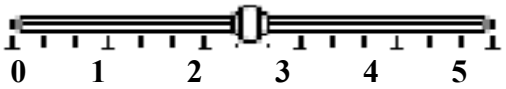
How SAD have you felt since you woke up this morning?



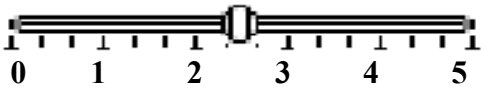
How ANGRY have you felt since you woke up this morning?



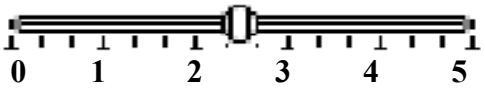
How TIRED have you felt since you woke up this morning?



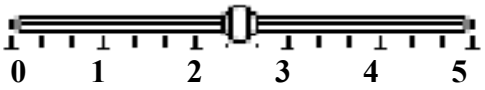
How IRRITATED have you felt since you woke up this morning?



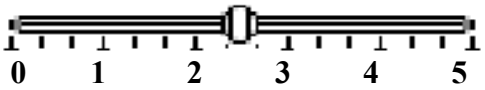
How STRESSED have you felt since you woke up this morning?



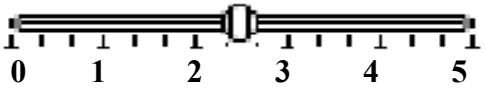
How LONELY have you felt since you woke up this morning?



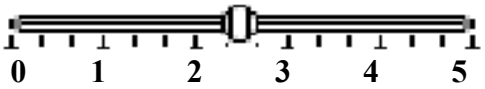
How FATIGUED have you felt since you woke up this morning?



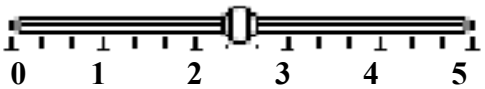
How TENSE have you felt since you woke up this morning?



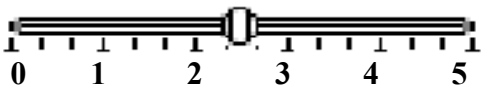
How PHYSICALLY ACTIVE have you been since you woke up this morning?



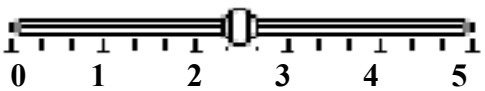
How DEPRESSED have you felt since you woke up this morning?



How DEPRESSED are you feeling right now?

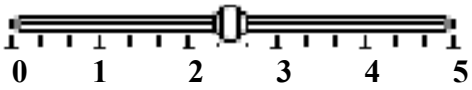


How do you think today will be? “0-Awful” to “5-Very Good”.

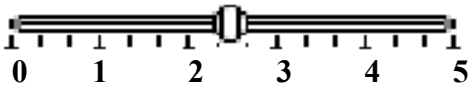


During the time since you last responded, how much have you been bothered by any of the following problems?

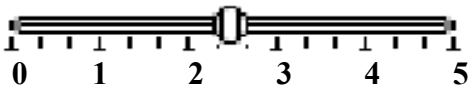
Any Pain (stomach, back, chest, joints, Headache)



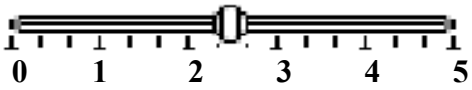
Dizziness or fainting spells?



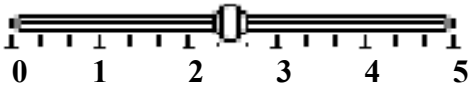
Feeling your heart pound or race?



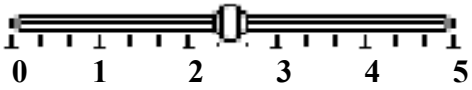
Shortness of breath?



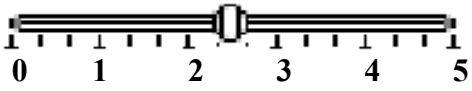
Upset Stomach (constipation, diarrhea, nausea, gas, or indigestion)?



Feeling tired or having low energy?



Trouble sleeping?



If you were bothered by sleep: did you (Circle one)

Have trouble falling asleep	Wake constantly thru the night
Wake early in morning	Combination of above

Thank you for taking time to complete this morning's questions

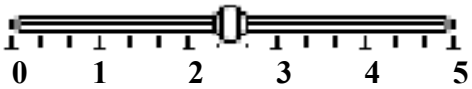
Finished Date: _____ Time: _____

Evening Questions

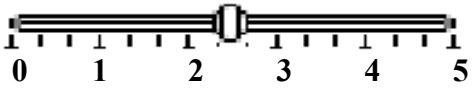
Begin Date: _____ Time: _____

On these questions please rate how you have felt throughout the day. We will use a rating scale from "0-Not at all" to "5-The most ever"

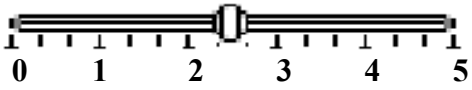
How ALERT have you felt today?



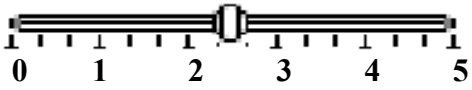
How FRUSTRATED have you felt today?



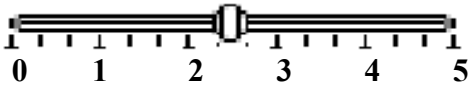
How ENERGETIC have you felt today?



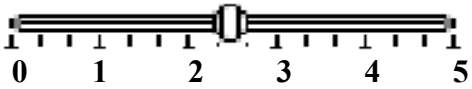
How ANXIOUS have you felt today?



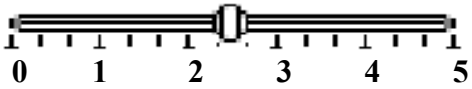
How HAPPY have you felt today?



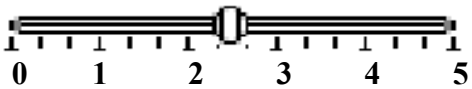
How SAD have you felt today?



How ANGRY have you felt today?

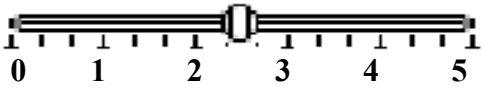


How TIRED have you felt today?

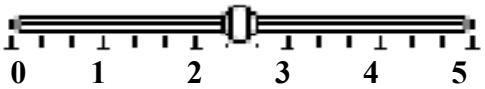


How IRRITATED have you felt today?

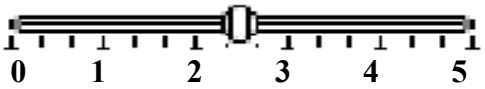
How STRESSED have you felt today?



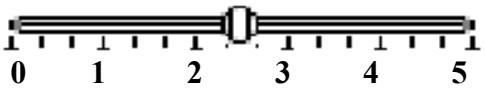
How LONELY have you felt today?



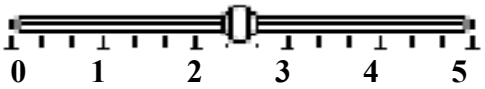
How FATIGUED have you felt today?



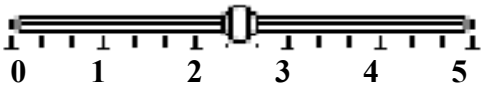
How TENSE have you felt today?



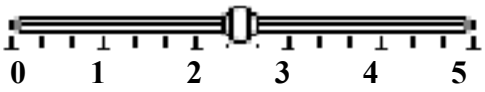
How PHYSICALLY ACTIVE have you been today?



How DEPRESSED have you felt today?

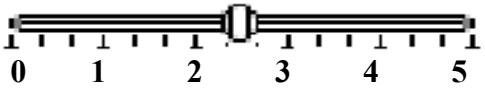


How DEPRESSED are you feeling right now?

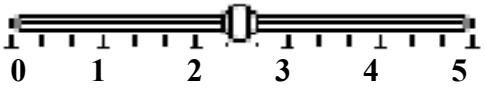


Please rate from 0 to 5, how much stress or tension you have experienced today with your: (Reminder “0 None at all” to “5 The most ever”)

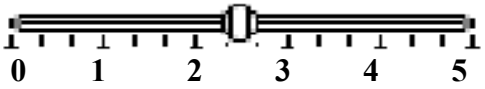
With your FAMILY and FRIENDS



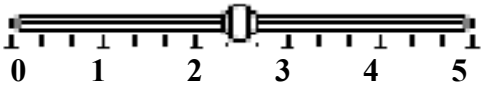
With your JOB or HOUSEWORK



With your FINANCES

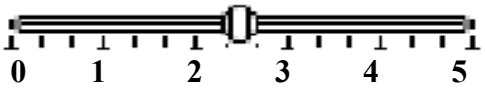


With your HEALTH PROBLEMS

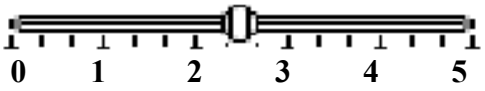


Please think about the most stressful event that happened today.

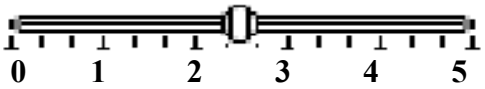
How stressful was this event? "0-No stress" to "5 Very Stressful".



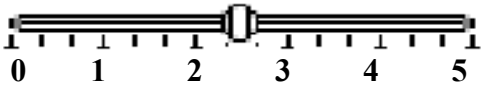
How much control did you have over the event? “0-No control” to “5-Complete Control”.



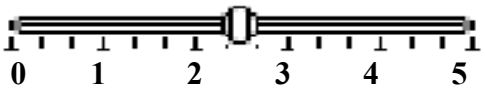
How desirable was the event? “0-Not desirable” to “5 Very Desirable”.



Were you able to cope with this stressful event? “0-Not at all” to “5 Completely”.



Did someone help you dealing with this event? “0-I received no help” to “5-It was completely handled by someone else”.



Did you take your medication today?

Yes No

Common side effects of medication include: dry mouth, constipation, drowsiness, wakefulness, blurred vision, dizziness, and headaches. Have you had any side effects from your medication?

Yes No

B. If YES, please remember to discuss side effects with your doctor at your next visit

Common benefits of medication can include: Improved sleep, better mood, or increased ability concentrate. Have you noticed any beneficial results from your medication?

Yes No

Pleasant activities and events include fun social activities that are positive and pleasurable. Success activities: Experiences that make you feel like you've done a good job or been successful at something.

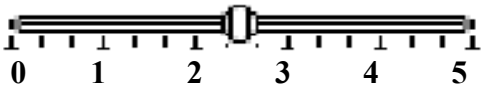
I completed ___ pleasant or success activities today. (Circle one)

0 1-3 4-6 7-10 11+

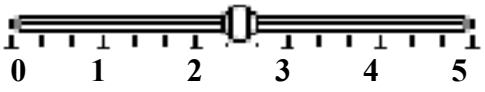
Of the most enjoyable of today's activities, who were you with:

Alone Family Friends Others Combination of these

In general, how did you feel this day? “0-Awful” to “5-Very Good”.



How do you think tomorrow will be? “0-Awful” to “5-Very Good”.



Common negative thoughts people have when depressed: I'm wasting my life, I'm scared, nobody loves me, I'll end up living alone, I'll never be successful, I don't have enough

patience, there's no use trying - I'll never get it right, I can't get close to people. These are just some of many negative thoughts.

Think of a negative thought you had today. Try to remember what your mood was like BEFORE having this thought. What happened to your mood after having this thought?

Got better Stayed the same Improved

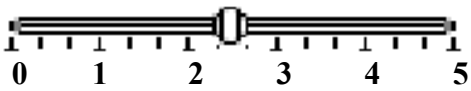
How long did you dwell on this thought throughout the day?

Less than 1 hour 1-3 hours 4-6 hours over 6 hours

Positive thoughts include: Life is interesting, I feel great, I'm having fun, I'm as good as other people, I can learn to have control over my thoughts and actions. These are just some examples. While it may be difficult at time to come up with positive thoughts try your best.

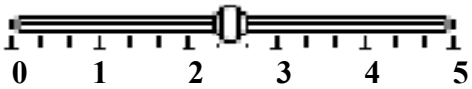
Think of a positive thought you had today. Try to remember what your mood was like BEFORE having this thought?

Try to remember what your mood was like AFTER having this thought. Did your mood improve? "0-No Improvement" to "5-Very Improved".

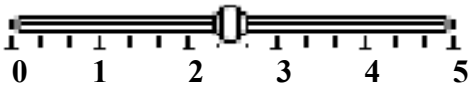


During the time since you last responded, how much have you been bothered by any of the following problems?

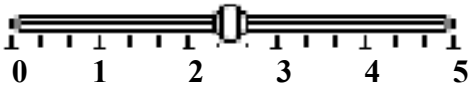
Any Pain (stomach, back, chest, joints, Headache)



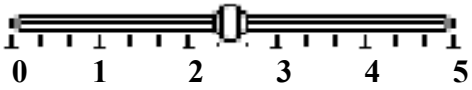
Dizziness or fainting spells?



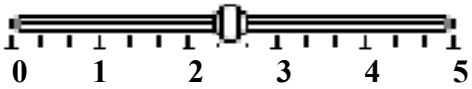
Feeling your heart pound or race?



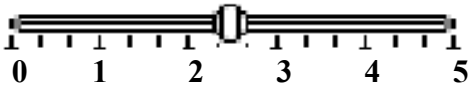
Shortness of breath?



Upset Stomach (constipation, diarrhea, nausea, gas, or indigestion)?



Feeling tired or having low energy?



Thank you for taking time to complete today's assessment.

Finished Date: _____ Time: _____