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2014

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A Computerized Intervention for Depression: A Randomized Clinical Trial

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A Computerized Intervention for Depression: A Randomized Clinical Trial

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Dissertation

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Doctor in Philosophy

The University of Texas at Austin

December 2014

Dedication

To my wife Abbie and my son Lucas who are my greatest inspiration and joy and who have always been there for me, and have helped me to keep going in life.

To my parents Jaime and Bertha and my brother and sister for their unconditional support, love, and strength.

To my friends, J.C. Boy, and Lalo Pons, for their friendship and constant presence in my life.

Lastly, to my grandfather Jose T. Gonzalez, who taught me to enjoy life to the fullest.

Acknowledgements

My deepest gratitude to my dissertation chair, Dr. Ricardo Ainslie. You have been a great mentor, role model, and friend to me. You believed in me since the beginning of this journey and always encouraged me to fight for my dreams. I can't thank you enough. Similarly, I would like to thank my dissertation committee Dr. Drum, Dr. Tombari, Dr. Rude, and Dr. Hegel for their invaluable research, clinical input, and for spending the time to be my mentors. Next, I want to thank Dr. De Jesus and Dr. Sparks for their multiple advices and support throughout my academic career. Special thanks to Dr. Cartreine for let me use ePST for my dissertation project and for his support during these years.

I would also like to acknowledge Dr. Stone who took a chance on me when he agreed to be the principal investigator/ sponsor for my research study at the Beth Israel Deaconess Medical Center. You are a great mentor and you were very supportive with my research protocol and all the detailed paperwork involved for the IRB. Thank You! I want to express my gratitude to Dr. Wolf, Dr. Morse, Dr. Medrano, and Dr. Pershonok for their invaluable counsel and supervision during my internship and time in Boston. Finally, I want to acknowledge the CRC Staff for their collaboration and assistance during my research.

A Computerized Intervention for Depression: A Randomized Clinical Trial

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The University of Texas at Austin, 2014

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One in ten adults in the U.S. report depression, and thirty-eight percent of those receiving treatment are receiving minimally adequate treatment. Studies show that evidence-based Internet interventions are highly effective in treating depression at a low cost. The aim of this study was to reduce symptoms of depression in subjects through the use of a new, electronic Problem Solving Treatment (ePST). Adult participants with moderate to severe depression symptoms were randomly assigned to either treatment or a wait-list condition. The Beck Depression Inventory-II was used as the primary outcome measure. A Repeated Measure Design with one factor in the between (treatment vs control) and one factor in the within (pre, mid-point, and post-treatment) was used in the analysis. Study results showed that participants in the ePST group improved their depression symptoms (from Moderate to Mild levels of depression) after receiving 3 session of ePST, as well as after receiving six session of ePST (from moderate to minimal levels of depression). On the other hand, participants assigned to the control group remained with Moderate levels of depression.

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CHAPTER 1: INTRODUCTION

The World Health Organization (WHO) estimates that depression is affecting about 121 million people worldwide, and it is associated with the death of over 850 thousand individuals by suicide per year worldwide (WHO, 2012). According to the Global Burden report, depression is the second cause of death in developing regions for men aged between 15 and 44. It is also projected that in 2020, depression will reach the 2nd place of the ranking of Disability-Adjusted Life Year (DALY's)[1] affecting all ages and both sexes (WHO, 2012).

In the Unites States, the Center for Disease Control and Prevention (CDCP) estimates that one in ten adults report depression (CDCP, 2012), with an overall prevalence rate of 6.7% in the adult population in a 12-month period (National Institute of Mental Health, [n.d.]). The prevalence of Major Depressive Episode, characterized by symptoms such depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration (WHO, 2012; APA-DSM-IV, 2000)varies by race/ethnicity and by age. For example, The Substance Abuse and Mental Health Services Administration (SAMHSA) estimated that among adults aged 18 or older, Asians showed the lowest (2.9%), while the rate was 12.1% among persons reporting two or more races, 9.2% among American Indians or Alaska Natives, 8.1% whites, 6.3% Hispanics, and 6.1% blacks (SAMHSA, 2008).

[1] The Disability-adjusted life year (DALY), is a time-based measure that combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health.

In terms of access, 51.7% of individuals in the U.S. with major depression within a 12-month period received treatment. However, just 38% of those receiving treatment are receiving minimally adequate treatment (Kessler et al., 2005). Although, the numbers of individuals that received treatment for major depression have improved over the years (i.e., 51.7% in 2005 versus 71% in 2008) (National Survey on Drug Use and Health, 2008), continuing to provide access to depression treatment to the overall population still remains a challenge.

Furthermore, the health care literature demonstrates that depression detection occurs mainly in the primary care sector with 50% to 70% of the individuals who seek help with their symptoms of depression and communicate their symptoms to their primary care physician. Only 16% to 23% initially communicate their symptoms to a mental health specialist (Arnau, Meagher, Norris, & Bramson, 2001). However, treating and preventing depressive disorders in the primary care sector is difficult for various reasons. First, the number of depressed people in the U.S. is alarming: one in ten (CDCP, 2010). Second, less than 50% of the depressed population receives effective treatment (WHO, 2012; Kessler, 2005); Third, the primary care sector does not have enough specialized personnel to treat depressive disorders. Fourth, when it does occur, the cost of treatment is high.

For these reasons a psychological intervention is necessary with the following characteristics: (1) evidence-based; (2) effective; (3) brief; (4) noninvasive; (5) easily delivered in primary care sectors; (6) administrable by non-mental health providers; (7)

easily learned by mental and non-mental health providers; and (8) capable of reducing either the direct and/or indirect economic costs.

Problem Solving Treatment (PST) has been shown to be an effective intervention and fulfills the above criteria. PST is a positive approach to clinical intervention that focuses on training in constructive problem-solving attitudes and skills. The theory on which PST is founded involves two interrelated conceptual models: (1) the Social Problem-Solving (SPS) model, and (2) the Relational/Problem-Solving model of stress and well-being (RPS). Social problem-solving model is founded on the idea that SPS is a self-directed learning process, a versatile coping strategy, and a self-control method with important implications for the maintenance and generalization of treatment effects, and capable of increasing the probability of adapting coping outcomes across a wide range of problematic situations (D'Zurilla & Goldfried, 1971; Mahoney, 1974; Nezu, 1987). Further, the Relational/ Problem-Solving model of stress and well-being assumes that problem solving is a coping strategy that influences the relationship between stressful life events and well-being by functioning as a mediator. The theory further states that when functioning as a mediator if a problem solving coping strategy is ineffective, negative well-being ensues (e.g., anxiety, depression), while effective problem solving has positive consequences for well-being (e.g., fewer negative emotions, and more positive emotions) (D'Zurilla, 1990; D'Zurilla & Nezu, 1999, 2007; Nezu, 1987; Nezu & D'Zurilla, 1989).

The aims then of PST are to reduce psychopathology and to enhance psychological and behavioral functioning. Additionally, the treatment aims to prevent

relapses and the development of new clinical problems, as well as to maximize quality of life by helping individuals cope more effectively with stressful problems in living (Dobson, 2009).

PST is a brief intervention. The treatment lasts between four and eight sessions and mental health as well as non-mental health providers such as nurse practitioners, physician assistants, and family physicians (Gath & Catalan, 1986; Mynors-Wallis, 1996) can be trained to administer the intervention (Mynors-Wallis, Gath, Day, & Baker, 2000). In addition, the treatment can occur in primary care facilities and behavioral health clinics.

Another important component is the use of telemedicine as a low-cost channel to disseminate evidence-based psychological interventions for depression to those who prefer a different treatment approach or to those that do not have access to traditional therapy. Studies have shown that telemedicine is an effective tool to provide high quality services remotely in consultations, diagnosis and treatment to patients. Similarly, results have shown that combining telemedicine and psychological interventions (telepsychology) can reach hundreds of thousands of people worldwide and could be used in public sector settings to augment existing offerings and provide service not currently available such as prevention interventions (Muñoz, 2010).

Over the past decade the development of Internet-based intervention studies have increased worldwide in order to further efforts to prevent and treat mental health conditions among adolescents, adults, and seniors in primary care settings. However, a limited number of studies have occurred in the U. S. appraising the effectiveness of this

approach. To date most have been developed and conducted in Europe. Therefore, the present study contributes to U.S. and international mental health literature by examining how well adults in the U.S. who live with depression respond to a new Internet-based intervention created in the U.S. and for individuals in the U.S.

This interactive multimedia Computerized based treatment program was developed to provide an electronic version of problem solving therapy for depression (ePST)[2]. The program is entirely automated and does not require the involvement of a live clinician, although it is designed to provide a "virtual therapy" experience that feels more like interacting with a person than with a computer. The ePST program was built to help individuals who do not have access to traditional therapy due the living conditions or individual preferences (e.g. rural, poor and persons desiring privacy or with significant time constraints). Internet-based treatment of depression offers several advantages. It can be used anywhere without a therapist present and can offer a standardized and consistent approach.

The ePST program provided a simulated therapy session based on the Problem Solving Treatment for Primary Care (PST-PC) treatment manual used in depression clinical trials (Hegel & Arean, 2003). A "virtual" therapist (who appears onscreen throughout the user's engagement with ePST™ and who interacts flexibly via branching algorithms that provide personalized responses from the therapist to the user based on

[2] Although ePST is a computerized-based intervention for the purposes of the present study ePST is treated as an Internet-Intervention since it overall goal is to be adapted and uploaded to the World Wide Web and since study on computerized interventions have shown similar treatment effects.

their input about their problem solving experiences and depressive symptoms) provided programmed instruction on the steps and skills of problem solving, emotional support, and tailored feedback to the user's input. The ePST program required minimal reading skills because the therapist guided the user through the problem solving process via audio and video.

In order to prove the efficacy of the ePST treating depression**,** a randomized clinical trial with a clinically depressed adult population was assigned to two treatment conditions (treatment and control). The current study took an important first step towards the creation of novel Internet-based interventions to treat depression in primary care as well as in remote and isolated environments. In addition, this study aimed to expand the current limited Internet intervention studies to treat depression available in the U.S. Further, this study expanded the understanding of how psychological theories, interventions, and technology could work together in order to provide quality access to those who did not have the resources. Future research will be required to replicate these findings, test them in isolated environments, as well as with different severity of depressive symptoms.

CHAPTER 2: LITERATURE REVIEW

Defining Depression

Feeling sad, tired and demoralized, as well as experiencing low self-esteem, and changes in sleep or eating habits are normal conditions for any human being. However, when such feelings and experiences increase in frequency, intensity and duration they can become symptoms of an emotional or physical disorder (Muñoz, 2012). If the majority of the symptoms appear for the most part within a set time period, then the symptoms form a syndrome, such as major depressive episode (DSM-IV, APA 2000). Finally, if the syndrome has a long enough duration, intensity and recurrence, it can become a disorder, such as major depressive disorder (MDD) (Muñoz, Beardslee, & Leykin, 2012). Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration (WHO, 2012), and it is frequently associated with suicidal thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or specific plan for committing suicide (APA, 2010-DSM-IV). Depression affects everyone regardless of gender, age and socio-economic status and background. When depression is not treated promptly and effectively, it becomes chronic or recurrent and could lead to substantial impairments in an individual's ability to cope, take care of his or her everyday responsibilities as well as interact with others (WHO, 2012).

Prevalence of Depression in the U.S.

A recent study conducted by the Centers for Disease Control and Prevention (CDCP) estimated that one in ten adults report depression (CDCP, 2012). This estimation

was determined based on responses to the Patient Health Questionnaire 8 (PHQ-8) (Kroenke et al., 2009)[3]. In other words, about 30 million adults[4] in the U.S. (US Census Bureau, 2012) meet the criteria for a depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders (CDCP, 2012).

Another study conducted by Kessler and colleagues estimate that 9.5% of the adult population presents some type of mood disorder. Of these mood disorders major depressive disorder accounts for 6.7%, followed by bipolar disorder with 2.6%, and dysthymia disorder with 1.5% (Kessler, 2005). Among adults with major depressive disorder, 30.4% were classified as severe, 50.1% classify as moderate, and just 19.5 % as mild (Kessler, 2005). Among those with dysthymia disorder, 49.7% of the cases were classified as severe, 32.1% as moderate, and 18.2% as mild (Kessler, 2005). In sum, if major depression disorders are accounted for, there are about 600 thousand adults with severe symptoms of depression and about 1 million more who present moderate depression. In the U.S. major depressive disorder is so common that it ranks as one of the top five sources of premature death and disability (Michaud et al., 2006) and the leading cause of disability among major ethnic and racial groups and a common problem in medical comorbidity (González, Tarraf, Whitfield, & Vega, 2010).

Several factors affect the prevalence of depression. A study conducted in 2010 by the Centers for Disease Control and Prevention reported several significant factors: sex, race, age, level of education, marital status, and employment status. In regards to sex, the

[3] The PHQ-8 is measure of current depression in the general population which covers eight of the nine criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) for diagnosis of major depressive disorder (American Psychiatric Association)

[4] The U.S. estimated population in June 2012, is 313,570,767

report indicates that women were significantly more likely than men to report major depression (4.0% versus 2.7%) while the NIHM reported that women are 70% more likely than men to experience depression during their lifetime. The Substance Abuse and Mental Health Services Administration (SAMHSA) estimated that among adults aged 18 or older, past year prevalence of major depressive episode varied by race/ethnicity. Asians reported the lowest (2.9%), while rates were 12.1% among persons reporting two or more races, 9.2% among American Indians or Alaska Natives, 8.1% whites, 6.3% Hispanics, and 6.1% blacks (SAMHSA, 2008). In reference to age, the NIMH reports that in a 12 month prevalence, major depression among 18 to 25 years old is 8.7%, for those between 26 to 44 year olds is 7.4%, and 50 or more is 4.5% more likely (Kessler et al., 2005).

Regarding the level of education, individuals with less than a high school diploma (6.7%) and high school graduates (4.0%) were more likely to report major depression than those with at least some college (2.5%). In terms of marital status, depression prevalence among individuals that have never been married was 4.1%, while depression levels for married individuals was 2.2% and 6.6% to those that have divorced. Lastly, individuals who are disabled (22.2%) or unemployed (9.8%) compared with homemakers and students (3.0%), persons employed (2.0%), and retired persons (1.6%) (CDCP, 2010).

Consequences of depression

The degree of disability produced by depressive disorders in the U.S. is high and affects medical costs, employment, work productivity and daily functioning at the individual, social, and national levels.

a. Medical Expenses

Depression is the leading cause of medical disability for individuals aged between 14 and 44 (Stewart, Ricci, Chee, Hahn, & Morganstein, 2003); this selected sector of the population represents more than 40% of the U.S. Population[5]. According to the National Research Council (NRC) and the Institute of Medicine (IOM) 2009 report, the cost of depression affects much more than the mental health system it also affects the education, justice, and physical health care (NRC & IOM, 2009b). Moreover, research has found that direct and indirect cost per capita of Depression disorders is comparable to the total costs for other major illness like hypertension, coronary artery disease, diabetes, and back problems (Druss, et al., 2000 in Johnston, Westerfield, Momin, Phillippi, & Naidoo, 2009).

In a study conducted with treatment-resistance depression patients (TRDP) findings suggested an increment of 40% in their medical care cost with an annual cost per patient of $1,530 higher than those with non-TRDP, while a cost per patient with complex TRD was of $4,425 higher than those for non-TRDP (Pincus, et al., 2001;Gibson et al., 2010). Similarly, another study found that TRD patients had more severe depression and have higher medical **costs** for imaging tests, physician visits,

[5] http://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf. Table1

psychiatric hospitalizations, and number of working days lost (Fostick, Silberman, Beckman, Spivak, & Amital, 2010).

Consequently, depressed patients use three times more health care services and seven times more the emergency room visits than individuals who are not depressed (Pincus, et al., 2001). It is also estimated that the total cost of depression is 2.1 trillion dollars for the total group over the course of their lifetimes (Smith & Smith, 2010).

b. Employment Status

Depression disorder affects employment and unemployment rates as well**,** and its cost burden is expressed in dollars lost due to absenteeism, disability, and presenteeism (i. e. being present at work but working at a reduced capacity) (Johnston et al., 2009). For example, studies performed by the Center for the Epidemiologic Studies Depression (CESD), focused on the effects of depression in employment and unemployment rates with adults. Researchers found that depression was a predictor of subsequent unemployment and decreases in income even after controlling for baseline education, marital status, and history of prior unemployment (Kessler et al., 2008). Also, it was found that children or adults who suffer from depression have lower income, lower educational attainment and fewer days working each year (Smith & Smith, 2010). Furthermore, depressed individuals are seven times less likely to be employed (Ettner, Frank, and Kessler, 1997; Lerner, et al., 2004; Kessler et al., 2008), and those who are employed work less hours and receive lower wages (Ettner, Frank, and Kessler, 1997; Kessler, Heeringa et al., 2008).

c. *Work Productivity*

In terms of work productivity, it is estimated that depressed people lose 5.6 hours of productivity every week when they are depressed (Stewart, 2003). A study conducted in a major U.S. corporation found that depressive illness was associated with a mean of 9.86 annual sick days, significantly more than any of the other conditions (Druss et al., 2000).

Additionally, fifty percent of the loss of work productivity is due to absenteeism and short-term disability (Kessler, et al., 1999), and in any 30 day period depressed workers have 1.5 to 3.2 more short-term disability days (Druss, Schlesinger, & Allen, 2001), and could lead to seven fewer weeks of work per year, which represents a loss of 20% in potential income (Smith & Smith, 2010). It is estimated that at least 80% of depressed people are impaired in their daily functioning (Pratt & Brody, 2008). The cost of depression, including the lost productivity and increased medical expense, is $83 billion each year, which is more than eight times the projected budget in 2012 for supportive education and outreach programs and for the prevention of drug abuse for young people and treatment services for substance abusers (Office of National Drug Control Policy, 2011).

Health Care Access and Quality of Treatments for Depression

Access and quality of care is fundamental for the prevention and treatment of depression in the overall population, and it is fundamental to have such services in the primary care system since primary care is the center of medical care (Starfield, 1998) and the where most mental health care is provided (Regier et al., 1993). Among mental health

disorders, depression can be reliably diagnosed in primary care settings (WHO, 2012), and it is suggested that depression can be prevented (Muñoz et al., 2012); however, health care access and the quality of treatments available to treat individuals with depression are still limited. These limitations include but are not limited to: access, shortage in providers and costly treatments.

In terms of access, in the U.S. in a 12-month period, 51.7% of the individuals with major depression received treatment, however, 38% of those receiving treatment are receiving minimally adequate treatment (Kessler et al., 2005). Although, the numbers of individuals that received treatment for major depression have improved over the years (i.e., in 2005 the number was 51.7% and in 2008 it was 71%) (National Survey on Drug Use and Health, 2012) continue providing access to depression treatment to the overall population still remains a challenge. In addition, there is a shortage of mental health personnel. A recent study estimated that in the U.S., about 84 million people do not receive mental health care services, or they receive reduced services, because of the shortage of community mental health care providers (Carlson, 2010). Today, the health care challenge is still to provide access with high quality and at low cost rates to anyone who is in need of treatment for depression.

Treatment for Depression

Brief overview of Cognitive Behavioral Treatment

There is vast evidence that Cognitive Behavioral Therapy (CBT) is an effective treatment for depression (Butler et al., 2006; Hollon et al., 2006;; Bright, Baker, & Neimeyer, 1999; Bruns & Nolen-Hokesema, 1991; Elkin et al., 1989; Beck, Rush Shaw,

& Emery, 1979) and also a prevention intervention (Muñoz et al., 2012) for depressive disorders. In private practice settings and in primary care settings **(**Høifødt, et al., 2011) there is an overall mild to moderate effect size across studies. The goal of CBT is to reduce and keep depressive symptoms below the clinical threshold; in this way potential clinical episodes of depression could be prevented and/or reduced (Muñoz, 2012).

In a seminal article by Elkin and colleagues (1989) found that CBT has a therapeutic effect that is comparable to antidepressant medication (Elkin et al., 1989). Another study that reviewed 78 controlled clinical trials, with patients with major depression or dysthymia, proved that Cognitive Therapy was an effective intervention for mild to moderate levels of depression. This study also demonstrated that CBT had significantly better results when compared with waiting-list and antidepressants (Gloaguen et al, 1998). Furthermore, a recent meta-analysis conducted by Cuijpers et al., (2013), where a total of 115 studies compared CBT vs. control groups, showed that CBT is undoubtedly an effective treatment for adult depression. Finally, it is important to note that the National Institute of Mental Health (NIMH) recognizes CBT as one of the most effective intervention to treat minor to moderate depression.

Treating Depression in Primary Care Settings

Detection of depression occurs mainly in the primary care sector with 50% to 70% of the individuals communicating their symptoms of depression to their primary care physician while just 16% to 23% initially communicate their symptoms to a mental health specialist (Arnau et al., 2001). As a result, over the past decade the primary care sector has been one of the principal settings for treating and managing depressive

disorders (Regier, 1988; Eisenberg 1992; Brody & Larson, 1992) in the general population.

The primary care sector primarily prescribes medication to treat patients with depressive disorders, and in the best cases, physicians refer their patients to therapists that provide behavioral evidence-based interventions or interpersonal therapy (Barrett et al., 1999). Although such services exist within the primary care sector, receiving psychological treament is difficult since those treatments are available only through referral to the specialty sector. In addition, many barriers exist to accessing mental health care services in the primary care sector; these include, but are not limited to, patients' poor insurance coverage, distance from care facilities, time commitments, and lack of trained clinicans, not to mention the stigma associated with receiving psychological interventions (Lovell & Richards, 2000).

Additionally, treating depression with medication is costly and not everyone is amenable to taking medication. Also, not everyone benefits from psychopharmacological treatment (Simon et al., 1996; Kirsch et al., 2008; Hollinghurst et al., 2010). Furthermore, implementing CBT in the primary care sectors requires highly trained specialists and time commitment (12-16 sessions) (Mynors-Wallis, Gath, Lloyd-Thomas, & Tomlinson, 1995), and this is an opportunity that most primary care settings cannot offer..

Because older adults are more likely to seek mental health services in primary care medicine (Arean & Miranda, 1996), a growing number of health care settings, such as the Veterans Affairs (VA) system and health maintenance organizations (HMOs), are beginning to provide brief mental health treatment within primary care. A dilemma faced

by these settings is that even the briefest interventions like CBT are not designed in consideration of the primary care setting or with the patient in mind, since primary care settings are not designed for visits longer than 30 minutes, and they do not typically employ staff with mental health expertise (Arean, Hegel, Vannoy, Fan, & Unuzter, 2008). Given these considerations, I will argue that Problem-Solving Treatment for Primary Care interventions (PST-PC) can address psychological problems within the parameters of time and resources available in most primary care settings.

Consequently, treating and preventing depressive disorders via the primary care sector is difficult given that these settings do not have enough specialized personnel to treat depressive disorders and given that pharmacological treatment is quite costly. In addition, the sheer number of depressed people and the fact that less than 25% receive effective treatment further underscores the complications involved in using the primary care sector. As the main delivery point for interventions aimed at individuals suffering from depression, the primary care setting must contend with the following issues: a) the number of depressed people in the U.S. is alarming: one in ten (CDCP, 2010); b) less than 25% of the depressed population receives effective treatment (WHO, 2012; Kessler, 2005); c) the primary care sector does not have enough specialized personnel to treat depressive disorders; d) when it does, treatments are highly costly.

For these reasons what it is needed is a psychological intervention with the following characteristics: (1) evidence-based; (2) effectiveness; (3) brevity; (4) noninvasiveness; (5) Easily delivered in primary care sectors; (6) administrable by non-

mental health providers; (7) easily learned by mental and non-mental health providers; (8) capable of reducing either the direct and/or indirect economic costs.

One solution that addresses the current difficulties of treatment and prevention of depressive disorders in the primary care sector is Problem Solving Treatment for Primary Care (PST-PC) since it meets all of these requirements.

Problem Solving Treatment Theory

Introduced in 1970 by D'Zurilla and Goldfried (1971), PST promotes behavior modification, emphasizing cognitive mediation as a way to facilitate self-control and maximize the generalization and maintenance of behavior changes (Kendall & Hollon, 1979). Furthermore, Problem-Solving Treatment for Primary Care (PST-PC) is a therapeutic intervention based on cognitive-behavioral principles (Williams, 2000). It was developed by Gath at Oxford University as an alternative to medication based treatments for medical outpatients with depression and anxiety (Barrett et al., 1999; Catalan, Gath, Bond, Day, & Hall, 1991). It is a positive approach to clinical intervention that focuses on training in constructive problem-solving attitudes and skills. The aims of PST are both to reduce psychopathology and to enhance psychological and behavioral functioning to prevent relapses and the development of new clinical problems, as well as to maximize quality of life by helping individuals cope more effectively with stressful problems in life (Dobson, 2009). The theory on which PST is founded involves two interrelated conceptual models: (1) the Social Problem-Solving Model and (2) the Relational/ Problem-Solving Model of Stress and Well-Being.

The Social Problem-Solving Model

Social problem solving (SPS) refers to problem solving as it occurs in the natural social environment (D'Zurilla & Nezu, 1982). Social problem solving is a self-directed learning process and coping strategy and a self-control method with important implications for the maintenance and generalization of treatment effects (D'Zurilla & Goldfried, 1971; Mahoney, 1974; Nezu, 1987). SPS is a versatile coping strategy capable of increasing the probability of adapting coping outcomes across a wide range of problematic situations. Also, SPS qualifies as a learning process because problem solution results in a change in performance capability in specific situations (Gagné, 1966). Social problem solving has three major components: (1) social problem solving, (2) the problem, and (3) the solution.

a) Social problem solving

Social problem solving is a self-directed cognitive-behavioral process where an individual attempts to identify or find effective solutions for specific problems encountered in his/her everyday life (Dobson, 2009). SPS through a conscious, rational, effortful, and purposeful activity seeks to improve problematic situations, and/or reducing or modifying the negative emotions generated by these situations. As it was presented by Dobson (2009) SPS is more than a simple coping strategy to overcome daily situations, SPS is a metaprocess of understanding, appraising and adapting to stressful events. Therefore, SPS is capable of dealing with real-life problems such impersonal problems (e.g., financial problems, property damage), intrapersonal problems (e.g., cognitive,

emotional, behavioral, health), and interpersonal problems. (e.g., marital conflicts, interpersonal conflicts)

b) The problem

In the context of SPS a "problem" (or a problematic situation) is defined as: a) the imbalance or discrepancy between adaptive demands and the availability to effectively cope with the situation, b) any life situation or task (present or anticipated) that demands an effective response to achieve a goal or resolve a conflict, but no effective response is immediately apparent or available to the person (Dobson, 2009).

The challenges associated with effective response to the adaptive demands may originate within the person, (e.g., personal goals, needs, commitment) and/or the environment (e.g., job demands, behavior expectations of significant others). The obstacles associated with these challenges depend on the problem. A single time event (e.g., forgetting an important appointment) is distinguishable from a series of similar or related events (e.g., an ongoing pain or loneliness). Other factors that inhibit an individual's capacity to improve their situation are: the complexity associated with situation or problem, amount of resources needed, and the any skills required.

c) The solution

A solution is the outcome of the problem-solving process when it is applied to a specific problematic situation. In addition, it is considered an effective solution if the situation is changed for the better. An effective solution reduces negative emotion and symptoms, and on the other hand, increases positive emotions. An effective solution

maximizes other positive consequences at the same time minimizes negative consequences. These consequences include long-term and short-term, as well as personal and social outcomes.

In summary, problem-solving therapy borrows a key principal from the social problem- solving model. The adapted approach is the process to change problematic situations or life events for better by identifying and/or finding effective solutions to specific problems that demands effective response. Such changes will increase positive consequences and reduce negative emotions and symptoms in an individual.

The Relational/Problem-Solving model of stress and well-being

First, PST takes from the Relation/Problem-Solving Model (R/PSM) the assumptions that psychopathology symptoms can be understood and effectively prevented or treated if they are viewed as ineffective, maladaptive, and self-defeating coping behaviors that in turn have negative psychological and social consequences, such as anxiety, depression, low self-esteem, and impaired interpersonal functioning (D'Zurilla & Goldfried, 1971). Second, PST adopts from R/PSM the idea that social problem solving is a general and versatile coping strategy. This coping strategy increases adaptive functioning and positive well-being, and as result reduces and prevents the negative impact of stress on well-being and adjustment (D'Zurilla, 1990; D'Zurilla & Nezu, 1999, 2007; Nezu, 1987; Nezu & D'Zurilla, 1989).

In the R/PSM, stress is viewed as a function of the reciprocal relations among three major variables: (1) stressful life events, (2) emotional stress/well-being, and (3) problem-solving coping.

a) Stressful life events

Stressful life events are any life experiences that present a person with demands for personal, social, or biological readjustment (Bloom, 1985). In this model, two major types of stressful life events are considered: a) a major negative event, and b) daily problem. Major negative events are broad life experiences that require gradual readjustment in a person's life (e.g., a major illness, the lost of a love one, a job loss), while daily problems are viewed as narrower and specific stressful life events (e.g., see problem definition). Although these two types of stressful life events are independent from each other, they are often related. For example, a diagnosis with a chronic illness (major negative event) will create new stressful problems for a person such as difficulties paying bills, following treatment procedures as prescribed, and health problems. Equally, the accumulation of poor decision making, lack of healthy activities such as frequent exercise, getting enough sleep hours (daily problems), will cause or contribute to a chronic illness: a major life event.

b) Emotional Stress (ES)

In this model, emotional stress is a key part of a broader construct of "well-being" that also encompasses cognitive, behavioral, social, and physical functioning (Lazarus & Folkman, 1984), and it refers to the immediate emotional responses of a person to stressful life events, as modified, modulated, or transformed by cognitive appraisal and coping processes (Lazarus, 1999). Also, emotional stress theory explains that depending on the nature of stressful life events, cognitive appraisals, and coping behavior, emotional

stress responses may be negative (e.g., anxiety, anger, depression) or positive (e.g., hope, relief, exhilaration, joy).

Negative and positive emotions will be dictated by the life circumstances that surrounds the individual. For example, an individual will experience negative emotions when: 1) a stressful event is perceived as threatening or harmful to his/her well-being, 2) doubt exists regarding his/her ability to cope effectively, 3) coping responses are ineffective, maladaptive or self-defeating. In contrast, such an individual will experience positive emotions when 1) he/she perceives a stressful event as an opportunity for his/her benefit, 2) an individual believes that he/she is capable to cope effectively with the problem, and 3) his/her coping responses are effective, adaptive and self-enhancing (Dobson, 2009).

c) Problem-solving coping

The most important concept in the relational/problem-solving model is "problem-solving coping," a process that integrates all cognitive appraisal and coping activities within a general social problem-solving framework. A person who applies the problem-solving coping strategy effectively (1) perceives a stressful life event as a challenge or "problem to be solved," (2) believes that he or she is capable of solving the problem successfully, (3) carefully defines the problem and sets a realistic goal, (4) generates a variety of alternative "solutions" or coping options, (5) chooses the "best" or most effective solution, (6) implements the solution effectively, and (7) carefully observes and evaluates the outcome. Regardless of what goals are set, the ultimate expected outcome

of problem solving is to enhance adaptive coping and positive well-being, and to reduce the negative impact of stress on well-being and adjustment (Dobson, 2009).

The hypothesized relationships among the major variables in the relational/problem-solving model of stress and well-being shows that major negative events and daily problems are the two types of stressful life events in the model, and that they are assumed to influence each other. It is important in PST to identify the daily problems that might be created by major negative events and to focus on solving these daily problems, as well as coping with the major negative event itself.

The model assumes that problem solving influences the relationship between stressful life events and well-being by functioning as a mediator or a moderator. The model recognizes two different mediational hypotheses. The first hypothesis is based on the ABC model, where stressful life events (A) are assumed to set the occasion for problem-solving behavior (B), which, in turn results in personal and social consequences (C) that affect well-being. If problem solving is ineffective, negative well-being ensues (e.g., anxiety, depression), but effective problem solving has positive consequences for well-being (e.g., fewer negative emotions, more positive emotions).

Purpose and Protocol

PST-PC interventions aim to reduce treatment time and enhance personnel resources in primary care settings where patients with depression are treated. Furthermore, PST-PC teaches patients the close link between their everyday problems and their symptoms of depression and anxiety. Simultaneously, patients learn to use their

own skills and resources to cope with both present and future problems (Mynors-Wallis, 1996).

PST-PC is a brief intervention that lasts between four and eight sessions where mental health as well as non-mental health providers such as nurse practitioners, physician assistants, and family physicians (Gath & Catalan, 1986; Mynors-Wallis, 1996) can be trained to administer the intervention (Mynors-Wallis, Gath, Day, & Baker, 2000) in primary care facilities and behavioral health clinics.

As a CBT branch, PST-PC is a collaborative treatment between the therapist and patient in which there are three main steps: (1) the patient's symptoms are linked with their problems in living; (2) the problems are defined and clarified; and (3) an attempt is made to solve the problems in a structured way (Williams, 2000; Dowrick et al., 2000). Within the three main steps in PST-PC six stages are encompassed: (1) identifying and clarifying the problem; (2) setting clear achievable goals; (3) brain-storming to generate solutions; (4) selecting a preferred solution; (5) clarifying the necessary steps to implement the solution; and (6) evaluating progress (Mynors-Wallis et al., 1995); an additional stage (7) scheduling enjoyable activities is recommend (Cartreine et al., 2013). On subsequent sessions, participants and trained providers evaluate their success or lack of success at implementation, troubleshooting, and begin the cycle again.

The CBT main components of PST are: 1) behavioral activation, 2) sense of control, and 3) the relationship between brain, body and behavior. *Behavioral activation:* PST activates the individual to take steps toward changing their situation rather than being passive. *Sense of control*: PST instills a sense of control and self-efficacy, which

can combat feelings of learned helplessness that can cause depression. *Brain-Body-Behavior*: PST teaches a strategy of approaching life problems that can be used throughout the individual's lifetime as a way of both managing and preventing depression. Finally, the elimination of problems in and of themselves can be of significant benefit, particularly for reducing stress. Although some problems may or may not be completely solved in treatment, the underlying idea of PST-PC is that once the patient starts tackling his/her problems, he/she will begin to reassert control over his/her lives. In other words, regaining a sense of control over life's problems is likely an important factor in resolving emotional symptoms (Barrett et al., 1999).

In summary, PST-PC's ultimate goal is that once the technique has been learned, the patient will use it as a toolbox to address, prevent, cope and solve past, present and future problems or subsequent depression episodes. As stated, PST-PC is a brief treatment and ranges between four to eight individual sessions, with an approximate time of one hour for the first session, and 30 minutes for each subsequent session (Dowrick et al., 2000; Barrett et al., 1999; Williams, 2000).

Effectiveness of PST

PST has been tested in primary care settings to determine whether it was an efficient and viable intervention in community care settings in urban and rural areas. In community care settings when PST -PC was compared with community-based psychotherapy in treating late-life major depression and dysthymia, adults who received PST-PC had more depression-free days at 12 and between 12 and 24 months, and they had fewer depressive symptoms and better functioning at 12 months than those who

received community-based psychotherapy (Arean et al., 2008). In urban and rural areas, a study conducted in nine urban and rural communities in Finland, Republic of Ireland, Norway, Spain, and the United Kingdom, found that the proportion of problem solving participants depressed at six months was 17% less than that for controls, and when PST was offered to adults with depressive disorders in the community it was more acceptable than a course on prevention of depression (Dowrick et al., 2000).

Recent meta-analyses on problem-solving therapy conducted by Cuijpers, van Straten et al., (2007) and Malouff, Thorsteinsson, & Schutte, (2007), found that PST was superior to no treatment, treatment as usual, and attention placebo for treating major depressive disorder. In addition, PST was demonstrated to be more effective than placebo and as effective as amitriptyline (an antidepressant) in treating major depression (Mynors-Wallis et al., 1995). Likewise, PST has proven to be an effective treatment for major depression (Mynors-Wallis, 2002; Mynors-Wallis, Gath, Lloyd-Thomas, & Tomlinson, 1995; Oxman, Hegel, Hull, & Dietrich, 2008) and minor depression (D'Zurilla & Nezu, 1999) in primary care.

Furthermore, PST was found to be an effective treatment for older adults (Alexopoulos, Raue, & Areán, 2003) ; Charney et al.,2003; Kendrick et al., 2005; Mynors-Wallis et al., 2000), and as effective as an antidepressant medication in treating major depression in younger patients (Mynors-Wallis et al., 1995; Mynors-Wallis, Gath, Day, & Baker, 2000) in primary care settings. Additionally, in a study that examined if PST could be administered by research general practitioners or research practice nurses to treat depressive disorders, researchers found that PST was an effective treatment for

depressive disorders in primary care, and most importantly, PST could be delivered by suitably trained practice nurses or general practitioners (Mynors-Wallis et al., 2000). Similar findings were obtained by Unutzer et al., (2002) where nurse practitioners with no prior mental health treatment experience were able to deliver this brief intervention in a reliable fashion.

Application of Computerized PST

Because PST is highly structured and modular, brief, has good "common sense" face validity, low attrition rate, and can be delivered by non-mental health providers or specialists, it is uniquely suited for adaptation to computerized delivery. The National Space Biomedical Research Institute (NSBRI) and the National Aeronautics and Space Administration (NASA) are attempting to take this next step by moving PST-PC from a provider-administered treatment to a self-administered one. If successful, it will enable this brief but effective intervention to be delivered at any location at any time via computer—including rural areas, isolated communities and even in outer space (Cartreine et al., in press).

Telemedicine & Telepsychology

Telemedicine

Telemedicine (from its Greek roots '*tele', meaning* far or distance, and medicine), refers, in general terms, to the ability to provide medical care at a distance. The primary objective of telemedicine is to provide high quality medicine and care without the physical presence of the provider, and the overall assumption is that telemedicine will address particular unfulfilled necessities that a nation's health care system has in terms of

its medical services (Ferrer-Roca, 1998). Telemedicine can help medical centers that lack or have limited infrastructure, limited resources or are geographically isolated, by connecting them to centers that have highly trained on-site personnel in order to provide health services through long-distance communication (Heinzelmann et al., 2005; Zundel, 1996). Telemedicine can also reduce times of consultation, diagnosis and treatments while reducing the need for clinical visits (Fong, Fong, & Li, 2010). It facilitates the exchange of medical data between, and within, health care systems. Moreover, telemedicine reduces medical disparities when there is a lack of specialized personnel across health care systems. Finally, telemedicine improves health care access and can bridge the gap between patients and providers regarding social and cultural barriers (Currell et al., 2000; Craig et al., 2005; Heinzelmann et al., 2005; Muñoz, Cuijpers, Smit, Barrera, & Leykin, 2010).

Telemedicine can be as simple as two doctors talking about a patient through the telephone or internet, or as complex as a sophisticated global hospital enterprise network that supports real-time remote surgical operations with surgeons simultaneously situated in different parts of the world controlling an operation that takes place in one hospital (Fong et al., 2010).

Telemedicine has been used in hospital, clinics, communities, and satellite health care units in urban and rural areas since the 1960's. One of the earliest documented uses of telemedicine was in 1967 between the Boston Logan Airport and the Massachusetts General Hospital where a black and white image microwave link was established for emergency services at the airport (Dwyer *1973;* Ferrer-Roca, 1998). In 1970, the Miami

School of Medicine delivered telemedicine (medical appointments) for prisoners, demonstrating to be successful in 70% of cases, and it was cost effective as well (Sassmore & Sander, 1978).

Focus on Rural areas

Between the 1960's and 1970's the federal government funded the project INTERACT based at the Dartmouth Medical School. This project, developed in mostly rural areas, consisted of supporting and implementing seven telemedicine research and demonstration projects[6] nationwide where medical staffing had been a critical issue (Zundel, 1996). Another project using telemedicine in rural areas was in 1989 by the Texas Tech Health Science University through the MedNet project that provided support to 37 rural communities (Ferrer-Roca, 1998). By the late 1980's the North-West Telemedicine Project demonstrated that the introduction of new communication facilities could improve the quality of health care for persons living in isolated areas or environments (Watson, 1989). In 1994, Oklahoma Telemedicine Network provided diagnostic services to 38 rural hospitals (Ferrer-Roca, 1998). Twenty years after the first pioneer project of telemedicine, the American Telemedicine Association (ATA) was established in 1992 offering services such as: support to patients under dialysis, distant consultation in dermatology, neurology, pediatrics, oncology, psychiatry, various forms of diagnosis or care at a distance on neuroradiology, cardiology, gastroenterology, orthopedics, and speech treatment (Ferrer-Roca, 1998).

[6] The seven projects happened in: 1) New Hampshire, 2) Maine; 3) Puerto Rico; 4) Minnesota; 5) Alaska 6) Washington, and 7) Arizona.

Clinical Care Applications: Telepsychiatry and Telepsychology

In the 1970s a study that used a two-way television network, found that telepsychiatry was an effective way to support non-psychiatric physicians in helping them improve their knowledge of psychiatry and treat emotionally ill patients, and most importantly, it was not a significant barrier to the establishment of rapport between doctors and patients or to the perception of emotional nuances, with patients reporting high acceptance (Zundel, 1996). Telepsychiatry was also tested with paranoid patients, and the circumstances of the interviews did not seem to foster additional anxiety, nor did the television system become the object of psychotic elaboration (Solow et al., 1971).

Further testing on telepsychiatry has been conducted in community centers to treat behavioral problems, anxiety, PTSD and sexual abuse. For example, Rusking et al., (2004) in a randomized clinical trial that compared telepsychiatry with in-person treatment services with depressed veterans using psychotropic medication, psycho-education, and brief supportive counseling for 6 months in an outpatient clinic, found that remote treatments of depression have comparable outcomes and equivalent levels of patient adherence, patient satisfaction, and health care cost when compared to in-person interventions. Yuen et al., (2010) used telepsychology through Skype videoconferencing- a type of Internet intervention, to treat social anxiety disorder where patients were able to engage exposure during sessions by practicing social situations (e.g., initiating conversations with strangers, group conversations at a party, public speeches) and performed role plays seated in front of a Webcam in the same room as the therapist. The

study reported that patients' anxiety increased when first engaging in the exercise but then they got habituated to the exposures.

If telemedicine solutions are wisely introduced into everyday practice, in the broad spectrum in the health care settings and system then the "tele" will be dropped, as will simply become an integral part of medicine.

Internet-Based Interventions

In a meta-analysis of 92 empirical articles, Barak et al., (2008) examined the effectiveness of Internet-based psychological interventions, including different forms of delivery. The study revealed that Internet-based psychological interventions have an overall effect size of d= 0.53 (large effect size) which is similar to the average effect size of traditional face-to-face therapy. It was also found that depression interventions had an overall effect size of d=0.32 (medium effect size). Moreover, interventions based on CBT models had an effect size of d=0.83, while psycho-education interventions had an effect size of d=0.46. Meta-analysis concluded that Internet-based psychological interventions were more effective with patients between ages of 25-39 with an effect size of *d*=0.69, followed by ages between 19 -24 with a *d*= 0.48.

Another meta-analysis conducted by Anson and Cuijpers (2009) about the effects of studies treating depression using computerized psychological interventions with control groups (care as usual, wait list) showed main effects between Internet-based and other computerized psychological treatments vs. control groups at posttest of *d=0.41;* however, effects sizes were significant greater for those studies that had support (e.g., therapist involved, automated, telephone, email) with a *d*=.61, as compared to treatments

that were unsupported (d=0.25). These results are consistent with Newman et al., (2011) and Titov's (2011) meta-analyses.

Another meta-analysis that examined the efficacy of internet-delivered intervention with a CBT or a PST model in treating adult patients diagnosed and/or with elevated symptoms of depression confirmed that both interventions were effective (Titov, 2011); however, guided internet-delivered psychotherapy interventions were superior to those that were self-guided programs.

Another study conducted by Reynolds et al., (2011) about possible resources that can be used in primary care facilities and by general practitioners for anxiety and depression, argued that online interventions can benefit both the general practitioner and the client. For example, the client will receive appropriate evidence-based mental health interventions and the time to receive treatment will be shorter. From the point of view of the general practitioner, online interventions can be used as adjunct to their traditional interventions, and they will be more involved in the mental health process. Reynolds presented a list of seven websites providing information about anxiety and/or depression and nine other based-interactive Internet programs for anxiety and/or depression.

At this time there is significant scientific evidence supporting the effectiveness of Internet and/or computer-delivered psychotherapy interventions (Kaltenthaler et al., 2006; Kaltenthaler et al., 2008; Marks et al., 2007; Marks and Cavanagh, 2009; Spek et al., 2007) used as treatment for anxiety and depression symptoms in primary care settings. Evidence indicates that Internet interventions can be used as adjunctive interventions and/or as standalone treatment. Finally, Internet interventions are effective

enough in reducing health disparities that the National Institute for Health and Clinical Excellence in the UK has approved such treatment as a viable possibility in primary care.

How it is used

Over the past decade studies and development of Internet interventions have increased worldwide in order to fill the gaps in our efforts at preventing and treating physical and mental health conditions with adolescents, adults and seniors in primary care settings. In addition to depression studies, research about the use of Internet interventions for mental health conditions included but are not limited to: Anxiety (White et al., 2000; Hayward et al., 2007; Shneider et al., 2005; Craske et al., 2009); OCD (Mouton-Odum et al., 2006; Greist et al., 2002); PTSD, (Hirai & Clum, 2005; Lange et al., 2003; Zucker et al., 2009).

The efficacy of Internet-based interventions for depression

Since the early 2000s there has been a scientific push to demonstrate the effectiveness of Internet-based interventions for depression (Warmerdam et al., 2010). However, most of the clinical trials to date have been conducted in European countries. For example, in 2003, in a randomized clinical trial in England with depressed and anxious adults, participants were assigned to either a treatment by an interactive multimedia program based on cognitive behavioral techniques, [beating the blues ^{tm} (BtB) program,] or to a General Practitioner Treatment as Usual (TAU) in primary care. Results showed that patients who received BtB had significant improvement in depression and anxiety compared with TAU by the end of treatment at 2 and 6 months follow-up. It was demonstrated that BtB by itself, and under minimal clinical supervision, brought rapid clinical and statistically significant improvement, decreasing symptoms of

depression and anxiety as well as in work and social adjustment relative to TAU (Proudfoot et al., 2003). Another randomized control trial was conducted in England for depressed adults placed participants at a website offering information about depression (BluePages) or a CBT therapy website (MoodyGYM) or a control intervention using an attention placebo (weekly contact with a lay interviewer to discuss lifestyle factors such as exercise, education and health habits) group. Results indicated that both CBT and psycho-education delivered via the Internet were effective in reducing symptoms of depression compared with a credible control intervention in reducing symptoms of depression in a community sample with an overall effect size of d=0.30 (Christensen et al., 2004).

Similarly, in 2005, Andersson and colleagues conducted an RCT in England with people with mild to moderate depression and were allocated to either treatment (Internet-delivered psychotherapy based on CBT model) or waitlist. Consistent with previous studies, results showed that the treatment group experienced greater reduction of depressive and anxiety symptoms, with a between-group effect size at post-treatment on the BDI-II of .94 (Andersson et al., 2005). In another RCT conducted in Europe, participants with elevated symptoms of depression were assigned to either the six version of the MoodGym program or to a control group found that the treatment group had a significant improvement with a within-group effect size of the Goldberg Depression Scale ranged from .20 to .40 (Christensen et al., 2006).

Perini et al., 2009 RCT's study with Australians and New Zealanders participants that met the criteria for major depression according to the DSM-IV were assigned to

either treatment using an Internet-intervention based on a CBT model or a waitlist control group. Results indicated that the treatment group had a large reduction in depressive symptoms, with a between-group effect size at post-treatment on the BDI of 0.89.

Furthermore, when Warmerdam and colleagues examined in a RCT in the Netherlands the utility and cost-effectiveness of Internet-based cognitive behavioral therapy (IBCBT), Internet-based problem solving treatment (IBPST), and waiting list with clinically significant depressive symptoms, study outcomes showed that IBCBT and IBPST were superior compared with waiting list control group in reducing symptoms of depression and enhancing quality of life after week 12 (data was collected at baseline and 5, 8 and 12 weeks follow-up) (Warmerdam et al., 2008). From a cost-effective point of view, IBCBT and IBPST showed a 91% and 89% probability respectively of being more cost-effective in the general population, even when the society had a limited willingness to pay for a reliably improved patient (Warmerdam et al., 2010).

Other European studies that used Internet-interventions that have been effective include: Van Voohees et al., (2009), Alvarez, Sotres, Leon, Estrella, & Sosa (2008), and Wright et al., (2005). The first study demonstrated that when CBT Internet Intervention was added to a 5 to 10 minute physician directed motivational interview, plus 3 motivational phone calls, it was superior to 1-2 minutes of physician's advice (Van Voohees et al., 2009). The second study showed that when university students used a therapy assisted computer program in conjunction with researcher assistance, results indicated improvement in cognitive impairment, academic performances and depressive symptoms, whereas antidepressants only improved depressive symptoms (Alvarez,

Sotres, Leon, Estrella, & Sosa, 2008). Finally, the last study compared a 250 minute lab-based computer program with 450 minutes with therapist-delivered therapy and results indicated no significant difference between the interventions (Wright et la., 2005). In a new RCT for depressed adolescents and young adults or higher health service utilizers in the United States, subjects were assigned to a pure Internet-based CBT interactive self-help program plus treatment as usual (TAU) or to TAU plus access to a health management organization (HMO) website with statistical information about depression. The results showed a between-group treatment effect size on the Patient Health Questionnaire-8 Item (PHQ-8) at 32 weeks of .020, with a moderate effect size among women of 0.42 (Clarke et al., 2009).

Contrary to previous studies, De Graaf et al., (2009) in a clinical randomized trial that compared Computerized Cognitive Behavioral Therapy (CCBT) using the "Colour Your Life program" without support, Treatment as Usual (TAU) by a general practitioner (GP); or online, and unsupported CCBT plus GP combined, results suggested that although all three groups improved in their depression symptoms substantially at 6 months follow-up (within group effect size = 0.86, 0.81 and 0.89 respectively), CCBT did not outperform usual care by itself and the combination of both did not have additional effects. De Graff also suggested that CCBT without any support is not beneficial for all people with depression; however, the use of CCBT plus therapist support could be beneficial as a secondary treatment. In a follow-up critique of De Graff's study, it was hypothesized that factors that contributed to CCBT not being effective in treating depression was that participants were recruited from a normal

community sample and many of them might not ever have sought treatment (Andrews, 2010).

In summary, for more than a decade, scientific curiosity for adapting psychological theories (e.g., cognitive behavioral therapies) with computer software and/or web designs has resulted in new ways to treat individuals with mental health disorders and behavioral problems. Internet-based interventions, since their development, have been tested through randomized clinical trials mainly in Europe, Australia, New Zealand and the Netherlands, and these studies have demonstrated their effectiveness for treating symptoms of mental disorders.

Although these Internet interventions for depression are effective (e.g., MoodGym, and Beating the Blues), most of them are text oriented, contain minimal audio and video, and the intervention is guided by cartoons and/or by animations. In comparison, ePST is unique. This approach to Internet intervention is more dynamic (i.e., the intervention is heavy in audio and video, and is less text oriented). Moreover, this approach enhances accessibility, even to those who are not highly literate.

Currently there is a gap in the literature with respect to Internet interventions for depression. As mentioned, the effectiveness of Internet-based interventions have been conducted, though they are few in number. Furthermore, very few studies have assessed the effectiveness of this approach on populations in the U. S. Moreover, no study has been performed to determine the effectiveness of the ePST intervention for depression on a population in the U.S. Accordingly, the present study aims to fill the gap in the literature.

PROPOSED STUDY

Interventions and proof-of-concept studies have demonstrated that evidence-based Internet interventions can reach hundreds of thousands of people worldwide and could be used in public sector settings to augment existing offerings and provide service not currently available such as prevention interventions (Muñoz, 2010).

An interactive multimedia computer-based treatment program was developed to provide an electronic version of problem solving therapy for depression (ePST). The program was entirely automated and did not require the involvement of a live clinician, even though it was designed to provide a "virtual therapy" experience that feels more like interacting with a person than with a computer. The ePST program was built to help individuals who did not have access to traditional therapy due the living conditions or individual preferences (e.g. rural, poor and persons desiring privacy or with significant time constraints). This computer-based treatment of depression offered several advantages. It can be used anywhere without a therapist present, and offered a standardized and consistent therapeutic approach.

The ePST program provided a simulated therapy session based on the PST-PC treatment manual used in depression clinical trials (Hegel & Arean, 2003). A "virtual" therapist (presented via audio and video) provided programmed instruction on the steps and skills of problem solving, emotional support, and tailored feedback to the user's input. The ePST program required minimal reading skill because the therapist guided the user through the problem solving process via audio and video. Below are the three primary research questions and a sub-question of this study:

Research Questions:

1. Does ePST improve depression when compared to a wait list control group at mid-point and post-test treatment? _
2. Are there significant changes in the ePST group and in the control group across the three assessment times?
3. Is there a treatment interaction between Groups and the times assessments?

As a supplementary analysis the following question was examine:

4. Is ePST a user-friendly software for the treatment of depression?

CHAPTER 3: METHODS

Hypotheses

The following null hypotheses were tested: 1) There was no differences in depression level between groups at pre, mid-point and post-test treatment; 2) there was no differences in depression levels across testing occasions (mid-point treatment and post-test) for both treatment and control group. 3) There was not interaction effect between group and times.

Research Design

This research employed a two factor [Ax(B)] mixed method factorial experimental design with one between subject factor (ePST vs Delay Entry Control) and one within subject factor: Time (pre, mid-point, and post treatment). The between factor has two levels and the within factor has three levels.

Recruitment

Participants were recruited through announcements in the local media, university health centers, hospitals, churches, workplaces, and community center bulletins in the greater Boston area. The Beth Israel Deaconess Medical Center IRB's Committee as well as The University of Texas-Austin IRB's Committee approved the study protocols. There were no adverse events for any participants.

Screening

Participants over 18 years of age, who reported interest in the clinical trial and were eligible, were contacted by the Principal Investigator to do a pre-screening interview over the phone. The purpose of this pre-screening process was to explain the

study to potential participants and to pre-screen them. This screening interview contained three components: 1) Brief description of the study, 2) Inclusion criteria, and 3) Exclusion criteria.

Pre-screening phone interview

Brief description of the study: In this phase, the PI contacted potential participants who had indicated interest and asked them whether they were interested in participating in a study that was examining the use of a computerized psychological intervention to treat adults who present symptoms of depression. Only potential participants who verbally consented to be screened, were asked questions regarding the pre-screening to see if they met inclusion criteria.

Pre-screening inclusion criteria: In this component potential participants were asked demographic questions (e.g., age, gender, ethnicity, educational level, and computer usage). Furthermore, potential participants were asked for their current use of psychological services and/ or psychiatric medications (See full description of the inclusion criteria in Section page. 50). Additionally, potential participants were screened for depression using the Patient Health Questionnaire-9 (PHQ-9), and for current use of psychological services and/or psychiatric medications (See full description of the inclusion criteria in Section C and the Inclusion Criteria Questionnaire in Appendix 3**).** During this phase, questions regarding possible suicidal ideation, plans or attempts or thoughts about hurting themselves (i.e., Item 9 "Thoughts that you would be better off dead, or of hurting yourself" in the PHQ-9), were omitted, by recommendation of the IRB Committee. These questions however, were asked during the In-Person Intake

Session (see below), in order to guarantee the safety of the participants, and to provide them, if that was the case, with local referral numbers so they can contact other services in the area.

Pre-screening exclusion criteria: In this component potential participants were asked questions – to the best of their knowledge, about current and/or previous diagnoses of medical and psychological conditions, and about their current use of antidepressant and/or antipsychotic medications. (See full description of the Exclusion criteria in Section C and the Exclusion Criteria Questionnaire in Appendix 2).

If potential participants did not meet any pre-screening exclusion criteria and did meet the inclusion criteria, and if they consented verbally and indicated interest in participating in the study, they were then invited by the PI to the Beth Israel Deaconess Medical Center- Clinical Research Center (BIDMC-CRC) facilities for an In-Person Intake Session. Potential participants who reported having met any of the exclusion criteria were not eligible to participate in the study, and they were informed that the present study was not suitable for them at this time. The study coordinator provided them with some local referral numbers so they can contact other services in the area (See script in the Appendix 5, Script 2a). No other data, including the participant's history, was collected at this time. The description of participants screened out and excluded are show in Figure 1.

Week 0: In-Person Screening

The goals of the intake session were: A) To enroll potential participants who met enrollment criteria and who agreed to participate in the study by signing the informed

consent form; and B) To measure his or her baseline level of depression. The intake session was conducted in person by the PI with the potential participant in a designated private room at the BIDMC-CRC facilities.

The Intake Session was conducted face-to-face at the CRC. It was divided into 7 parts:

1) Explanation and description of study
2) Sign informed consent form
3) Evaluation regarding inclusion criteria
4) Evaluation regarding exclusion criteria
5) Administration of baseline assessment
6) Random assignment to group
7) Scheduling of participants

The informed consent process as well the ePST treatment sessions took place in a designated room on the BIDMC-CRC.

Explanation and description of the study: During this phase, the PI gave a detailed description of the study to potential participants in a private room at the CRC facilities. During this time participants had the opportunity to ask questions about the study, as well as about the study's benefits and risks. Once the potential participant agreed to be part of this screening he/she continued with the second component of this phase: Sign informed consent form.

Sign informed consent form: The PI explained in detail the informed consent form to the participants. Only participants who signed the consent form continued with the administration of the baseline assessment.

Evaluation regarding inclusion criteria: In this component subjects were asked questions about the inclusion criteria (Appendix 3). A trained psychology student administered the PHQ-9, a psychometrically validated screening instrument for clinical depression. In order to meet the inclusion criteria, participants needed a score between 10 to 20 on the PHQ-9, which indicates a Moderate to Moderately severe Depression level. At this time, participants were asked suicidality questions. It was part of the study protocol, that in the event that participants indicated a score of 1, 2, or 3 on item 9 on the PHQ-9, the trained psychology student would implement the safety protocol (See Appendix 5).

Evaluation regarding exclusionary criteria: Once the participant met the inclusion criteria, he/she was asked questions based on the exclusion criteria questionnaire (see Appendix 2). In addition to the questionnaire, the use of the Mini International Neuropsychiatric Interview **(MINI)** helped to make diagnoses and identified potential subjects who did not meet the study criteria. The MINI is a brief, structured diagnostic interview that assists in the diagnosis of psychiatric disorders, based on DSM-IV and ICD-10 criteria (Sheehan et al., 2009). In the current study, depressed mood was assessed via self-report (PHQ-9, BDI-II and Hopkins) and confirmed by a clinical interview conducted by a trained clinician.

Administration of baseline assessment: The baseline dataset was based on the demographic protocol (see Appendix 1), and the depression questionnaire (BDI-II, PHQ-9, and The Hopkins Symptom Check List-20-d). Once participants completed the measures, they continued with the last step of the In-Person Intake Session: random assignment to group.

Random assignment to group: Participants were informed that they were being randomly assigned to one of the two possible groups: Electronic Problem Solving Treatment (ePST) or Delayed Entry Control group (DEC). The PI gave an envelope to participants that contained a randomly assigned unique number and a randomly selected study group (ePST or DEC). A computerized random number generator determined randomization. The use of block randomization was used to ensure equal number of subjects in each.
Scheduling of participants: Participants in the ePST were scheduled to use the software, while DEC participants were scheduled for a 4-week follow-up.

Study Criteria

Inclusion criteria

In order to be part of the study, potential participants had to meet the following criteria:

1. Be 18 years of age or older.

2. Present symptoms from the following criteria based on the DSM-IV-TR: Major Depressive Episode, Mood Disorder Due to a General Medical Condition and/or Adjustment Disorder with Depressed Mood.
3. Depression must be the primary diagnosis and not occur secondary to any other diagnosis such as PTSD, anxiety disorders, social phobia, or complicated bereavement.
4. Not receiving psychological treatment (e.g., face to face) at the time of the study.
5. Not currently receiving Problem Solving Treatment in any other context.
6. Not reporting/reported suicidal attempts in the year prior to their participation in the study.
7. Be able to write and speak English according to Rapid Estimate of Adult Literacy in Medicine (REALM) test scores.

Potential participants who were taking anti-depressants were included, but were questioned about changes in medication or in dosage at the start of each scheduled appointment. Subjects who reported discontinuing psychiatric medications on their own, changing dosages on their own or who otherwise showed clinical instability or worsening symptoms were referred to medical backup for evaluation, in accordance with safety protocols (see Appendices 6and 7);

Exclusion criteria

Potential participants were excluded from the study for any of the following reasons:

1. Current suicidal ideation, history of suicidal attempts or self-injurious behavior at any point during the protocol.
2. Have been diagnosed with schizophrenia, bipolar I disorder, with psychosis, other disorder with psychotic symptoms, and/or brain injuries that includes loss of consciousness > 15 minutes and /or posttraumatic amnesia of any duration.
3. Any history of treatment with antipsychotic medication.
4. A felony conviction.
5. Any current or recent (i.e. within the previous 6 months) substance abuse/dependence diagnosis (other than nicotine or caffeine).
6. Undergoing current psychological treatment (e.g., face to face).

Participants who indicated suicidality or self-injurious behavior during the screening process were assessed by medical staff and if needed, they were referred for services. Other participants who indicated having been diagnosed with schizophrenia, bipolar disorders, or presented with psychotic symptom (e.g., hallucinations), and/or brain injuries as well as presenting with current substance abuse/dependence (other than nicotine or caffeine) and/or were currently undergoing to psychological treatments (e.g. face to face) were excluded from the study. No participant was excluded based on gender, race, ethnicity, and sexual orientation.

The optimal time for completion of the study is illustrated in Table 1, see below.

Table 1. Optimal time for completion of the trial

Optimal time for completion									
	Pre-Screening	Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7
ePST	---------	Intake/ Baseline	Session 1	Session 2	Session 3	Mid-Point assessment and Session 4	Session 5	Session 6	Post-Treatment evaluation
DEC	---------	Intake/ Baseline	----------			Mid-point assessment	----------		Post-Treatment evaluation and beginning of ePST if desired

1. *Procedures*

Once participants were screened and randomized, they were assigned to their groups (N=45). Those in the intervention condition –ePST group, (ePST=56) received the computerized intervention via flashdrive and they were able to use it in the designated room at the CRC. Participants who had been randomized into the ePST were asked to do six ePST sessions. The first session occurred within one week of enrollment, and most of the following sessions were scheduled at the outset as close to a weekly basis as possible. Participants in the DEC group (DEC= 20) were scheduled to come for a mid-point assessment (4 weeks after baseline) and for a post-treatment assessment point (7 week after baseline). Both treatment groups were equally economically compensated for every time they filled out the clinical measures.

2. *Intervention*

Electronic Problem Solving Treatment (ePST)

ePST is an interactive multimedia computer-based treatment program that was developed to provide an electronic version of problem solving therapy for depression (ePST). The program is entirely automated and does not require the involvement of a live clinician, although it is designed to provide a "virtual therapy" experience that feels more like interacting with a person than with a computer. The ePST program was created to help individuals who do not have access to traditional therapy due to particular living conditions (e.g. rural, poor, or with significant time constraints) or individual preferences (e.g. persons desiring privacy). Also this computer-based treatment of depression was developed to offer several advantages: it can be used anywhere and following the person's own schedule, effective treatment without needing a live therapist, and increases the number of evidence-based interventions, and addresses the lack of mental health providers nationwide).

The ePST program provides a simulated therapy session based on the PST-PC treatment manual used in depression clinical trials (Hegel & Arean, 2003). A "virtual" therapist (presented via audio and video) provides programmed instructions on the steps and skills of problem solving, emotional support, and tailored feedback to the user's input. The ePST program requires minimal reading skills because the therapist guides the user through the problem solving process via audio and video (Cartreine et al., in press).

The first session is comprised of seven components: 1) A welcome to the ePST by the virtual psychologist; 2) Depression self- assessment of current depression symptoms; 3) Psycho-education about depression; 4) Introduction to Problem Solving Treatment (PST); 5) Explanation and exercise of the PST components (i.e., stating a problem,

stating a goal, brainstorming, choosing solutions, creating an action plan and scheduling enjoyable activities). At the end of the session, a print out of the treatment plan is generated.

Subsequent sessions (sessions 2 to 6) include: 1) a welcome to the current session; 2) Depression self-assessment of current depression symptoms using an in-built PHQ-9; 3) Comparison between previous and current depression symptoms; 4) Check of the status on how the problem solving unfolded and the level of participant satisfaction; 5) Troubleshoot the action plan; 6) Suggestions for improvement; 7) Development of an action plan; 8) Evaluation of the action plan; 9) Option to work on other problems or not; 10) Schedule enjoyable activities; and 11) Read about PST cases.

As a security measure for this clinical trial, the ePST software created a printed evaluation report of patient's depressive symptoms. The report showed whether the participant expressed any suicidal intent or ideation or increment in their depression symptoms. The PI or Research Nurse verified the reports and then decided whether or not the participants were at risk. A second print out was automatically generated, for the convenience of the participant, at the end of the session. This report included the objectives, the goal, the step-by-step treatment plan, and the list of the enjoyable activities planned for the week. Only the participant had access to this print out.

Delay Entry Control (DEC) Group

Participants in the waitlist group were asked to attend the intake session, and came from a Mid-point depression assessment four weeks after baseline and for a final depression assessment session at week seven. The PI or CRC staff called participants two

days before their assessment time session to schedule the appointment. The same logistic procedures were applied between Mid-point assessment and Post-treatment session.

Assessment time points

To monitor participants' depression levels, clinical deterioration, and other clinical concerns as well as their progress, the intervention set up three time assessments points: 1) Baseline (week 0), 2) Mid-point assessment point (week 4), and 3) Post-Treatment assessment point (week 7).

Baseline (week 0)

During the In-Person Intake Session (at Week 0), and prior participant randomization, participants were asked to complete a series of self-assessment measures. These assessments, administered by the PI, served to set participants' baseline.

Mid-point assessment (week 4)

Participants in both group conditions were contacted by the PI or by one of the CRC staff via email and/or phone to return for the completion of the Mid-point assessment. DEC participants were assessed 4 weeks after baseline assessment, while ePST participants were assessed before starting session 4 of the ePST. Mid-point measures were identical to baseline measures.

Post-Treatment (week 7)

Post-treatment measures were identical to baseline and mid-point assessments, with the addition of an adherence scale for those in the ePST group. This scale was the System Usability Scale (in-built in the ePST software). After completing these assessments, only ePST participants were invited to participate in a 30-minute debriefing

session. This procedure was voluntary and optional for them. The goal of the debriefing session was to find out what the participants liked or disliked about the ePST and suggestions for improvement. Data collected from the debriefing session was analyzed qualitatively and compared to their responses on the System Usability Scale (SUS).

Safety Measures and Protocols for Participants with Suicidal Ideation or Other Symptoms of Clinical Deterioration

There were several ways in which the PI identified and responded to suicidal ideation or other forms of clinical deterioration. They included:

1. Screening and Selection
2. Monitoring of Depression and Risk of Suicide Protocol
3. Procedural Manual for Safety – Clinical Coverage
4. Monitoring for Clinical Deterioration
5. Monitoring Risk for Suicide Protocol
6. Informed Consent Process

Screening and Selection

The present study had set up multiple measures in order to ensure the safety of its participants. The first safety measure was reflected in the study's inclusion and exclusion criteria (see Section C-Subjects selection). The rigor of these criteria reduced the likelihood that participants had active suicidal ideation or suicide attempts. However, in the event that participants presented suicide risk or experienced severe symptoms of depression, a second safety measure and protocol was designed. This protocol was called 'Monitoring of Depression and Risk of Suicide'.

Monitoring of Depression and Risk of Suicide protocol

In this protocol, the Study Coordinator and the CRC staff monitored participants' level of depression and risk for suicide every time they came to their session. Participants' depression scores were reported weekly or as needed to the PI and to the psychiatric staff backup in order to ensure the safety of the participants. The monitoring process for risk of suicide began immediately when the participant logged into his or her session and answered the Depression Self-Assessment measure (the PHQ-9) that is built into the ePST program.

Immediately after the PHQ-9 was completed, the ePST program automatically generated a printout, and simultaneously put the session on hold. This printout included the participant's PHQ-9 responses and a unique safety code number (this code differed for every session). While the ePST session was on hold, the Study Coordinator or the CRC staff (who was/were waiting outside of the room) reviewed the depression self-assessment scores, paying particular attention to how question 9 "Thoughts that you would be better off dead, or of hurting yourself" was answered. ePST sessions remained on hold until the Study Coordinator or CRC staff entered the safety code and clicked the continue button. The Study Coordinator or CRC staff inserted this safety code number only if there was no indication of suicidality. On the other hand, if a participant answered question 9 with a score higher than 1 (on a 0 to 3 scale), the Study Coordinator and/or the CRC staff followed the procedural manual for safety (see Appendix 5). The printout served as a guide so the Study Coordinator could monitor participants' severity of

symptoms and presence of suicidality. Note: For a detailed description of this process, see Appendix 6.

Procedural Manual for Safety – Clinical Coverage

A third safety measure was called Procedural Manual for Safety. This manual guided the PI, the Study Coordinator, and the research staff (e.g., CRC personnel) on what to do in the event that a participant reported suicidality. The procedural manual for safety was implemented immediately if participants reported suicidal ideation, suicide attempts, or other self-injurious behavior during the intake process, the course of their study participation, or during any session. As explained in the procedural manual for safety, regardless of the severity of the plan or ideation, the Study Coordinator and the CRC staff contacted the study medical back-up. This team then proceeded with the necessary and standard diagnostic procedures and therapeutic interventions, as needed. Note: See the detailed description of the procedural manual for safety in Appendix 5.

Monitoring for Clinical Deterioration

A fourth safety measure was the plan for participants who experienced clinical deterioration during the study. Although it was unlikely that participants deteriorated clinically as a result of interacting with the ePST software, there was a possibility that factors external to the study may cause them to experience clinical deterioration.

Through this plan, multiple measures were developed to address the possibility of clinical deterioration and to guarantee participants' safety. The first measure was the ongoing monitoring system built into the ePST software, which alerted the study personnel to observe participants' depression levels, symptom severity, and risk of

suicidality throughout their participation. This built-in monitoring system allowed study personnel to track participants' symptoms during their participation and thus facilitate rapid responses to potential risks. Participants were evaluated with the PHQ-9, which stratifies depression on five levels (Minimal, Mild, Moderate, Moderate-Severe, and Severe). Individuals who scored in the severely depressed range (21 to 27) for two consecutive sessions were excluded from the study (See Vignette 1). Similarly, ePST participants were excluded if their overall depression score increased two levels within 3 consecutive sessions (See Vignette 2).

> **(Vignette 1):** Participant X scored 10 points in his intake session (Moderate Depression). Participant X scored 21 (Severe Depression) in sessions two and three.
>
> **(Vignette 2):** Participant Y scored 7 points (Mild Depression) in his intake session. He scored 13 points (Moderate Depression) in session two and 19 points (Moderately Severe Depression) in session three.

In either event, participants were referred immediately (i.e. within 10 minutes of observing the increased score) to the psychiatric backup for a face-to face evaluation. In these circumstances, participation in the study resulted in suspension. A referral was made for treatment; however, the data was included in the final analysis.

Note: Regardless of participants' levels of depression, deterioration, or symptom severity, an affirmative response to question 9 ("thoughts that you would be better off dead or of

hurting yourself") or report of suicidality at any point in the study resulted in the implementation of the procedural protocol for safety.

Other measures to ensure that professional help was available to the participants at all times included the Monitoring Risk for Suicide Protocol (Appendix 6), the Procedural Manual for Safety (Appendix 5), and the physical location of the clinical trial (i.e. at the BIDMC- CRC facility).

Note: Protocols to respond to participants who reported any level of suicidal ideation, severe levels of depression, and/or clinical deterioration are provided in the following appendices:

- Appendix 5- Procedural Manual for Safety
- Appendix 6- Monitoring for Depression and Risk of Suicide protocol

Measures

Demographic questionnaire: Information was collected on participants' age, ethnicity, sex, educational level, and computer frequency usage.

Depression Measures

Patient Health Questionnaire (PHQ-9) (*see Appendix 4, letter A*): The PHQ-9 is the 9-item depression module from the full PHQ. The PHQ-9 was used for two reasons, including: 1) Participant selection and, 2) Monitoring depression levels in the ePST group in each session. The PHQ-9 was designed for depression screening and has been validated with 3,000 primary care patients. Responses for these 9 items (from the DSM-IV) range from 0 for "not at all" to 3 for "nearly every day." A total score is calculated by adding the scores for each of the 9 symptoms. Higher scores indicate greater depression

symptom severity. As a severity measure, the PHQ-9 score can range from 0 to 27, since each of the nine items can be scored from 0 (not at all) to 3 (nearly every day). The psychometric properties of the PHQ-8 are nearly identical to those of the complete PHQ-9 (Corson, Gerrity, & Dobsha, 2004); it possesses excellent sensitivity (.97), specificity (.97), and positive predictive value (.75) for detecting major depression (Kroenke & Spitzer, 2001).

Beck Depression Inventory II (See Appendix 4, letter B): The Beck Depression Inventory Second Edition (BDI-II) is a 21-item self-report instrument used to assess the existence and severity of symptoms of depression as listed in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (APA, 1994). There is a four-point scale for each item ranging from 0 to 3. The cutoff scores are: 0-13 - minimal depression; 14-19 - mild depression; 20-28 -moderate depression; and 29-63 - severe depression (Beck et al., 1996). The psychometrics of the BDI-II are quite sound. BDI-II has a Coefficient alpha of .92 with outpatient and 0.93 with nonclinical samples, and the test-retest reliability coefficient across the period of a week of 0 .93 (Beck, 1988; Dozois, et al., 1998). The BDI-II was used as the primary outcome measure of depressive symptoms and to monitor depressive symptoms throughout treatment. BDI-II was used during the three data points: intake, mid-point and post-test session in both treatment conditions.

Hopkins Symptom Checklist 20-item Depression Scale (HSCL-20-d)(see *Appendix 4, letter C*): The HSCL-20-d is a validated self-reported measure of depressive symptoms, and functioned as the primary, self-report measure of depressive symptoms in

the present study. This 20-item depression scale (Katon et al., 1995) is derived from the 90-item HSCL (Lipman, Covi, & Shapiro, 1979). Items are rated on a 5-point scale (0 to 4) according to how much the symptom has been experienced during the past week. Scale scores are determined by dividing the sum of the items by the total number of items, yielding a range of 0-4. A Score of 1.72 has been shown to be associated with a high positive predictive value for a diagnosis of major depression in adult primary care patients (Mulrow et al., 1995).

The HSCL-20-d item scale has been used in other studies that used Problem Solving Treatment. Thus, the results of the present study allowed for comparisons with other PST studies. The HSCL-20-d has also been shown to be a valid measure of depressive symptom improvement (Katon et al, 1995, 1996, 1999; Ware, 1996), and has been used as the primary outcome measure in many depression collaborative care studies, including IMPACT and RESPECT-D, thus allowing for direct comparisons between studies (Hegel et al., 2003). The HSCL-20-d with depressed adults has a coefficient alpha of .86 (Williams et al., 2004).

Mini International Neuropsychiatric Interview (MINI): The MINI is a brief, structured diagnostic interview that assists in the diagnosis of psychiatric disorders, based on DSM-IV and ICD-10 diagnostic criteria. It is used only to establish eligibility for the study. In the MINI, if a participant answers key questions negatively, the participant 'skips out' of that section. If the subject responds positively to one or more of the key screening questions, more detailed questions are then asked. The MINI demonstrates strong diagnostic concordance with the Structured Clinical Interview for DSM-III-R

diagnosis of major depression, with a Cohen's kappa of 0.84; in addition, the MINI has an excellent inter-rater reliability (.75to .80) and test-retest reliability (above .75) (Sheehan et al., 1997; Sheehan et al., 1998). The MINI was used in the enrollment interview and in the post-treatment session.

System Usability Scale (SUS) (*see Appendix 4, letter D*): The System Usability Scale (SUS) is a 10-item self-report measure of the ease of using computer programs with odd-numbered items worded positively and even-numbered items worded negatively. Items are scored on a 5-point scale (0-4) on the strength of agreement with each of 10 statements (e.g., "I found the system unnecessarily complex", "I felt very confident using the program"). Cronbach's alpha for inter-item agreement is a robust 0.91 (Bangor, Kortum, and Miller, 2008). Factor analysis shows only one significant factor, suggesting that the overall score is the best measure of usability. The sum of the individual items (range 0-40) is multiplied by 2.5 to obtain the total score, ranging from 0-100. SUS scores that are 68 or higher are at least average, while scores below 68 are below average (Sauro, 2011). The SUS scale was built as part of the ePST software and was administered to the participants at the end of sessions 1 and 6 in the ePST group.

CHAPTER 4: RESULTS

SPSS (version 21.1 for Windows) was used to conduct all the quantitative analyses. The primary outcome variable—depression—was measured using the BDI-II and the HSCL-20-d.

Demographic characteristics at the Pre-screening phone interview and at the In-Person Screening

Of the 100 responders to the advertisements, 97 were pre-screened. In the pre-screening phone interview 33 participants were excluded, 23(70%) were male and 10(30%) were female. Among the 33 participants, 12 (37%) were African American, 11 (34%) were Caucasian, 3 (9%) were Hispanic / Latino, 2 (6%) were Asian, and 2 (3%) reported being Other. The average age mean for males was 36.8 (SD= 14.1) and for females was 36.8 (SD=8.31). Among these 33 participants, 25(75%) were excluded from the study due to having psychotic symptoms. Another 4(12%) were excluded because they reported having problems with substance abuse, and the last 4(12%) were excluded because they were in psychological therapy at the time.

An additional 19 individuals from the original 97 pool were excluded during the In-Person intake screening (18 male and 1 female). 8 (42%) were African American, 7 (37%) were Caucasian, 2 (11%) were Hispanic / Latino, 1 (5%) was Asian, and 1 (5%) reported being Other. The average age mean among these males was 29.5 (SD= 10.2) and for the only female was 45 (SD=0). Among these 19 participants, 11 (75%) were excluded because they had suicidal ideation and attempts in the past, 4 (6%) were excluded because they did not want to be part of the study (i.e., not willing to wait six

weeks to start the program) and another 4 (6%) were excluded because the clinical study did not meet their expectations (i.e. thought they would be receiving anti-depressants).

Demographics of the final Study sample

After applying inclusion and exclusion criteria, forty-five participants completed the study trial. 28 (62%) were women and 17 (38%) were men. The women's average age was 30.36 (SD=7.91), and the men's average age was 26.74 (SD= 10.38). Regarding ethnicity, 65% of the participants were Caucasian, 22% were Hispanic/Latina, 9% were African American, while 4% were Asian. The level of education of the participants was divided in the following manner: 33% have some college or associate's degree (most of them were in college at the time), 31% were college graduates, 25% were postgraduates, 7% did not complete high school, and 4% were high school graduates. Finally, 42% of the participants reported using the computer more than 3hrs. a day but less than 5hrs, 22% reported using the computer more than 8hrs. a day, another 22% reported using the computer less than 1hr. a day, and finally 13% of the participants reported using the computer more than 6 hrs. but less than 8hrs. a day**.**

Table 2. Study's Descriptive Demographics

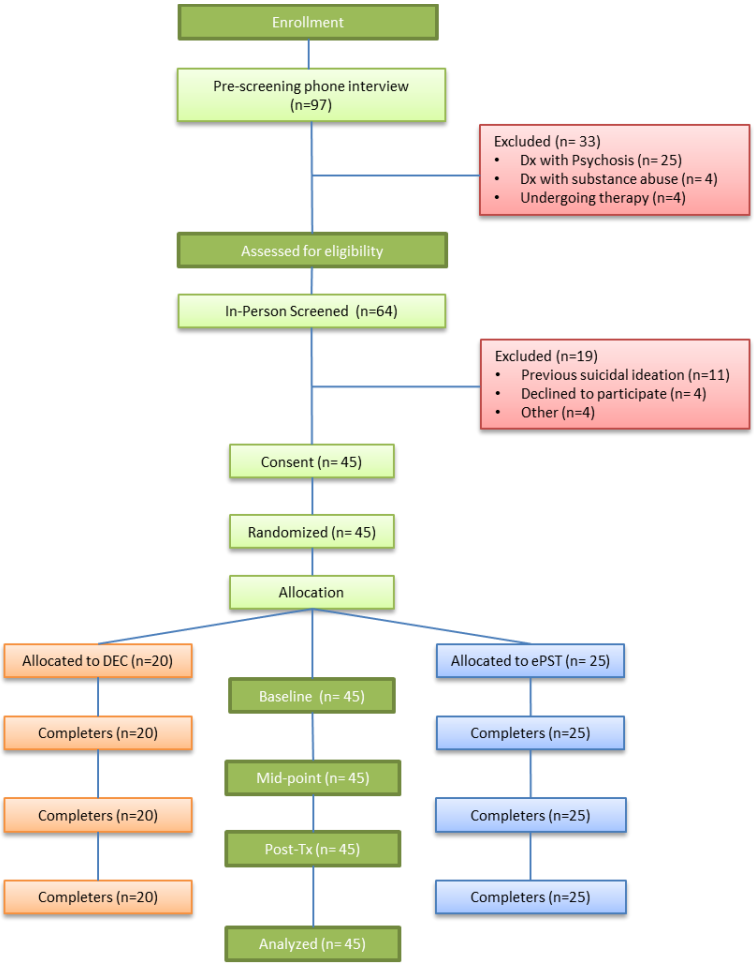
		Control (n= 20)		Treatment (n= 25)	
		n	%	n	%
Gender					
	Male	13	65	4	16
	Female	7	35	21	84
Age					
	Male	24.5	SD = 10.01	29.23	SD= 10.75
	Female	29.86	SD = 7.09	30.9	SD= 8.73
Race					
	White/Caucasian	10	50	19	76
	Black/African American	4	20	-	-
	Hispanic/Latino	5	25	5	20
	Asian	1	5	1	4
	Other	-	-	-	-
Educational Level					
	Some high School	3	15	-	-
	High school graduate	1	5	1	4
	Some college or Associates degree	8	40	7	28
	College graduate	5	25	9	36
	Masters level graduate	3	15	7	28
	Doctorate level Graduate	-	-	1	4
	Did not respond	-	-	-	-
Computer Skill					
	> 1h.r a day	7	35	3	12
	< 3 hrs. a day but less than 5hrs.	7	35	12	48
	< 6 hrs. a day but less than 8hrs.	2	10	4	16
	< than 8 hrs. a day	4	20	6	24

Retention Rates

Of the 45 participants who agreed to participate and met study criteria, 100% completed the three time assessments. Attrition rates were significantly higher even though these numbers (e.g. attrition and dropout rates) did not correspond to what the computerized intervention literature has reported (i.e., dropout rates of 20% to 50%

(Christensen & Griffiths, 2002; Christensen et al., 2006; Perini et al., 2009). These numbers are discussed in the results and discussion sections further below.

Figure 1. Flow of participants throughout the clinical trial



Diagnoses and Depression level

All participants (N=45) met the cut-off criteria between 10 and 20 on the PHQ-9, (with a *M*=14, SD= 2.9), indicating a moderate level of depression. By post-treatment, the mean score of 8 indicated that the depression levels were in the non- depressed range. Participants' scores of depression measured by the Beck Depression Inventory-II, at

Baseline with an *M*= 21.9, SD= 4.32, reported a moderate level of depression. Additionally, participants' scores on the HSCL, at Baseline with a mean of 1.5, SD=0.5, expressed mild to moderate levels of depression as well. Finally, the results of the structured clinical interview showed that 70% of the participants met the criteria for Major Depressive Disorder, 20% met comorbidity diagnosis of Depression with Anxiety, 5% met diagnosis of Dysthymia while just 1% met diagnosis for PTSD.

Statistical analyses were performed on all participants that completed the study.

Preliminary Analyses

Preliminary analyses were conducted prior to testing the study hypotheses. The descriptive analyses of the data were inspected (including frequencies, means, standard deviations, skewness, and ranges of values) to determine accuracy of entry and to look for outliers. The analyses were based on the intention-to-treat principle (i.e. those who provided follow-up data irrespective of treatment adherence).

Scatterplots and boxplots of the data were checked. Results in this phase showed that data met the assumptions of normality. These results were confirmed with visual representation of the boxplots and scatterplots indicating no outliers and with the transformation of the raw scores into Z-scores Z<2.5.

Table 3. Descriptive statistics for the outcome measures by time assessments points

Table 3. Descriptive Statistics for Outcome Measures by Time Assessment Points															
	Delay Entry Control						ePST						Test Statistics		
	Baseline		Mid-point		Post-Treatment		Baseline		Mid-point		Post-Treatment				
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	F	P-value	Effect sizze, d
BDI-II	21.75	4.24	22.5	5.76	23.3	5.6	22.04	4.46	18.04	4.22	14.52	3.73	58.78	0.001	0.57
HCLS-20-d	1.47	0.49	1.49	0.49	1.6	0.46	1.54	0.53	1.43	0.43	1.2	0.41	24.91	.001.	0.36

Intervention efficacy

To provide context to our findings, we hypothesized the following: 1) Depressive symptoms will not be different between groups across time assessments, 2) Depressive symptoms would not show significant improvement over time, and 3) There would not be a treatment interaction between groups across the three time assessments (i.e. pre, mid-point, and post-treatment).

To test the main hypotheses, multiple repeated-measures analyses of variance (ANOVA) were performed. The means of BDI-II and HSCL were used to test for significant difference between groups. Partial eta square ($\eta 2$) was computed as a measure of effect size. There were only two levels of factor A (i.e., ePST and DEC). Alpha level was set at .05

As presented in Figure 2, there was a significant time effect observed for the BDI-II outcome. Importantly, there was a significant Group x Time interaction effect suggesting that the patients receiving ePST had a significantly greater improvement compared to the patients in the DEC group.

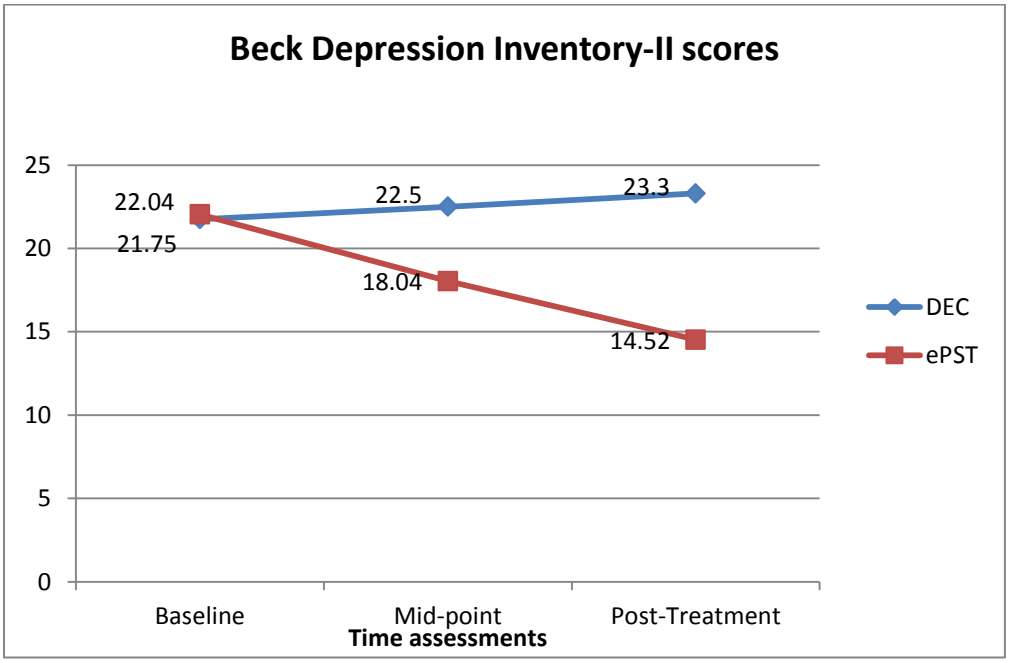
The main difference in the ePST group happened between Baseline and Mid-point, and continued decreasing between Mid-point and Post-treatment. Mean differences among the three testing occasions were tested for statistical significance. Effect sizes were examined using partial Eta squared. Mauchly Test of Sphericity was used to test for homogeneity of covariance across the three levels of the within groups factor. The Mauchly test of Sphericity sets the alpha level at .05; however, this test was significant ($p < .29$), therefore the Greenhouse-Geisser test was used to test homogeneity of variance and modify the ANOVA F. The Greehouse-Geisser test indicated a $p= .866$, which is sufficient to fail to reject the null hypothesis. There was a significant Time x Group interaction effect: F (1.73, 43)= 58.78; $p <.01$; $\eta 2 = .578$, which indicates a 'large' effect (Kinnear & Gray, 2010).

Pairwise mean comparisons were performed for the Time factor using the Bonferroni procedure. The Bonferroni test was used because we planned to have multiple comparisons protecting the inflation of the alpha level. The familywise significant level was set at .05. There was a significant reduction in the BDI-II scores from Baseline to Mid-Point (MD=1.67; $p < .001$) and from Baseline to Post-treatment (MD= 3.0; $p < .001$). We also observed a significant reduction on the BDI-II scores between Mid-point and Post-treatment assessments (MD= 1.32; $p < .001$). The 95% confidence intervals for the values of the population mean difference were: 0.58 to 2.76; 1.87 to 4.12; and 0.53 to 2.14 according to the group order above.

Group differences across times were analyzed, and results indicated a statistical difference between groups $F (1; 43)=11.81; p< .001;$ $\eta 2 = .216$. Post hoc test showed

simple main effects to be significant at Mid-Point assessment F (43,1)=10.04, p< .003, and at Post-Treatment $F(43,1)$=41.73; p < 0.001), but no significant at Baseline F (43,1) = .02; p < 0.89.

Figure 2. Beck Depression Inventory-II scores

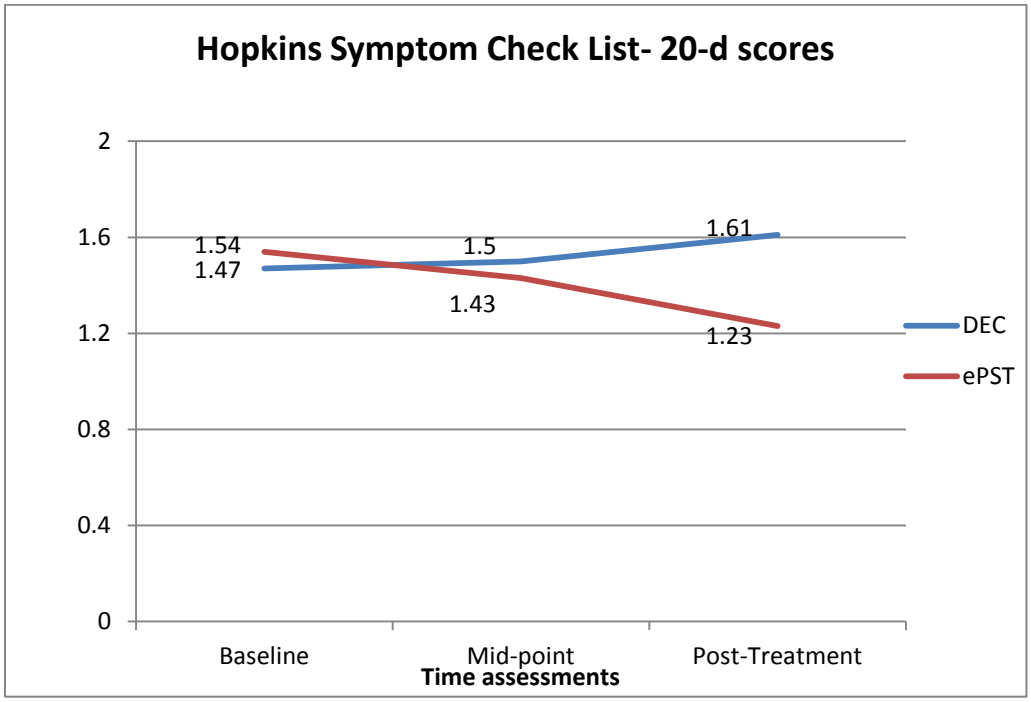


In regards to the HSCL-20-d outcome measure, the statistical analysis of the means showed a significant interaction between Time x Group, as is illustrated in Figure 3. Effect sizes were then examined using partial Eta squared. Mauchly Test of Sphericity was used to test for homogeneity of covariance across the three levels of the within groups factor; however, this test was significant (p=0.001), therefore the Greenhouse-Geisser test was used to test homogeneity of variance and modify the ANOVA F. The Greehouse-Geisser test indicated a p= .781, which was sufficient to fail to reject the null

hypothesis. There was a significant Time x Group interaction effect: $F(1.56, 43)= 24.91$; $p <.001.$; $\eta 2 = .36$, which indicates a 'moderate' effect (Kinnear & Gray, 2010). The test between-subjects groups were not significant at the 0.05 level ($p = .32$). Although there was a reduction in the HSCL-20-d scores between Baseline and Mid-Point (MD=0.03; $p < .92$) and between Baseline and Post-treatment (MD= 0.09; $p < .075$), as well as between Mid-point and Post-treatment assessments (MD= 0.49; $p < .109$) the Pairwaise comparison test, using Bonferroni, showed no significant differences between the Time factor. The 95% confidence intervals for the values of the population mean difference were: -0.54 to 0.13; -0.006 to 0.18; and -0.007 to 0.10 according to the group order above.

Finally, group differences across times were analyzed and results indicated no statistical difference $F(1,43)= 0.88; p <.035; \eta^2= 0.020$. Post hoc test found no difference between groups at Baseline $F(43,1)= .23$; $p < .633$ and at Mid-Point $F(43,1)= 0.23$; $p < .634$; however, a main effects at the Post-treatment assessment point was found $F (43,1)= 9.71$; $p < .003$.

Figure 3. Hopkins Symptoms Check list- 20-d



In summary, the clinical trial showed that participants in the ePST group improved their depression symptoms (from Moderate to Mild levels of depression) after receiving 3 session of ePST, as well as after receiving six session of ePST (from moderate to minimal levels of depression). On the other hand, participants that were assigned to the DEC group remained with Moderate levels of depression for seven weeks. The difference between the groups suggests that ePST, a computerized evidence-based intervention for depression, showed a significant improvement to treat symptoms of depression after four weeks and six weeks of use.

User Satisfaction and Program Usability

We also hypothesized that ePTS would be perceived as user-friendly. To test this hypothesis, the SUS score means were examined to determine whether the subjects found

the software treatment to be user-friendly or not. In Table 2, the group mean and standard deviations were reported for the overall average rating of user-friendliness, and means and standard deviation were reported for each question.

Table 4. Summary of the System Usability Scale scores

	Baseline		Post-treatment	
	M	SD	M	SD
1. I think that I would like to use this system frequently	2.92	0.75	3.96	0.54
2. I found the system unnecessarily complex	1.12	0.83	0.92	0.86
3. I thought the system was easy to use	3.16	0.74	3.64	0.86
4. I think that I would need the support of a technical person to be able to use this system	1.12	0.83	0.96	0.74
5. I found the various functions in this system were well integrated	3.04	0.67	3.64	0.81
6. I thought there was too much inconsistency in this system	0.92	0.86	0.76	0.72
7. I would imagine that most people would learn to use this system very quickly	2.88	0.72	3.44	0.77
8. I found the system very cumbersome to use	1	0.7	0.84	0.55
9. I felt very confident using the system	3.08	0.75	3.64	0.49
10. I needed to learn a lot of things before I could get going with this system	1.08	0.86	0.68	0.63

Note:SUS' scores ranged from 0 to 4. For the Odd itmes, higher scores indicate more agreement with ePST user-friendlyness. For the pair items, lower scores represent a more positive scores.

Participants (*N*=25) rated ePST using the SUS at Week 1(M= 76.6, SD= 7.17) and Week 6. (M=85.4, SD=5.62) on a 1-100 scale. The *T*-test was performed to determine significant changes between time points. Results showed that these changes were significant *t(24)= -9.60; p< 001*. The statistical results also indicated that participants found the program (i.e., ePST) to be usable. According to Bangor et al., (2008) in their meta-analysis, suggest that the average system score is 70 points, while Sauro (2011) suggested 68 points to be considered as average. In either case, the present

scores put ePST in the Good to Excellent range. Furthermore, these scores were consistent with another two studies where ePST was evaluated for its user-friendliness (Cartreine et al., 2013; Berman et al., 2014).

Qualitative analysis

To further understand the study's results and the efficacy of ePST to treat symptoms of depression, a semi-structured, open-ended interview was conducted at the end of the study with participants who used ePST. The goal of this debriefing session was to find out what the participants liked or disliked about the software, and to give them an opportunity to suggest improvements to the program. Of the 25 participants who completed ePST, 11 agreed to be part of this qualitative component. The interview focused on the following questions: 1) what were the things that you liked about the program?, 2) what are the things that you would change/improve in the program?, and 3) What things/factors do you think helped you improve your depression?

Things that participants liked about the ePST

Overall, participants found ePST easy to use and easy to interact with. Participants liked how straightforward and accessible the 'virtual therapist' presented the steps to identify and work on each of their problems. This feature allowed participants to have control over the time they would dedicate to their own problem solving each week. Participants also liked that they could choose what problems to work on instead of being told what to do. Furthermore, participants valued the idea of not having a 'time limit' in their session instead of feeling rushed through the time as in traditional face-to-face

therapy. Additionally, they also liked not having the pressure to talk about things that they were not ready to talk about. Another feature that was highly valuable was the fact that participants could go back and forward between the content, in other words, if they needed more time to process or better understand what the 'therapist said' they could pause the session without having to worry about losing time or waiting until the next session.

Things to improve in ePST

Participants suggested improvements to ePST regarding: Generalization, Limited Interaction, and Portability.

Generalization: participants sometimes felt that the intervention needed to be *less computer-like and more human*, meaning being more approachable and personal. For example, some of the participants would have liked to hear their name at the time of the greeting or when terminating the session with the virtual therapist.

Limited interaction: Some participants reported wanting to have additional interaction with the 'virtual therapist' (e.g., to consult other personal issues or to follow-up on other questions, alternative treatment plans and unresolved issues). For that reason, they suggested to complement ePST with a type of "live online chat" or "hotline" so they could discuss other issues that required a higher level of support (e.g., which services are the right ones for their situation). Also, they recommended using voice commands versus typing.

Portability: Although participants knew ePST was tested in a controlled clinical trial, they suggested, for practical reasons, that ePST should be accessed through the Internet instead of having to use a flash drive. Participants thought that having ePST on the web would give them real freedom to use and access the intervention 'virtually' from anywhere, at any time, and through various means (i.e., laptop and smartphones) instead of having to carry a flash drive with them all the time.

During this interview another concern raised was the protection and confidentially of their personal information, and even though it was not part of ePST, it would be relevant to consider in the future. The majority of the participants reported feeling "ambivalent" on sharing too much information about their psychological problems to the computer because they know "*that once you put something on a computer it will, or could, become public access*". Along the same lines, another fear reported was that third parties could have access to their records, and as such they could be labeled as 'psychiatric patients' and charged more from their insurance policies.

Things/Factors that helped them improve in their depression

Multiple factors were reported by the participants to be helpful in decreasing their levels of depression during the clinical trial. First, doing the study in a specialized research center where professional clinical help was available 24/7, allowed the participants to have control over their time. This notion was illustrated when one participant said, "I am finally able to schedule my therapy at a time that is most convenient to me and not to my therapist".

A second factor was that participants where encouraged to work on short-term and achievable goals instead of long-terms goals. When participants achieved their short-term goals, they not only experienced gratification—something important to feel especially if you are depressed – but also, they found that they could solve problems even though they were depressed. For example, a participant said, "I have been depressed for months and I am used to thinking that I can't do anything right because of my depression, but when I solved my first goal I realized that even though I am depressed I can do things… that made me feel happy and hopeful and also made me think that not everything is lost".

A third component was acceptance of their depression. Acceptance of their symptoms was present when participants were not excluded from the trial either because they were too depressed or because they did not want to take medication. The following statement illustrates how acceptance motivated a participant to work on their depression: "When I found that I was not rejected from the study because of my depression (i.e., moderate-severe depression) I felt hope because I was recently rejected from another depression study because 'they' found me to be too depressed to treat me… that made me feel that I was a lost cause and that I was really sick".

The last factor that participants found valuable was validation of their depression. Validation occurred in every session when participants checked in with the virtual therapist about the progress of their problems, as well as when they received tailored feedback about their levels of depression. This feedback helped participants to be aware of their thoughts, emotions, and behaviors by helping them monitor their symptoms as

well as thinking about other action plans that they could use to improve their depression. For example, a participant mentioned, “I always felt that my symptoms and my depression were something bad…but when I started my therapy I noticed that regardless of the severity of the depression the ‘virtual therapist’ always had a neutral and objective point of view and that made me feel that depression is something common, is treatable, and curable and is not an impossible mental health condition to overcome. I felt normal, and accepted by the Mark (the virtual therapist).

CHAPTER 5: DISCUSSION

Summary of the Overall Study

The current study was a randomized clinical control trial of a new computerized treatment intervention to reduce symptoms of depression in the adult population. Participants in the treatment group (ePTS group) received six sessions of the electronic Problem Solving Treatment (ePST), while participants in the Delayed Entry Control (DEC) group waited six weeks to receive ePST. An experienced clinician conducted the clinical interview, and depression measures were obtained to diagnose and detect symptoms of depression, as well as other psychological/ psychiatric illnesses. Overall, results indicated that ePST is an effective treatment to reduce symptoms of depression.

Summary of Study Results

Results indicated that depression symptoms in the ePST group significantly improved by the Mid-point time assessment and continued after the post-treatment time assessment. On the other hand, depression symptoms were maintained in the same level range (moderate to high) for the DEC group over the same time assessments, as indicated by the Beck Depression Inventory- II and the Hopkins Depression Checklist-20-d. The changes between groups regarding their depression symptoms are consistent with the Problem Solving Treatment literature (Barrett et al., 1999; Dowrick et al., 2000; Williams, 2000; Berman et al., 2013) and with several clinical trial studies that have used computerized evidence-based treatments to treat depression symptoms (Proudfoot, 2003; Warderam et al, 2008;Anderson, 2008; 2009; Meyer et al., 2009).

Treatment effects

Results indicated that ePST is an effective psychological treatment to treat adults who had moderate to moderate-severe levels of depression after three and six sessions. The efficacy of ePST to reduce symptoms of depression after three sessions is consistent with other studies where young adults and adults with depressive disorders improved their symptoms after 3 ½ hours of using problem solving therapy (Mynors-Wallis et al., 1995; Mynors-Wallis 1996). Additionally, the results from this study reinforced the notion that Problem Solving therapy, (either delivered face-to-face or via computer) is more effective when compared with no treatment, treatment as usual, and attention placebo for treating major depressive disorders (Cuijpers, van Straten et al., 2007; Malouff, Thorsteinsson, & Schutte, 2007). Also, these results prove that problem solving therapy can be administered in primary care settings by non-mental health professionals while still being an effective way of treating adults who suffer from depression (Mynors-Wallis, Gath, Day, & Baker, 2000). Additionally, these results are in line with other clinical trials where problem-solving therapy delivered via computer was seen to be as effective as face-to-face problem solving therapy (Kaltenthaler et al., 2008). Finally, these treatment results are consistent with a recent clinical trial that used ePST (Berman et al., 2014) to treat depressed patients.

Attrition rates

Our attrition rate of 100% should not be considered unusual when compared to similar computerized studies for depression. For instance, in a systematic review of computerized cognitive behavior therapy (CCBT) for depression, Kaltenthaler et al.

(2008), reported dropout rates for CCBT ranging from 0% to 75% in their studies. Furthermore, a recent study conducted by Berman et al., (2014) that used ePST, showed an attrition rate of 87%. Nonetheless, this 13% attrition rate difference in our ePST study could be attributed to the fact that our clinical trial had three study coordinators dedicated to the recruiting and monitoring of participants appointments. Therefore, these results should be interpreted with great caution.

However, it has been shown that internet and computerized interventions combined with live therapist support (i.e., interacting with study personnel) yield better outcomes and greater retention rates (Johansson & Andersson, 2012).

In summary, the study results concluded that ePST is an effective intervention to treat Caucasian women who are highly educated (i.e. at least some college) and who suffer from Moderate-Severe levels of depression.

STUDY LIMITATIONS

This clinical trial possesses multiple strengths and benefits; however, it is necessary to recognize its limitations and for that reason some cautions in interpreting the study findings are offered. The first limitation is based on the study sample and its demographics, including: educational level and computer skills, and the chosen targeted population.

Educational level and computer skills: Subjects were recruited through different media venues (e.g., flyers, emails, PCP referrals, word-of-mouth) and in diverse settings, although the majority of the participants who completed the study were college students

(i.e., undergraduate or higher level) and professional workers. Having an educated study sample, as occurred in this study, has been a common observation in computerized and Internet trials (Andersson and Titov, 2014; Beneling et al., 2011) across the board. These results could skew the outcome measures, as well as the attrition and dropout rates. For example, it is known that a typical CBT language has a reading age level of 17 years (Willliams & Garland, 2002) therefore; this may create a barrier for many individuals. Although, participants in this study were assessed for reading fluency using The Saint Louis University Mental Status Examination (SLUM), study results showed that participants with higher educational levels present with higher attrition rates, and gave higher scores to the ePST regarding its user-friendliness while participants with lower educational level gave lower scores to the same rubric**.** Although such demographic characteristics may reflect a higher socio-economic status (e.g., highly educated and having access to the Internet), it also raises the question about whether the characteristics of patients using this type of treatment interventions are similar to those accessing traditional face-to-face treatment in primary clinics (Anderssson and Titov, 2014). Nevertheless, this study proved ePST's efficacy to treat symptoms of depression and it also indicates that ePST, at this time, like other computerized interventions, needs to be tested with clinical groups and/or with groups that have lower educational backgrounds in order to assess reach. However, interpretation of these findings should not be generalized across different education and computer literacy levels.

On the other hand, the study's attrition rate could be explained by the level of education of the sample and by the design recruitment system design. As the literature

has shown, highly educated individuals tend to participate more in this type of computerized and Internet clinical interventions, thus it is common to observe high proactivity in their own recruitment and more motivation to participate in treatments; hence participants are more responsive (Andersson and Titov, 2014). Although more research is needed to draw definitive conclusions, this study offers valuable clinical implications for those Internet-based self-help treatment developers.

In summary, the majority of the studies in this field have been carried out with English-speaking individuals of higher socioeconomic status and educational levels above high school. Furthermore, additional research seems to be needed on the socio-ethnic-educational mismatch among computerized interventions. As is noted above, it is possible that this mismatch was a factor on the treatment effects by groups. Even though there have been few studies on this issue (Choi et al., 2012), there is very little research on this topic and further exploration is required. Until these interventions overcome the cultural, educational, and language barriers it cannot be determined if these innovative therapeutic interventions are a viable solution to treat mental health problems among different socio-demographic groups.

Another limitation is the use of self-reported measures (BDI-II, PHQ-9, and HSCL-20-d). Although all these measures are widely used in clinical trials and are practical tools to detect the severity of symptoms of depression, the accuracy and usefulness of the instruments depends on the individual's ability to rate him or herself accurately. This limitation might cause responders to skew their answers since some subjects may find the label of being depressed too strong; therefore, subjects may present

themselves in a positive light: more competent or in a better psychological state than they actually are; and thus their results may not be comparable across individuals. This has the potential to introduce bias as those who received the intervention may report improvement if for no other reason than being aware that they are expected to improve. The reliance on self-report measures might cause a bias on the impact of the intervention regarding participants' depression symptoms.

Although efforts to minimize this limitation were addressed in the study, (i.e., participants were clinically diagnosed by an experienced clinician before and after the trial using a clinical structured interview) study findings are based on self-reported measures, which are comprised entirely of participants' competency to complete self-reported surveys. In summary, online questionnaires work well and are helpful to the therapist to detect risks but psychiatric diagnoses cannot be reliably made using self-reported measures (Adersson and Titov 2014).

In addition to the self-reported measures and the possible limitations due to the nature of the targeted population, another limitation is the type of intervention by group. As is set in the study design, participants in the ePST group received the interventions for depression, while participants in the Delay Entry Control group did not receive any treatment. Even though several studies have used this methodology (treatment vs. waitlist or sometimes called treatment as usual) this is a considerable study limitation. The implication of this limitation lies in the possibility that it is easier to find a significant difference between treatment conditions. In other words, *getting something is better than nothing*. This effect is called a placebo effect. According to recent theories on the use of

placebo in clinical trials with patients who suffer from pain and from depression, placebo will affect the psychosocial context that surrounds the patient (Koshi & Short, 2007) and thus this context can play an important role in the outcome of treatment. In other words, if the patient perceives the study facilities as positive, the patient will feel better regardless of the intervention. The opposite is true as well, if the patient perceives the study facilities negatively, these too will have an impact on the patient's experience and performance.

One way to address this problem is by comparing ePST treatment versus self-help book intervention for depression for the same amount of sessions and through the same mechanisms (via on-line or via flashdrive). In that case, both groups would receive something that has been proven to work for depression and thus, the study will be able to show if there is a statistically significant improvement in one group over the other. By controlling the interaction of different treatments, a study could deduce if the results were caused by the ePST intervention and not by other factors.

Finally, three assessment points, in a seven week study, seems like a relatively short time to evaluate the efficacy of the intervention, in particular in assessing subjects' changes in their depression between the mid-point (week 4) and post-treatment (week 7) assessment times. Nevertheless, the Problems Solving Therapy literature has argued that patients who received PST will show significant improvements in their depression symptoms by the end of their third session (Berman et al., 2014).

In addition to this evidence, a recent meta-analysis on computerized interventions conducted by Warmerdam et al. (2008) and another study by Van Straten et al. (2008)

have highlighted that many participants have shown rapid improvement within the first five weeks of treatment. A similar study conducted by Meyer et al., (2009) observed lasting therapeutic effects on patients that received a fewer number of sessions. Finally, a meta-analysis conducted by Van Straten et al., (2008) and by Warmedarm et al., (2008) showed that treatments with less than 8 sessions showed similar treatment effects to those studies that have 8 sessions. Even though treatment effects are significant in this study, researchers in the field of computerized intervention have suggested conducting studies that incorporate longer follow-ups in order to detect the long-term treatment effects of the interventions (Chistensen et al., 2004); (Mackinnon et al., 2008), since these are lacking in the field. Therefore, further research with longer follow-up periods is needed, in particular because help-seeking and health care users might be affected over time as an effect of treatment (Christensen, Leach, Barney, Mackinnon, & Griffiths, 2006).

The last limitation of the study consists of the amount of interaction that participants had with the study personnel. Although we made several efforts to have minimal contact with participants (i.e., less than 3 min. per session) direct contact (e.g., make appointments, meeting with study staff during the time assessments, and meeting with professional mental health providers when participants reported being suicidal) and indirect contact (e.g., receiving emails by the study personnel to remind them about appointments) should be considered as external factors that could have influenced the treatment outcomes.

Therefore, our findings should be interpreted taking into account these interactions at the time to determine whether ePST could be used as a stand-alone

intervention for depression or as an adjunct treatment for depression. Furthermore, more research is recommended to determine the therapeutic status of ePST ™

In summary, despite the limitations described herein, the results of this randomized clinical control trial provide support for the significance and value of ePST as an evidence-based treatment intervention based on Problem Solving therapy to treat depression in adults. Further evaluation of this intervention is recommended in order to maximize its utility and impact.

POTENTIAL BENEFITS

It is not surprising that the World Wide Web could be the channel to reach individuals who present anxiety and depression symptoms worldwide, and that Internet interventions could be the solution to treat them. Given that health care is one of the most common reasons for using the Internet (Powel and Clarke, 2002), individuals with anxiety and depression are particularly likely to seek information and resources online (Berger, Wagner and Baker, 2005).

Internet-based interventions report multiple benefits, including: (1) being used as diagnostic tools (Slack et al., 1966; Robison et al., 1998; Budman, 2000; Muñoz, 2010), (2) as adjuncts to or as stand-alone treatments in health care facilities. For example, primary care physicians, non-mental health and mental health specialists can use these interventions during assessments and as a psycho-educational tool, before, during and after treatment, and throughout the recovery phases (Hikie, et al., 2010, Andrews and Titov, 2010).

As a primary treatment, computerized and Internet-based interventions are effective when health care resources are limited and when no other interventions for specific health problems are available (Muñoz, 2010); (3) Internet-based interventions are significantly cheaper in comparison with medical and psychiatric interventions, as well as for the maintenance of the program and the web site, and for adding new features to interventions; (4) interventions can be shared globally without taking resources away from the population where the interventions were developed (Muñoz, 2010); (5) accessibility decreases logistic barriers to treatment, portability and improved self-monitoring (Newman, Consoli, & Taylor, 1999; Palmer, Bor, & Josse, 2000; Yager, 2001), as well as reducing health care disparities; (6) Internet interventions can reach a mass audience, providing them with evidence-based psychological interventions 24/7, 365 days a year across the world (Christensen and Griffiths 2002; Muñoz, 2010); (7) technology-assisted therapy can increase access to services from remote and isolated environments (e.g., International Space Station, Antarctic research base), to rural satellite clinics as well as state-of-the-art hospitals in metropolitan areas (Newman, 2011); and (8) language barriers can be reduced with the use of Internet-based interventions in primary care clinics, since any Internet intervention can be developed according to the patient's language, sex and even race preferences, as well as in formats that do not require literacy (Muñoz, 2010).

There is a pressing need to provide evidence-based treatment to persons who do not have access to, or choose not to access traditional mental health services.

Interventions delivered via electronic technologies have the potential to meet this need (Cartreine, Ahern, & Locke, 2010).

FUTURE DIRECTIONS

Depression is a common mental disorder and it is the number one cause of disability worldwide (Murray & Lopez, 1996). Depression also affects the course and outcome of common chronic conditions (e.g., arthritis, asthma, cardiovascular disease, cancer, diabetes, and obesity); hence, increases the medical costs to the health care system ranging from $30-$50 billion dollars per year (Pincus, Pechura, Elinson, & Pettit, 2001). Depression studies have found that between 50% to 70% of depression detection happens in the primary clinic sectors (Depression Guideline Paner, 1993; Munoz, Hollon, McGrath, Rehm, & VanderBos, 1994 (Arnau, Meagher, Norris, & Bramson, 2001). Despite efforts from the government and the private sector to improve access to care and provide quality of treatments into the health care systems to treat individuals with depression, data suggests that more resources are needed to fulfill the demand; therefore it is important to devote our efforts into the primary clinic.

These efforts include implementation of reliable diagnostic tools (e.g., PHQ-9) and to provide effective evidence-based interventions that could be conducted by mental and non-mental health care providers as an alternative to medication treatments, such as Problem Solving Treatment. These interventions also need to help reduce the time and resources in primary care settings while at the same time have significant benefits treating patients with depression. Over the past two decades, the merging of evidence-

based interventions with Telemedicine (i.e., Tele-psychiatry) has shown to be a feasible and reliable option to treat depression and anxiety.

However, although computerized and internet interventions have been found to have multiple benefits as previously discussed (Marks, Cavanagh, & Gega 2007), and have been shown to be as effective as face-to-face therapy when treating depression (Cuijpers et al., 2010-is guided-self-help), these interventions need further research and improvements before they are treated as standalone psychiatric/psychological treatments and before they are fully implemented in health care systems. Possible directions are discussed below.

First, as has been previously discussed, one of the benefits of using computerized interventions is their easily portability and accessibility, as they can be delivered on flash-drives, PCs, laptops, smart phones, and through Internet links; nevertheless, a major concern is their poor security system, which could lead to a breach in patients' confidentiality. These therapeutic interventions seem to need to be handled as if they are medical devices in order to fulfill higher standards of confidentiality, and treat the information captured by them as if they are medical records. In other words, until computerized and/or Internet interventions establish a secure system where patients' private information is fully protected and their confidentially is granted, computerized interventions will not be able to cover some of the currents gaps (i.e., lack of mental health providers) in the mental health care system.

Second, despite that in the past decade several studies on the Internet and computerized-treatment interventions have shown the efficacy to treat depression,

conducting larger clinical trials in outpatient mental health clinics as well as in primary care settings will be required to determine and understand the real impact of these interventions. This could be done relatively easily since computerized and Internet interventions, unlike traditional therapy, can be used by hundreds and thousands of individuals simultaneously without losing its therapeutic power and at very low cost. For that reason, it is relevant to consider the potential impact of these interventions on access to evidence-based mental health care in the primary care system. Also, it is important to determine what would be the overall cost-benefit of this model in these settings.

Third, computerized and Internet interventions are flexible in their design by nature and can be adapted to reach specific target populations, including groups that historically have been marginalized or do not have access to care. For example, the program could be delivered in multiple languages (e.g., Chinese, Spanish, Portuguese and Russian), and its contents could be tailored to specific cultural backgrounds or to different levels of education. With such modifications, the effectiveness of this service could be investigated and possible barriers could be eliminated. Computerized interventions with these characteristics should be studied.

Fourth, by definition telemedicine provides assistance in certain places where limited services and resources are present. In order to implement this cost-effective method of increasing access, it is necessary to revise the current barriers to practice telemedicine. One of the most salient barriers is the question of licensing. For example, there are restrictions to practice across states. Furthermore, there are inconsistencies across states regarding regulation of telemedicine. As it is now, a number of states in the

United States do not provide licenses to practice telemedicine. Once the licensing issue is resolved, the next challenge is how to bill for the services. At the moment, the majority of health insurances in the United States health care system do not reimburse for telemedicine services. One possible solution, and an additional consideration for these interventions is the potential for these or similar interventions to be incorporated into collaborative care programs and/or into algorithm treatment care.

As we know, integrated care is an evidence supported (Cochrane and Huang, 2013) approach for treating depression in the primary care setting. The underpinnings of this approach include population tracking using technology and clinical measures, enhancing quality of care, using a multi-disciplinary team based approach, and caseload consultation. Increasingly, Integrated care models, and specifically collaborative care, have shown enhanced clinical efficacy while creating great potential for cost saving for the health care system (Katon, 2012). A critical component of the collaborative care model is the use of algorithmic treatment intervention. One such model, IMPACT, does it this way. Our study is not directly involved in an integrated model, however, given its low cost, evidence supported treatment efficacy, and flexible dissemination it lends itself to be an incorporated algorithm of care.

Finally, the current study took an important first step towards the creation of a new computerized intervention to treat depression in primary care and possibly in remote and isolated environments. In addition, this study could contribute to expanding the current limited literature on computerized and Internet interventions available in the U.S. and to treat individuals living in the U.S. who currently suffer from depression.

In summary, this study illustrated how psychological theories, interventions, and technology could work together to provide quality access to individuals, most of whom were from higher education and socioeconomic levels. The next step in this research is how to tailor the intervention to those that do not have the resources to do traditional psychotherapy, and/or from lower education and socioeconomic levels, or to those who prefer other treatment options.

APPENDICES

Appendix 1- Demographic Questionnaire
Appendix 2- Medical and Psychological Exclusionary Criteria Questionnaire
Appendix 3- Inclusionary Criteria Questionnaire
Appendix 4- Measures (PHQ-9, SUS, BDI-II, HSCL-20-d,)
Appendix 5- Procedural Manual for Safety
Appendix 6- Monitoring for Depression and Risk of Suicide protocol

Appendix 1- Demographic Questionnaire

Demographic protocol							
Ethnicity	Hispanic	Caucasian	Asian	African American	Pacific	Other	
Gender	M	F	Other				
Age > 18: Age =							
Date of birth							
College Student	Undergraduate Major	Graduate Major	Level of education				
Computer Skills > 3 times a week	Low	Mid 6 to 7	High >8				
Able to read and write English							
Meet the criteria						YES	NO

Appendix 2- Medical and Psychological Exclusionary Criteria Questionnaire

Script: I would like to ask you a couple of questions and please ***answer them*** *to the* ***best of your knowledge. If at any point you feel uncomfortable, you are free to stop the interview.***

Medical or Psychological Exclusionary Criteria Questionnaire			
	YES	NO	
Have you ever had a head injury? If yes, did you lose consciousness? If yes, for how long? If yes, do you remember the incident? How long ago was it? Did you experience problems afterward? What kind?			
How many drinks do you have in a regular week? Cutoff 25 or more*?			
Ask for: the size of the glass, and the substance type (e.g., beer, liquor, etc? Generic measure/*			
Have you been formally Dx with a substance used disorder?			
Are you currently taking antidepressant medication? Name:			
Are you currently taking antipsychotic medication?			
Have you been formally D x with a personality disorders (e.g., schizoid, Borderline)			
Have you been formally Dx with bipolar, schizophrenia, brain damage?			

Appendix 3- Inclusionary Criteria Questionnaire

Inclusionary Criteria

Script: I would like to ask you a couple of questions and please ***answer them*** *to the* ***best of your knowledge. If at any point you feel uncomfortable you are free to stop the interview.***

Inclusionary Criteria Questionnaire			
Depressed according to PHQ-9		YES	NO
How old are you?			
How often do you use a computer? How much time do you spend on a computer?			
Is English your first language? If not, which is it? Where did you learn English? For how long have you been speaking English?			
Are you receiving psychological or psychiatric treatment at this time? If yes, for how long?			
Have you been diagnosed with depression? If yes, When were you diagnosed?			
Are you planning to undergo to psychological treatment soon? If yes, where are you planning to attend?			
Administer PHQ-9, without item #9 (i.e., suicidality)	Score above 10=		

Appendix 4- Measures

A) Patient Health Questionnaire-9

PHQ-9					
		Not at all	Several Days	More than half the days	Nearly every day
1	Little interest or pleasure in doing things	0	1	2	3
2	Feeling down, depressed, or hopeless	0	1	2	3
3	Trouble falling or staying asleep, or sleeping to much	0	1	2	3
4	Feeling tired or having little energy	0	1	2	3
5	Poor appetite or overeating	0	1	2	3
6	Feeling bad about yourself-or that you are failure or have let yourself or your family down	0	1	2	3
7	Trouble concentrating on things, such as reading the newspaper or watching televisions	0	1	2	3
8	Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9	Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
Total					

Total Score	**Depression Severity**
1 – 4	Minimal Depression
5 – 9	Mild Depression
10 – 14	Moderate Depression
15 – 19	Moderately severe Depression
20 – 27	Severe Depression

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Appendix 4- Measures Contd.
B) Beck Depression Inventory-II

Roche | **Beck Depression Inventory** | **Baseline**

V 0477 | CRTN: _____ CRF number: _____ | Page 14 | patient inits: _____

BDI-II | Date:

Name: _____ Marital Status: _____ Age: _____ Sex: _____

Occupation: _____ Education: _____

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. Sadness
- 0 I do not feel sad.
- 1 I feel sad much of the time.
- 2 I am sad all the time.
- 3 I am so sad or unhappy that I can't stand it.

2. Pessimism
- 0 I am not discouraged about my future.
- 1 I feel more discouraged about my future than I used to be.
- 2 I do not expect things to work out for me.
- 3 I feel my future is hopeless and will only get worse.

3. Past Failure
- 0 I do not feel like a failure.
- 1 I have failed more than I should have.
- 2 As I look back, I see a lot of failures.
- 3 I feel I am a total failure as a person.

4. Loss of Pleasure
- 0 I get as much pleasure as I ever did from the things I enjoy.
- 1 I don't enjoy things as much as I used to.
- 2 I get very little pleasure from the things I used to enjoy.
- 3 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings
- 0 I don't feel particularly guilty.
- 1 I feel guilty over many things I have done or should have done.
- 2 I feel quite guilty most of the time.
- 3 I feel guilty all of the time.

6. Punishment Feelings
- 0 I don't feel I am being punished.
- 1 I feel I may be punished.
- 2 I expect to be punished.
- 3 I feel I am being punished.

7. Self-Dislike
- 0 I feel the same about myself as ever.
- 1 I have lost confidence in myself.
- 2 I am disappointed in myself.
- 3 I dislike myself.

8. Self-Criticalness
- 0 I don't criticize or blame myself more than usual.
- 1 I am more critical of myself than I used to be.
- 2 I criticize myself for all of my faults.
- 3 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes
- 0 I don't have any thoughts of killing myself.
- 1 I have thoughts of killing myself, but I would not carry them out.
- 2 I would like to kill myself.
- 3 I would kill myself if I had the chance.

10. Crying
- 0 I don't cry anymore than I used to.
- 1 I cry more than I used to.
- 2 I cry over every little thing.
- 3 I feel like crying, but I can't.

Subtotal Page 1 | Continued on Back

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11. Agitation

0 I am no more restless or wound up than usual.

1 I feel more restless or wound up than usual.

2 I am so restless or agitated that it's hard to stay still.

3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

0 I have not lost interest in other people or activities.

1 I am less interested in other people or things than before.

2 I have lost most of my interest in other people or things.

3 It's hard to get interested in anything.

13. Indecisiveness

0 I make decisions about as well as ever.

1 I find it more difficult to make decisions than usual.

2 I have much greater difficulty in making decisions than I used to.

3 I have trouble making any decisions.

14. Worthlessness

0 I do not feel I am worthless.

1 I don't consider myself as worthwhile and useful as I used to.

2 I feel more worthless as compared to other people.

3 I feel utterly worthless.

15. Loss of Energy

0 I have as much energy as ever.

1 I have less energy than I used to have.

2 I don't have enough energy to do very much.

3 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0 I have not experienced any change in my sleeping pattern.

1a I sleep somewhat more than usual.

1b I sleep somewhat less than usual.

2a I sleep a lot more than usual.

2b I sleep a lot less than usual.

3a I sleep most of the day.

3b I wake up 1–2 hours early and can't get back to sleep.

17. Irritability

0 I am no more irritable than usual.

1 I am more irritable than usual.

2 I am much more irritable than usual.

3 I am irritable all the time.

18. Changes in Appetite

0 I have not experienced any change in my appetite.

1a My appetite is somewhat less than usual.

1b My appetite is somewhat greater than usual.

2a My appetite is much less than before.

2b My appetite is much greater than usual.

3a I have no appetite at all.

3b I crave food all the time.

19. Concentration Difficulty

0 I can concentrate as well as ever.

1 I can't concentrate as well as usual.

2 It's hard to keep my mind on anything for very long.

3 I find I can't concentrate on anything.

20. Tiredness or Fatigue

0 I am no more tired or fatigued than usual.

1 I get more tired or fatigued more easily than usual.

2 I am too tired or fatigued to do a lot of the things I used to do.

3 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

0 I have not noticed any recent change in my interest in sex.

1 I am less interested in sex than I used to be.

2 I am much less interested in sex now.

3 I have lost interest in sex completely.

3 4 5 6 7 8 9 10 11 12 A B C D E

_____ Subtotal Page 2

_____ Subtotal Page 1

_____ Total Score

Appendix 4- Measures Contd.

C) Hopkins Symptom Checklist 20-item Depression Scale

HSCL-20-d

Instructions

Below is a list of problems and complaints that people sometimes have. Please read each one carefully. After you have done so, please circle the numbered answer that best describes HOW MUCH THAT PROBLEM HAS BOTHERED OR DISTRESSED YOU DURING THE PAST WEEK INCLUDING TODAY.
Circle only one answer for each problem and do not skip any items.

How much were you bothered by

	Not at All	A little bit	Moderately	Quite a bit	Extremely
1. Feeling low in energy or slowed down	0	1	2	3	4
2. Thoughts of ending your life	0	1	2	3	4
3. Poor appetite	0	1	2	3	4
4. Crying easily	0	1	2	3	4
5. Feeling of being trapped or caught	0	1	2	3	4
6. Blaming yourself for things	0	1	2	3	4
7. Feeling lonely	0	1	2	3	4
8. Feeling blue	0	1	2	3	4
9. Worrying too much about things	0	1	2	3	4
10. Feeling no interest in things	0	1	2	3	4
11. Trouble falling asleep	0	1	2	3	4
12. Loss of sexual interest or pleasure	0	1	2	3	4

13. Feeling hopeless about the future	0	1	2	3	4
14. Thoughts of death or dying	0	1	2	3	4
15. Overeating	0	1	2	3	4
16. Awakening in the early morning	0	1	2	3	4
17. Sleep that is restless or disturbed	0	1	2	3	4
18. Feeling everything is an effort	0	1	2	3	4
19. Feelings of worthlessness	0	1	2	3	4
20. Feelings of guilt	0	1	2	3	4

Appendix 4- Measures Contd.
d) System Usability Scale Measure

SUS					
	Strongly agree Disagree				Strongly
1. I think that I would like to use this system frequently.	1	2	3	4	5
2. I found the system unnecessarily complex.	1	2	3	4	5
3. I thought the system was easy to use.	1	2	3	4	5
4. I think that I would need the support of a technical person to be able to use this system	1	2	3	4	5
5. I found the various functions in this system were well integrated.	1	2	3	4	5
6. I thought there was too much inconsistency in this system.	1	2	3	4	5
7. I would imagine that most people would learn to use this system very quickly.	1	2	3	4	5
8. I found the system very cumbersome to use.	1	2	3	4	5
9. I felt very confident using the system.	1	2	3	4	5
10. I needed to learn a lot of things before I could get going with this system.	1	2	3	4	5

Appendix 5- Procedural Manual for Safety

This Procedural Manual for Safety addresses the following IRB requirements:

1. Principal Investigator (PI) and Co-Is have the responsibility to monitor all aspects of this study, including adverse events, on a continuing basis, and to report adverse events according to the IRB guidelines.
2. PI and Co-Is are responsible for notifying the IRB at the BIDMC about unexpected serious adverse events (AE's) within seven (7) calendar days.
3. PI and Co-Is are responsible for creating the guidelines for suspending any subject's participation in the study in the event of any serious adverse event or any unexpected moderate adverse event.

In this study, the Procedural Manual for Safety addresses the safety concerns listed above.

Note that participants who report a history of suicide attempts, substance abuse, or other major psychiatric comorbidities will be screened out of the study, as is stated in the study criteria.

A. Pre-Eligibility Screening Phone Interview

1. Research participants in this study are deemed to be at mid- to high risk of harm.

2. Potential Participants will be pre-screened over the telephone by a trained study coordinator to determine their eligibility to participate. No identifying information, hence no private health information, will be collected at this stage of recruitment, nor can any doctor-patient relationship be established. The pre-eligibility screening will occur during the recruitment process and prior to both enrollment and informed consent in order to eliminate participants with serious psychopathology that might require immediate psychiatric evaluation and treatment. The thoroughness of this pre-eligibility screening makes it unlikely that inappropriate participants will be enrolled. The study population will be selected to be mid- to high functioning with symptoms consistent with Major Depression Disorder (see protocol B, section C for inclusion/exclusion criteria). However, should a participant entered in the study later be determined to be in too much distress to participate, the study coordinators will speak with the participant and explain that the experimental treatments provided during the study may not be sufficient for their needs and will recommend that they speak with their primary care physician about seeking a mental health evaluation for treatment. Potential participants will be advised of this possibility during the recruitment pre-eligibility screening call and for those who are enrolled, it will also be documented in the Informed Consent Form (ICF).

2.a. Script for eligibility rejection (greater than the threshold for symptom severity or comorbidity exclusion)

Thank you for providing this information. Your answers indicate that the treatments we are testing may not be suitable for you. However, because of the symptoms you are having, I recommend you contact your primary care doctor and ask to be evaluated for possible depression. If you prefer or you don't have a primary care doctor there's a toll-free number for mental health treatment (800-981-4357). If you call that number, they will help you to set up an evaluation by a mental health professional. Do you have any questions?

3. The Pre-screening eligibility phone call interview will include administration of the PHQ-9, a measure that can detect the presence of depressive symptoms and assesses their severity. Note: Participants in this phase will be only required to answer the first 8 questions of the PHQ-9. Questions regarding possible suicidal ideation, plans or attempts or thoughts about hurting themselves (i.e., Item 9 "Thoughts that you would be better off dead, or of hurting yourself" in the PHQ-9), will only be asked during the In-Person Intake session by the Study Coordinator. Such measure was determined by the study personnel in order to provide, if necessary, safety to the potential participants.

B. 2) In-person Intake session (Safety plan was developed in coordination with the CRC Nursing)

During the In-Person Eligibility screening, it is possible that the Study Coordinator will detect levels of distress or psychiatric symptoms indicating that participants need additional care beyond the treatment offered in the study. Should this occur, the Study Coordinator will speak with the participant (who has been advised of this possibility during the eligibility phone call) and tell them that the level and/or nature of the distress they are reporting indicates that the treatment offered in the study would not likely be adequate for them and recommend that they speak with their primary care clinician and seek evaluation by a behavioral health specialist. The Study Coordinator will ask the participant to wait in the room while he/she contact responsible medical coverage in order to do the evaluation. Alternatively, they may choose to call the intake coordinator of their own health care network.

We will exclude from participation individuals who endorse PHQ-9 item #9 ("Over the last two weeks, how often have you been bothered by …thoughts that you would be better off dead, or of hurting yourself in some way") or endorse HSCL-20-d item # 14 ("How much were you bothered by …thoughts of death or dying?) to screen for suicide risk.

Participants who endorse Item #9 or #14 as "not at all" will be considered eligible but not those who endorse "several days", "more than half the days" or "nearly every day" on the PHQ-9 or "a little bit, "Moderately", "Quite a bit", and "Extremely" on the HSCL-20-d. Thus, the score for item #9 and #14must equal = 0 (Zero). Participants who score 1, 2, 3

on the PHQ-9 or 1- 4 on the HSCL-20-d will be excluded. In such instances, the study coordinator will explain the reason for exclusion as described in section 3a or 3b. When the participant has indicated a score of 1 or higher on item #9 or #14, the study coordinator will use the following script:

3a. Script for eligibility rejection (possible suicidal risk)

Thank you for providing this information.

> *Your answers indicate that the treatment we are offering in this study may not be suitable for you. However, because of the symptoms you are having, I am contacting the medical coverage right now, so you can be evaluated by one of them, please wait here in this room until help arrives. (A safety measure will be implemented according to the severity, risk and distress of the participants, see below). Also I will recommend you contact your primary care doctor as soon as possible. Because you checked off that you are having frequent thoughts you would be better off dead or of hurting yourself in some way, it's important that you be evaluated for treatment. Depression is a highly treatable condition and you need help right away. It is important that you call your primary care doctor within the next 24 hours and explain that you need to be seen as soon as possible, but definitely within the next two days. If your doctor cannot see you that quickly, ask where can you be referred for an urgent evaluation. If they are closed due to a weekend or holiday, you should go to your community hospital's emergency room. If you prefer, there's a toll-free number for mental health treatment (800-981-4357). If you call that number, they will help you set up an evaluation by a mental health professional and can make arrangements for you to be seen immediately. Do you have any questions? May I call you back in two days to check to be sure you've been able to find help?*

3.b Script for eligibility rejection (serious suicidal risk)

In the event that during the In-Person Intake session suggests that the prospective subject is in great distress and in urgent need of emergency psychiatric care with a considerable risk of self-harm, the patient should wait in the designed room at the BIDMC-CRC facilities while the Study Coordinator contacts the study medical coverage.

While participant is waiting the Study Coordinator will provide to participant the contact number for an emergency mental health crisis (*800-981-4357*) or 911 or refer to the nearest ED and assistance offered to facilitate a transfer of the person to a provider who can take responsibility for the person's safety. Also a specific plan will be implemented. The study coordinator should stay in contact with the patient until care has been arranged, or until a family member, friend, or ambulance has agreed to bring the person to an ED for evaluation.

I'm very concerned about how much distress you are in. You need medical evaluation and treatment right away. (A safety measure will be implemented according to the severity, risk and distress of the participants at this time- see below). Can you call your primary care doctor and see if s/he can arrange for you to be seen right away? Can you call 911 or 800-981-4357? Is there someone who can bring you to your local hospital emergency room? Is there a mental health clinician who has treated you whom you could call right now?

Suicide risk assessment

Patients eligible for participation in the study are deemed to be suffering from depression and to be at middle to low risk for suicide based upon interview and structured self-report measures. To be enrolled, participants must not have reported more than occasional suicidal ideation and must have no history of suicide attempts or intentional self-injurious behavior.
This will be determined by the following methods:
The Patient Health Questionnaire 9 or PHQ-9 will be administered during the Enrollment Evaluation. Participants must endorse item 9, "Thoughts that you would be better off dead, or of hurting yourself*"* as 0 = "Not at all."

0 Not at all
1 Several Days
2 More than half the days
3 Nearly every day

The Hopkins Symptom Check List-20-d (HSCL-20-d) will be administered during the following assessments: Baseline (week 0), Mid-point (week 4), Post-treatment (week 7), and Follow-up (week 14). Participants must endorse item 14 " thoughts of death or dying" as 0= "Not at all" to participate in the study.

0 Not at all
1 A little bit
2 Moderately
3 Quite a bit
4 Extremely

C. Evaluation During Treatment

What if a patient's depressive symptoms worsen during their participation in the study and s/he develops suicidal ideation or severe depression?
Each week during the study, participants in the ePST group will complete the PHQ-9. During treatment and after follow-up, they will again complete the HSCL-20-d. DEC group will fill the measures at baseline, mid-point, post-treatment, and a 2-month follow-up session.

During any of these sessions or time assessment points, if the participant indicates on the PHQ-9 or / and on the HSCL-20-d an increase to the score of 1 or greater on item 9 or item 14 (*suicidal ideas*) compared to the score on the previous visit, the Study Coordinator will contact immediately (i.e. within 10 minutes of observing the increased score) the psychiatric backup.

Suicide Risk Protocol

Severe Risk (ideation +, plan +, intent +, means +)

1. If the patient is deemed to be at severe risk of suicide the Study Coordinator will: 1) immediately (i.e. within 10 minutes of observing the increased score) contact the psychiatric backup; 2) Call Security to assist in monitoring patient safety during care and transfer. In this situation participants will never be left unattended and Security must be present until a mental health specialist comes to assess the situation.
3. The Study Coordinator will call the psychiatric backup and one of them will determine the situation and the course of action that must be taken.

High Risk (ideation +, plan +, intent +)

1. If the patient is deemed to be at high risk of suicide the Study Coordinator will: 1) immediately (i.e. within 10 minutes of observing the increased score) contact the psychiatric backup; 2) call Security to assist in monitoring patient safety during care and transfer. In this situation Patient will never be left unattended and Security must be present until a mental health specialist comes to assess the situation, and 3) The Study Coordinator will call the psychiatric backup and one of them will determine the situation and the course of action that must be taken

Moderate Risk (ideation +, plan+, intent -)

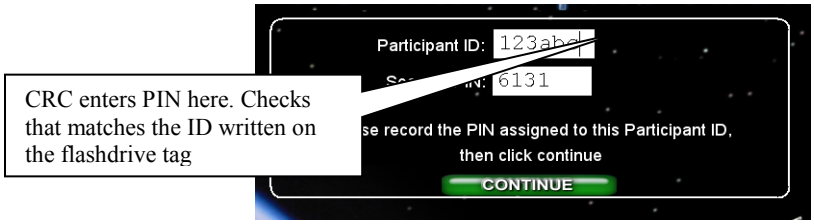
1. If participant's assessment of suicide risk is *moderate,* the Study Coordinator will: 1) immediately (i.e. within 10 minutes of observing the increased score) contact the psychiatric backup; 2) The medical coverage then will assess the situation and they will determine the course of action that must be taken.

Note: If the participant has no health insurance, the participant will be instructed to contact his or her local community hospital or community health center to arrange a mental health evaluation. Participants will be instructed to call the study coordinator within 24 hours to confirm that they have followed through and to report the date of their appointment for a mental health evaluation. 3) The Study Coordinator will call the psychiatric backup and one of them will determine the situation and the course of action that must be taken.

Appendix 6- Monitoring for Depression and Risk of Suicide protocol

Step 1: Research Nurse confirm that the Participant ID on screen matches that on the flashdrive tag.

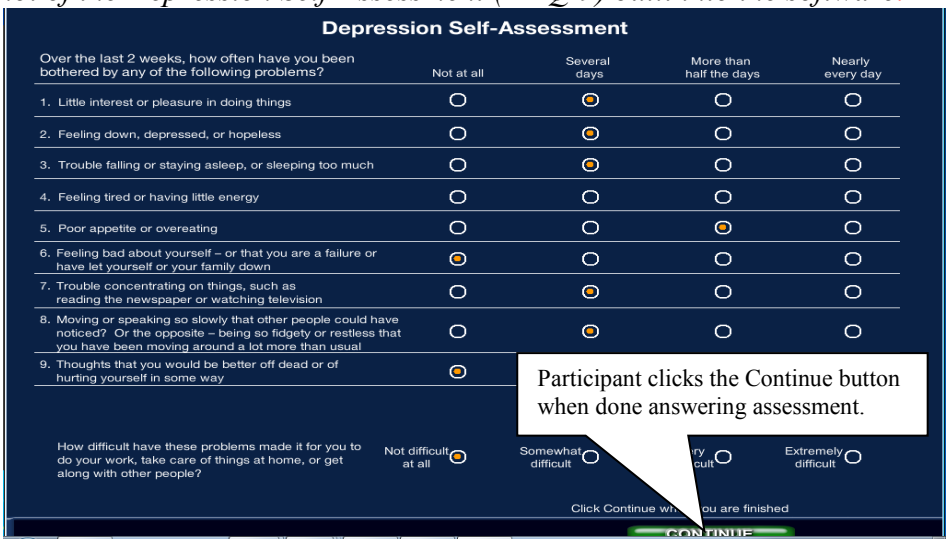
Step 2: Enter the Participant's PIN number (found on the tag).



Step 3: Participant completes the Depression Self-Assessment (called the PHQ-9).

Step 4: Participant clicks CONTINUE button when done.

Screenshot of the Depression Self-Assessment (PHQ-9) built into the software.



Step 5: Automated printout comes up.

Self-guided Treatment of Depression on Long-duration Space Flights

Confidential Patient Health Questionaire 9 Results

Indicates the level of depression

Participant ID: 123abc, on Sunday, March 31, 2013

Current depression level: 9 - Mild

1. Little interest or pleasure in doing things = 1
2. Feeling down, depressed, or hopeless = 1
3. Trouble falling or staying asleep, or sleeping too much = 1
4. Feeling tired or having little energy = 3
5. Poor appetite or overeating = 1
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down = 0
7. Trouble concentrating on things, such as reading the newspaper or watching television = 1
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual = 1
9. Thoughts that you would be better off dead or of hurting yourself in some way = 0

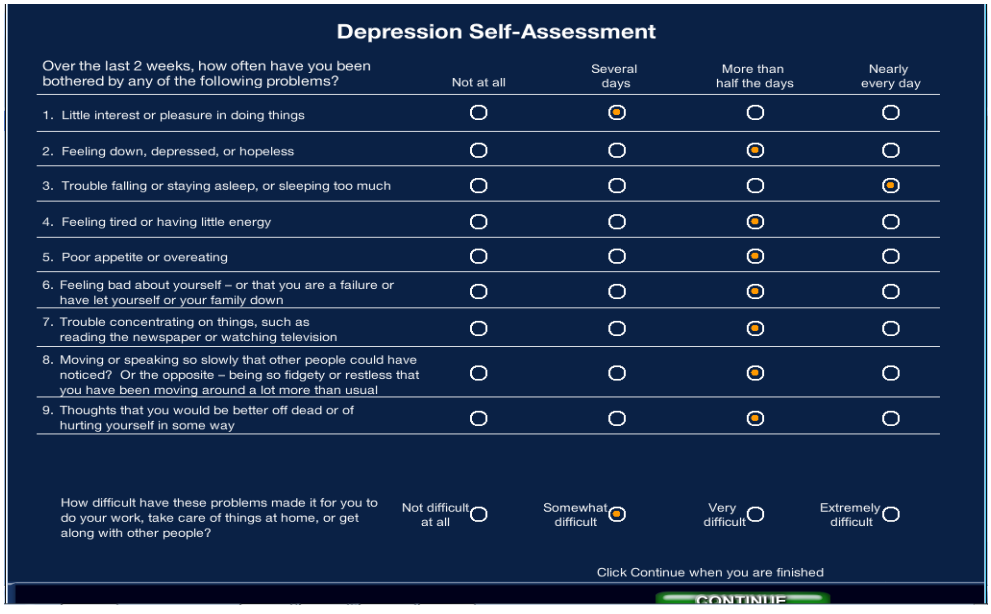
Your continuation code is 123775

Unique safety code number

Step 6: CRC nurse reviews printout. NOTE that question 9 asks about suicidal ideation.

- IF the Participant answers with a score of 1, 2, or 3 (on a 0 to 3 scale), Warning appears. (See printout example A). IF any Warnings appear, implement Procedural Protocol for Safety (*Appendix 6*).

Example of an answered Depression Self-Assessment with a score of 2 in question 9.



Depression Self-Assessment

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	○	◉	○	○
2. Feeling down, depressed, or hopeless	○	○	◉	○
3. Trouble falling or staying asleep, or sleeping too much	○	○	○	◉
4. Feeling tired or having little energy	○	○	◉	○
5. Poor appetite or overeating	○	○	◉	○
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	○	○	◉	○
7. Trouble concentrating on things, such as reading the newspaper or watching television	○	○	◉	○
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	○	○	◉	○
9. Thoughts that you would be better off dead or of hurting yourself in some way	○	○	◉	○

How difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
	○	◉	○	○

Click Continue when you are finished

CONTINUE

Example of printout A.

Self-guided Treatment of Depression on Long-duration Space Flights

Confidential Patient Health Questionaire 9 Results

Participant ID: 123abc, on Sunday, March 31, 2013

Current depression level: 18 - Moderately Severe

Indicates the level of depression

Ask patient about suicidal ideation.

Message indicates suicidal ideation. Implement procedural protocol for safety (Appendix 6).

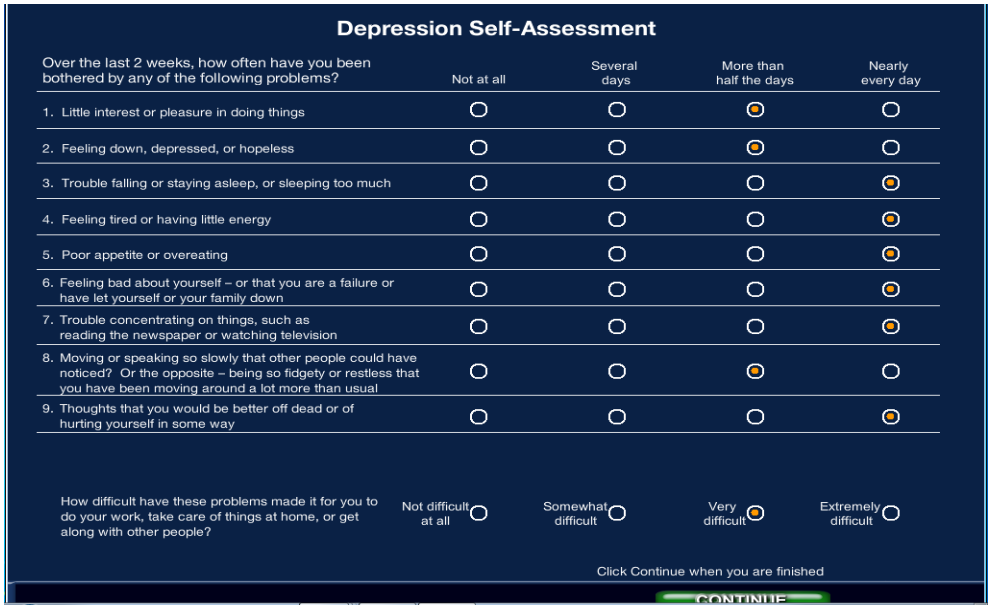
1. Little interest or pleasure in doing things = 1
2. Feeling down, depressed, or hopeless = 2
3. Trouble falling or staying asleep, or sleeping too much = 3
4. Feeling tired or having little energy = 2
5. Poor appetite or overeating = 2
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down = 2
7. Trouble concentrating on things, such as reading the newspaper or watching television = 2
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual = 2
9. **Thoughts that you would be better off dead or of hurting yourself in some way = 2**

Your continuation code is 123592

If the Q9 answer is greater than CERO, procedural protocol for safety is implemented.

- IF the Participant scores in the **Severe range** of depression, Warning appears. (See printout example B). IF any Warnings appear, implement Procedural Protocol for Safety (*Appendix 6*).

Example of a Depression Self-Assessment in the **Severe** range.



Depression Self-Assessment

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	○	○	◉	○
2. Feeling down, depressed, or hopeless	○	○	◉	○
3. Trouble falling or staying asleep, or sleeping too much	○	○	○	◉
4. Feeling tired or having little energy	○	○	○	◉
5. Poor appetite or overeating	○	○	○	◉
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	○	○	○	◉
7. Trouble concentrating on things, such as reading the newspaper or watching television	○	○	○	◉
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	○	○	◉	○
9. Thoughts that you would be better off dead or of hurting yourself in some way	○	○	○	◉

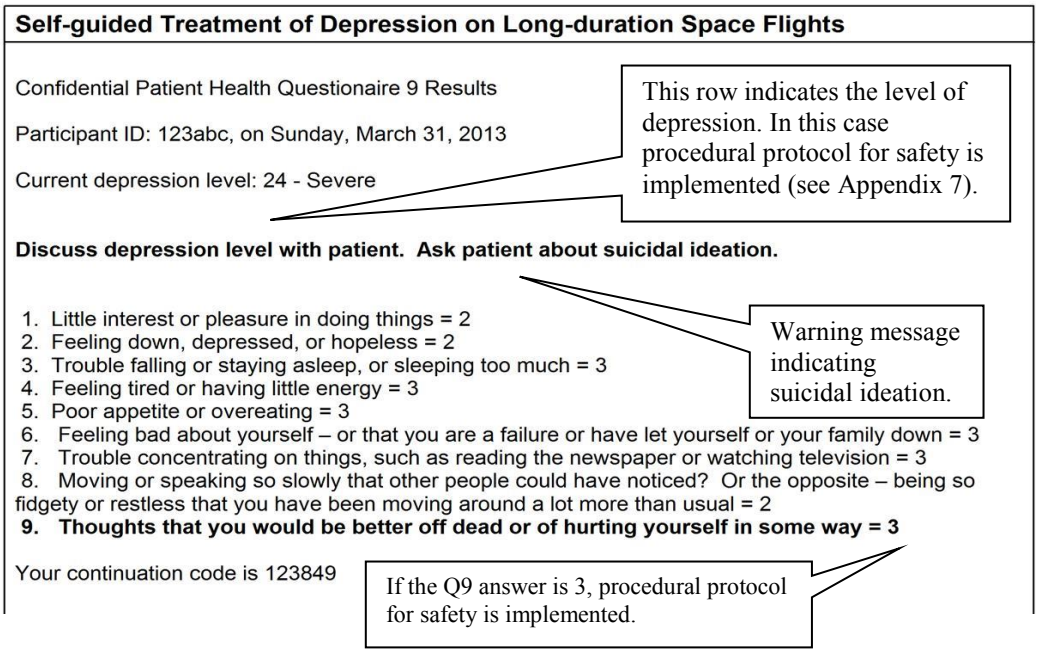
How difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all ○ Somewhat difficult ○ Very difficult ◉ Extremely difficult ○

Click Continue when you are finished

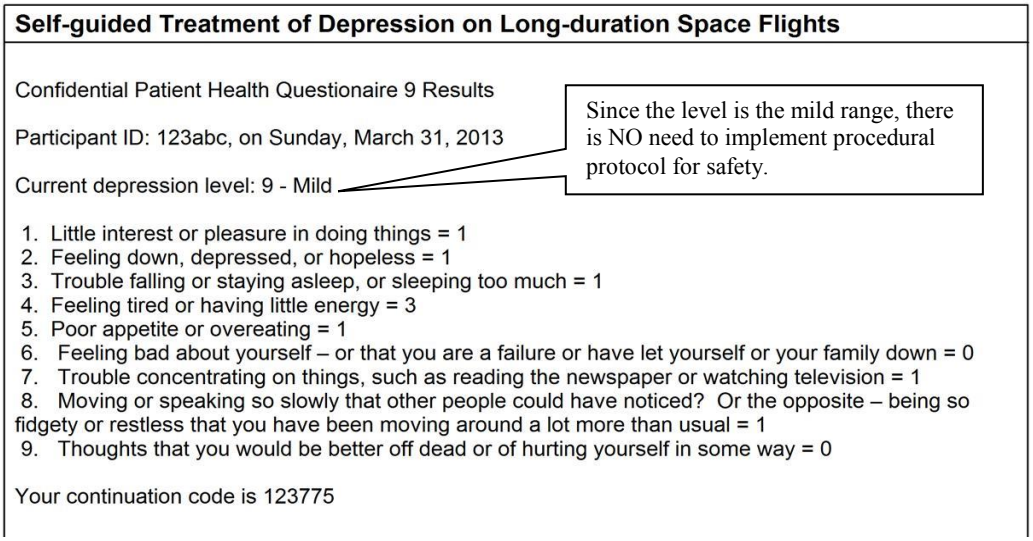
CONTINUE

Printout example B with warning message.

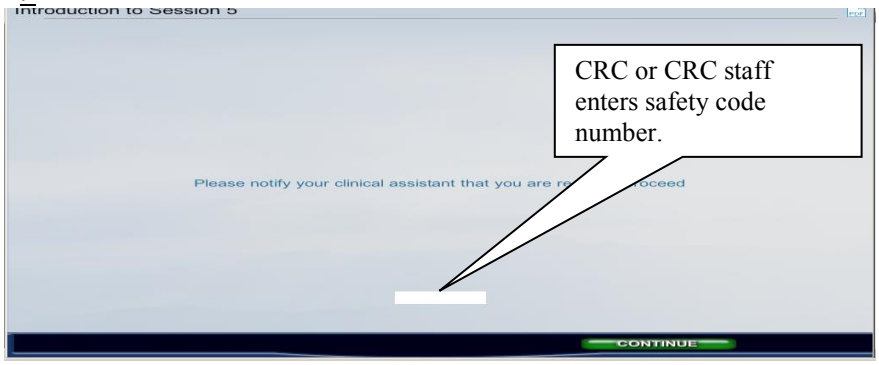


- IF the Participant scores in the **Mild** range, and does not indicate suicidal ideation, no warnings appear (see printout example C).

Printout example C



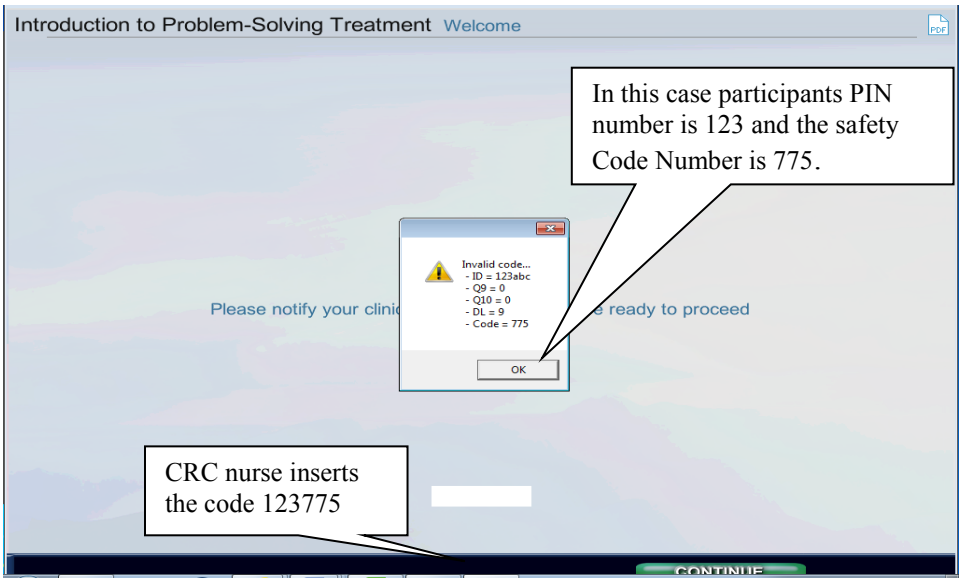
Step 7: Enter the Continuation Code, from last line of the printout.
Although the screen says "please notify your clinical assistant that you are ready to proceed, the safety code number will be only inserted by a Research Nurse if there is not suicidal risk.



Step 8: Entering PIN number with the Safety code number.

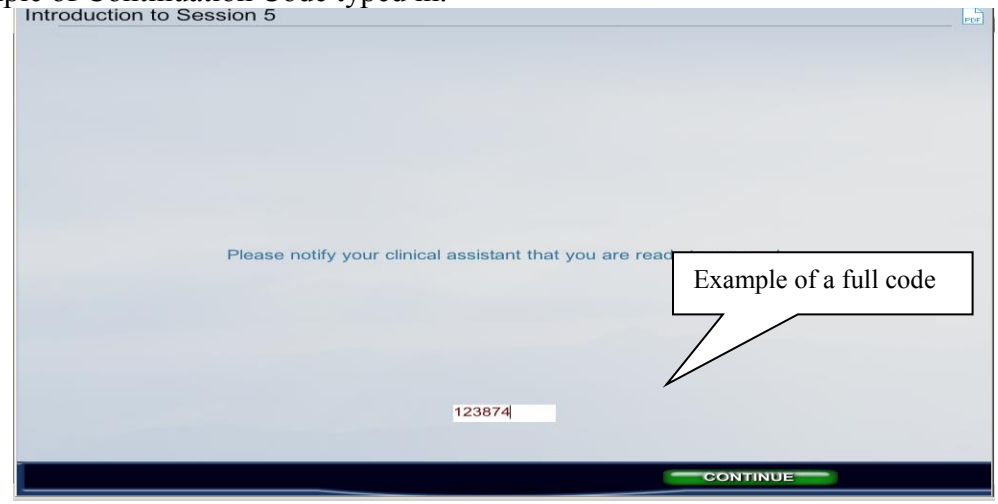
1. Continuation Code = first 3 digits of Participant Number + 3 digit "Code"
   NOTE: this screen was created to illustrate how both numbers are necessary to continue with the session.
2. [Ignore Q10. It is not relevant to this study.]CRC or Study Coordinator Clicks the CONTINUE .

   button



In this screen, the Continuation code would be 123775.

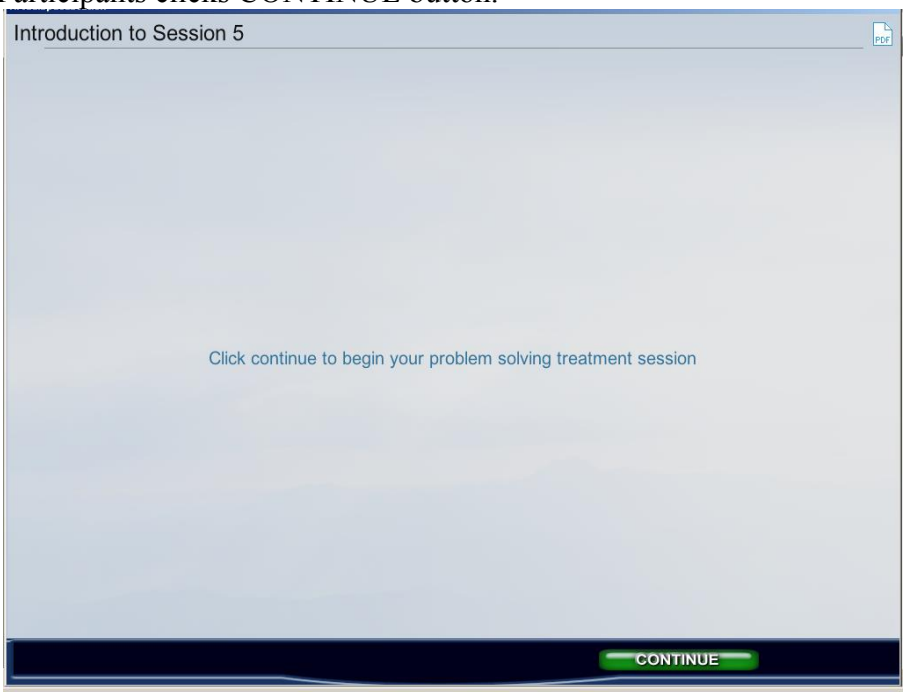
Example of Continuation Code typed in.



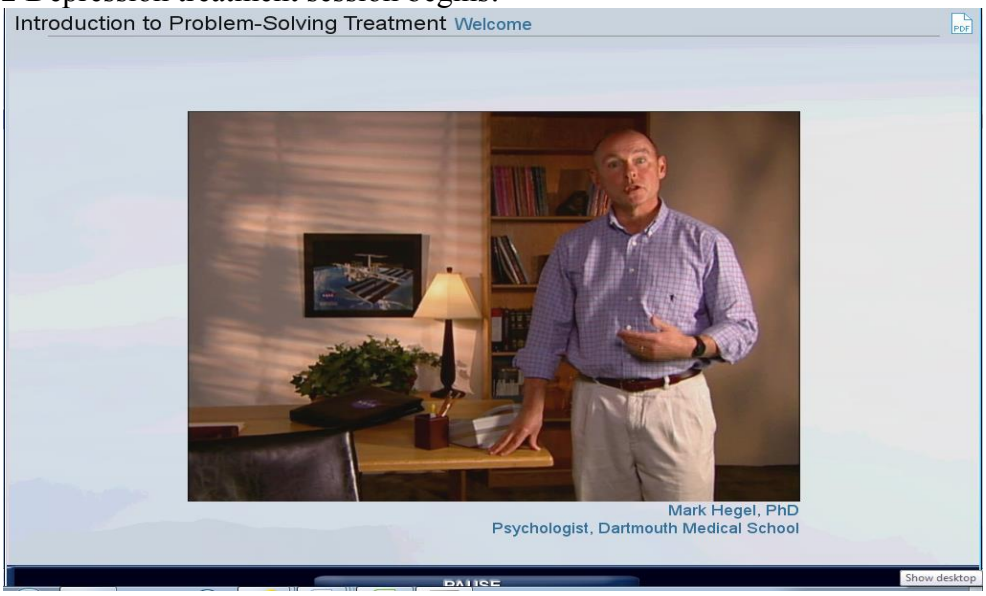
Step 9: the Research Nurse clicks CONTINUE button and authorize the participant continuing with his/her depression treatment session.

Step 10: Research Nurse leaves the room.

Step 11: Participants clicks CONTINUE button.



Step 12 Depression treatment session begins!



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