THE EFFICACY OF MULTIPLE NON-PHARMACOLOGICAL TREATMENT MODALITIES FOR DEPRESSIVE DISORDERS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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ABSTRACT

Physical activity has been theorized and shown to provide therapeutic benefits for those suffering from depressive disorders. Evidence based reviews have shown exercise to be an efficacious treatment modality to decrease depressive symptomatology. Although multiple reviews have demonstrated its effectiveness, exercise is yet to be defined as an evidence-based treatment for those suffering from depression. Thus, the aim of this review is two-fold: to perform an up-to-date meta-analysis examining the efficacy of physical activity in decreasing depressive symptomatology, and to compare physical activity, as an intervention, to three different evidence based psychotherapeutic treatment modalities.

Dedicated to the memory of my Grandfather,

Robert W. Black

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TABLE OF CONTENTS

Page

ABSTRACT …….iii

ACKNOWLEDGEMENTS……..……..v

LIST OF FIGURES…….....xi

CHAPTER

1. INTRODUCTION…….....1

Statement of the Problem…….3

Research Questions……..3

Limitations…….....4

Delimitations…….....4

Definition of Key Terms…….5

2. LITERATURE REVIEW……8

Understanding Depression……..…….…….....8

Theoretical Models of Depression…….. …….....16

Behavioral Models…….16

Cognitive Models……..…….20

Biological Models……..…….27

Integrative Model……..…….37

Interventions…….……..……...38

Cognitive Behavioral Therapy……..…….39

Behavioral Activation Therapy…….…….46

Non-Directive Supportive Therapy……...51

Physical Activity…….....57

Meta-Analysis……64

Network Meta-Analysis…….66

3. METHODOLOGY……..……..70

Research Design…….....70

Inclusion Criteria……..…….71

Participants……71

Types of Interventions……...72

Outcome Measures……74

Types of Studies…….75

Procedures……...……...75

Data Collection and Analysis.……..…….....76

4. RESULTS OF META-ANALYSES……81

Cognitive Behavioral Therapy……...81

Study Identification……81

Characteristics of Included Studies ……...81

Risk of Bias of Included Studies...…….....88

Effects of CBT Intervention with Subgroup Analysis ……..…….....94

Behavioral Activation Therapy…….....105

Study Identification……...105

Characteristics of Included Studies ……..105

Risk of Bias of Included Studies...…….....110

Effects of BA Intervention with Subgroup Analysis ……...…….....114

Non-Directive Supportive Therapy…….....121

Study Identification……..121

Characteristics of Included Studies …….122

Risk of Bias of Included Studies...…….....127

Effects of NDST Intervention with Subgroup Analysis ……..….....128

Physical Activity…….....135

Study Identification……..135

Characteristics of Included Studies …….136

Risk of Bias of Included Studies...…….....141

Effects of EX Intervention with Subgroup Analysis ……..….....145

5. RESULTS OF NETWORK META-ANALYSES…….....156

Overall NMA……...…….……...156

Waitlist NMA……...……166

Treatment as Usual NMA……176

6. DISCUSSION…….....186

Summary……...……..186

Limitations……...……200

Strengths……..203

Clinical Implications and Recommendations for Future Studies……205

Conclusion……...……....208

REFERENCES CITED…….....201

APPENDICES

A: PRISMA ITEM CHECKLIST …….....242

B: SEARCH STRATEGY……..…….....247

C: STUDY FLOW DIAGRAM ……...…….....298

D: CHARACTERISTICS OF INCLUDED STUDIES …….....299

E: NETWORK META-ANALYSIS CODES…….315

F: NETWORKK META-ANALYSIS STATA OUTPUTS……320

LIST OF FIGURES

Figure Page

1. An Integrative Model……....37

2. Risk of Bias Graph for CBT……..……89

3. Risk of Bias Summery for CBT…….90

4. Funnel Plot of Standard Error by SMD for CBT……..94

5. Overall Effect of CBT on Depression.…….96

6. Overall Effect of CBT by Control Type……..…….……98

7. Overall Effect of CBT by Treatment Length…….……...100

8. Overall Effect of CBT by Treatment Format..……..102

9. Overall Effect of CBT by Treatment Delivery Method…….…...104

10. Risk of Bias Summery for BA……..……...……...110

11. Risk of Bias Graph for BA……..111

12. Funnel Plot of Standard Error by SMD for BA……..113

13. Overall Effect of BA on Depression.……115

14. Overall Effect of BA by Control Type……..…….……...116

15. Overall Effect of BA by Treatment Format..…….117

16. Overall Effect of BA by Diagnosis Method…….…….118

17. Overall Effect of BA by Depression Severity……...119

18. Overall Effect of BA due to Number of Sessions……121

19. Risk of Bias Summery for NDST…..……...……125

20. Risk of Bias Graph for NDST……125

21. Funnel Plot of Standard Error by SMD for NDST.……...128

22. Overall Effect of NDST on Depression……129

23. Overall Effect of NDST by Control Type……..…….....130

24. Overall Effect of NDST by Treatment Format..……131

25. Overall Effect of NDST by Diagnosis Method…….……133

26. Overall Effect of NDST by Depression Severity…….....134

27. Risk of Bias Graph for EX……..……..…….141

28. Risk of Bias Summery for EX……...……142

29. Funnel Plot of Standard Error by SMD for EX..……...……145

30. Overall Effect of EX on Depression..…….……147

31. Overall Effect of EX by Control Type……..…….....148

32. Overall Effect of EX by Physical Activity Type……..……150

33. Overall Effect of EX by Exercise Frequency…….……..152

34. Overall Effect of EX by Exercise Intensity …….....153

35. Overall Effect of EX by Depression Severity……..155

36. Network Plot for Overall NMA……...157

37. Contribution Plot for Overall NMA……..…….....159

38. Inconsistency Plot for Overall NMA ……..……160

39. Funnel Plot for Overall NMA…….....161

40. Predictive Interval Plot for Overall NMA……163

41. Ranking Plot for Overall NMA…….……...164

42. Cumulative Ranking Plot for Overall NMA…….....165

43. Network Plot for WL NMA……167

44. Contribution Plot for WL NMA…….....169

45. Inconsistency Plot for WL NMA ……..……..170

46. Funnel Plot for WL NMA…….....171

47. Predictive Interval Plot for WL NMA…….173

48. Ranking Plot for WL NMA…….……174

49. Cumulative Ranking Plot for WL NMA…….....175

50. Network Plot for TAU NMA……..….177

51. Contribution Plot for TAU NMA…….....179

52. Inconsistency Plot for TAU NMA ……..……180

53. Funnel Plot for TAU NMA…….....181

54. Predictive Interval Plot for TAU NMA……183

55. Ranking Plot for TAU NMA…….……..184

56. Cumulative Ranking Plot for TAU NMA…….....185

LIST OF TABLES

1. Region and Countries of Included Trials……..……82

CHAPTER 1

INTRODUCTION

Depression is a common worldwide mental illness which, according to the World Health Organization, affects more than 300 million individuals worldwide (WHO, 2017). Major Depressive Disorder is one of the leading causes of disability in the world. In an epidemiological study of 10 high-income nations, it was found that depression had a lifetime prevalence rate of 14.6% (Bromet et al., 2011). According to the WHO, depression can be attributed to a decrease in an individual's ability to function at work, school, and other aspects of life (WHO, 2017). Although the current prevalence of depression is high, the burden of the disorder is expected to increase over time. As of 2002, depression ranked overall as the fourth disorder with the highest burden of disease, but it is projected to become the second highest worldwide, and highest in high-income countries, by 2030 (Mathers & Loncar, 2006).

Various treatment modalities have been used to treat depression, such as: pharmacological, psychotherapeutic, and psychosocial approaches. Second-generation antidepressants (selective serotonin reuptake inhibitors or selective serotonin norepinephrine reuptake inhibitors) are the most commonly used treatments for acute major depressive disorder and evidence based guidelines suggest that these medications are first step interventions (Jobest et al., 2016; Qaseem, Berry, & Kansagara, 2016). A meta-analysis published in 2008 found that up to 63% of patients on second generation antidepressants suffer adverse effects (Gartlehner et al., 2008). Due to the concerns of the general population surrounding the risks and possible harm of these medications, a trend

towards alternative treatments has been growing. There are a vast number of non-pharmacological therapies for depression. The Cochrane Depression, Anxiety, and Neurosis Group (CCDAN) lists 87 different psychological interventions (CCDAN, 2013). A recent network meta-analysis of seven psychotherapeutic treatments, including therapies such as cognitive-behavioral therapy, behavioral activation, and supportive counseling, found that all the interventions had comparable, significant benefits in decreasing depressive symptoms (Barth, 2013).

Physical activity, also referred to as exercise, has been suggested as a potential treatment for mild to moderate depression. Recent guidelines from the National Institute for Health and Care Excellence (NICE) and WHO recommend implementing exercise protocols in standard treatment for depression (NICE, 2016; WHO 2012). Several meta-analyses have shown that exercise is an effective treatment for depression. However, many of these analyses did not account for publication bias, which may cause overestimation of the effects of exercise on depression. In a 2016 meta-analysis, researchers accounted for publication bias and their statistical analysis found large antidepressant effects in patients who exercised compared to a non-active control. This study suggested the effectiveness of exercise as an evidence-based treatment for depression (Schuch et al., 2016). Most meta-analyses conducted on the effects of exercise focus on aerobic or mixed activity programs, and therefore these analyses exclude exercise programs such as yoga or tai chi. However, systematic reviews and meta-analyses do indicate the effectiveness of mindfulness- based exercise activity for depression and other mental health disorders (Larkey, Jahnke, Etnier, & Gonzalez, 2009).

The purpose of this systematic review is to analyze the body of literature surrounding multiple non-pharmaceutical interventions, suggested by NICE, for depression, as well as conduct statistical analyses to evaluate the differences in efficacy of the treatment options. Meta-analyses will be conducted on individual psychological and psychosocial interventions to evaluate changes in depression scores. If the basic assumptions for a network meta-analysis are determined have been met, and are feasible, an analysis will be run to analyze the direct and indirect comparisons between treatment options.

Statement of the Problem

Currently, there are multiple meta-analyses comparing the individual effectiveness of exercise and psychotherapeutic forms of treatment for depression. To provide well-rounded guidelines for the treatment of depression, comparisons between non-pharmaceutical interventions should be analyzed. The development of the network meta-analysis provides an effective framework by which indirect analyses can be run between individual treatment arms. If basic assumptions are determined to have been met, direct and indirect analysis will be able to compare the effectiveness of psychological and psychosocial treatments for depression.

Research Questions

The following research questions will be addressed in the study:

1) Is exercise an effective treatment for the management of depression?

2) Is exercise, as a treatment for depression, comparable to the effects of psychological forms of therapy?

Limitations

The following limitations are present in this study:

1) One potential limitation is the lack of studies with the highest methodological quality. In psychotherapeutic and psychosocial testing, it may be difficult to find studies that use blinded outcome assessment and allocation concealment.

2) Due to the basic assumptions of a network meta-analysis, it may not be feasible to conduct one, in which case, pairwise meta-analyses will be the end point.

3) Heterogeneity, or diversity, of the included articles may be high due to differences in various exercise treatments, treatment characteristics, and patient characteristics.

Delimitations

The following delimitations are present in this study:

1) Only studies in which all participants met criteria for increased depressive symptomatology will be included. This includes MDD (major depressive disorder) and dysthymia. Studies which included individuals with seasonal depression or bipolar disorder diagnosis were excluded (Kvam, 2016).

2)Studies included must have measured depression symptoms pre-and post-intervention or reported mean change and standard deviation through use of the Beck

Depression Inventory (BDI), Hamilton Rating Scale for Depression (HAM-D), or another valid screening measure.

3) All studies included were randomized control trials (RCTs) that included a usual care, waitlist control, or placebo control group.

4) Studies which included any kind of aerobic or mixed exercise protocol were included, even if it was in combination with antidepressant treatment. Studies which used mindfulness-based exercise (e.g. yoga) were excluded, but were considered as a separate treatment arm if there was deemed a significant number of RCTs to warrant analysis.

5) If the basic assumptions of transitivity and consistency were not met, any conclusions drawn from a network meta-analyses must be met with careful interpretation and limited sustainability.

Definition of Key Terms

Behavioral Activation (BA) - a form of psychotherapy where the treatment consists of registration of pleasant activities and the increase of positive interactions between a person and his or her environment (Barth et al., 2013)

Cognitive Behavioral Therapy (CBT) - a form of psychotherapy where the therapist focuses on the impact a patient's dysfunctional thoughts have on current behavior and future functioning (Barth et al., 2013)

Control group -Any group of individuals in an RCT that undergoes usual-care or waitlist control conditions (Schuch, 2016)

Depression - As defined by the DSM-5, it is a medical condition that negatively affects how a person feels, thinks, and acts, and can include the following symptoms: feeling sad, loss of interest, change in appetite, trouble sleeping, loss of energy, difficulty thinking or concentrating, and feelings of worthlessness. Symptoms must be present for at least two weeks (APA, 2017)

Exercise - a planned, structured, repetitive and purposeful physical activity (Caspersen et al, 1985).

Heterogeneity - the variation in study outcomes between studies.

Network Meta-Analysis (NMA) - An analysis that synthesizes information over a network of comparisons to assess the comparative effects of more than two alternative interventions for the same condition. It synthesizes direct and indirect evidence over the entire network, so that estimates of intervention effect are based on all available evidence for that comparison (Cochrane, n.d).

Similarity - In NMA, the situation in which different sources of direct and indirect evidence are similar with respect to the moderators of intervention effects (Cochrane, n.d).

Supportive Counseling (NDST) - typically referred to as counseling or supportive therapy in the literature; it is unstructured therapy without specific psychological techniques other than aspects such as helping people ventilate their emotions (Barth et al, 2013)

Transitivity - In NMA, when an intervention effect measured using an indirect comparison is valid and equivalent to the intervention effect measured using a direct comparison (Cochrane, n.d).

CHAPTER 2

LITERATURE REVIEW

Understanding Depression

Definition of Depression

In today's society, depression is a term that has various meanings to different individuals. For mental health practitioners, depression is a psychiatric disorder or illness that is characterized by a depressed mood and concurrent symptoms such as loss of appetite, lack of concentration, sleep inference, and suicidal thoughts (Ingram, 2012). Kendall, Hollon, Beck, Hammen, and Ingram (1987) developed an inclusive overview of the meaning of the term depression:

> The professional use of the term depression has several levels of reference: symptom, syndrome, nosologic disorder. Depression itself can be a symptom – for example, being sad. As a syndrome, depression is a constellation of signs and symptoms that cluster together (e.g., sadness, negative self-concept, sleep and appetite disturbances). The syndrome of depression is itself a psychological dysfunction but can also be present, in secondary ways, in other diagnosed disorders. Finally, for depression to be a nosologic category, careful diagnostic procedures are required during which other potential diagnostic categories are excluded. The presumption, of course, is that a discrete nosologic entity will ultimately prove to be etiologically distinct from other discrete entities, with associated differences likely in course, prognosis, and treatment response. (Beck, 1967, p. 290)

The American Psychiatric Association defines major depressive disorder as a mental illness that affects how an individual feels, thinks, and behaves, causing persistent feelings of sadness and loss of interest in previously enjoyed activities (APA, 2013). The

professional and clinical definition of depression is provided by the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). The DSM-5 is a classification system developed by the American Psychiatric Association and is used as a diagnostic tool to diagnose depression

DSM-5 Classification of Depression

In 2013, the fifth edition of the DSM was released by the American Psychiatric Association (APA, 2013). The DSM-5 separated the diagnosis of "Depressive Disorders" from "Bipolar and Related Disorders," both receiving separate chapters (APA, 2013). Within the DSM-5 there are multiple classifications of depression, which include: major depressive disorder (MDD), persistent depressive disorder (PDD), premenstrual dysphoric disorder (PMDD), disruptive mood dysregulation disorder (DMDD), depressive disorder due to another medical condition, and other specified depressive disorder and unspecified depressive disorder (Bentham, 2013). The common feature to all these disorders is the presence of sadness or irritable mood, which will be accompanied by somatic or cognitive changes that will severely affect an individual's ability to function. Differences in diagnosis are due to issues of duration, timing, or possible etiology.

Major Depressive Disorder

Major Depressive Disorder (MDD) is the most prevalent mental disorder worldwide (Kessler et al., 2005). The core symptoms of MDD, as described by the DSM-5, are the same as in the DSM-IV TR. The two core symptoms of MDD include: 1) depressed mood and 2) loss of interest or pleasure (Bentham, 2013). In order to be diagnosed with MDD,

symptoms should be present for at least two weeks and each symptom should be present each day at sufficient severity (NICE, 2013). The DSM-5 diagnostic criteria for MDD state that at least five of a possible nine symptoms need to be present during a two week period. These symptoms must not be attributable to another condition, and are:

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (Note**:** In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (Note: In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide (APA, 2013).

In addition to presenting at least five of these symptoms, individuals must clearly be in distress or be suffering from some impairment. The symptoms must involve obvious changes in affect and cognition (APA, 2013).

Persistent Depressive Disorder

As of 2013, the DSM reclassified dysthymia as persistent depressive disorder (PDD) (APA, 2013). PDD is a chronic condition defined by a depressed mood, but with symptoms not as severe as MDD (Hurley, 2017). Symptoms of PDD may fluctuate over time but in order to be diagnosed with PDD individuals must be symptomatic for 2 years (Hurley, 2017). However, it is not uncommon for individuals with PDD to feel that depression is just part of their character, and therefore may not discuss it with their doctor (Harvard Health, 2000). The DSM-5 diagnostic criteria for PDD requires an individual to have present (while distressed) two or more of the following symptoms: poor appetite or overeating, insomnia or hypersomnia, low energy, low self-esteem, poor concentration, or feelings of hopelessness (APA, 2013). These symptoms must not be absent for more than two months at a time over the two year span. Clinicians must rule out other possible explanations of symptoms such as cyclothymic disorder, schizoaffective disorder, delusional disorder, or symptoms due to the psychological effects of a substance.

Disruptive Mood Dysregulation Disorder

Disruptive mood dysregulation disorder (DMDD) is a new diagnosis in the DSM-5. DMDD is characterized by chronic, severe persistent irritability in patients (Gilea & O'Neil, 2015). The clinical manifestations of irritability include frequent temper outbursts

and a chronic and persistently irritable or angry mood between outbursts (APA, 2013). The DSM-5 criteria state that individuals must suffer from several temper outbursts that are inconsistent with their developmental level and that occur three or more times per week (APA, 2013). Individuals must be diagnosed between the ages of 6 and 18 and must have had symptoms for more than 12 months (APA, 2013). This diagnosis was added to the DSM-5 in an attempt to distinguish between children who presented with persistent irritability versus those children with a classic bipolar disorder presentation (Gilea & O'Neil, 2015).

Premenstrual Dysphoric Disorder

Premenstrual Dysphoric Disorder (PMDD) is characterized by mood swings, depressed mood, irritability, and anxiety during the luteal phase of the menstrual cycle (Grady-Weliky, 2003). The DSM-5 defines the essential features of PMDD as symptoms of mood lability, irritability, dysphoria, and anxiety symptoms that occur repeatedly during the premenstrual phase of the menstrual cycle and remit during the onset of menses (APA, 2013). At least a total of five of the following symptoms must be present, at least one symptom from each criterion.

Criterion 1:

1. Marked affective lability (e.g., mood swings; feeling suddenly sad or tearful, or increased sensitivity to rejection).
2. Marked irritability or anger or increased interpersonal conflicts.
3. Marked depressed mood, feelings of hopelessness, or self-deprecating thoughts.

4. Marked anxiety, tension, and/or feelings of being keyed up or on edge.

Criterion 2:

1. Decreased interest in usual activities (e.g., work, school, friends, hobbies).
2. Subjective difficulty in concentration.
3. Lethargy, easy fatigability, or marked lack of energy.
4. Marked change in appetite; overeating; or specific food cravings.
5. Hypersomnia or insomnia.
6. A sense of being overwhelmed or out of control.
7. Physical symptoms such as breast tenderness or swelling, joint or muscle pain, a sensation of "bloating," or weight gain (APA, 2013)

If physical or behavioral symptoms are present in the absence of mood symptoms then there is not sufficient evidence for a diagnosis of PMDD.

Substance/Medication-Induced Depressive Disorder

The features of substance-induced depressive disorder are similar to other depressive disorders, but the symptoms are associated with the intake of a substance. In addition, depressive symptoms must last beyond the expected length of the physiological effects and withdrawal period (APA, 2013). The DSM-5 diagnostic criteria for substance-induced depressive disorder require that individuals suffer from depressed mood and/or diminished interest in activities. In addition, there must be evidence that symptoms developed after the occurrence of substance intoxication or that a substance is capable of

producing the symptoms of depression. It is paramount to determine that the symptoms cannot be better explained by other depressive disorders (APA, 2013).

Depressive Disorder Due to Another Medical Condition

According to the DSM-5, the essential feature of depressive disorder due to another medical condition is persistent depressed mood that is thought to be related to the effects of another medical condition (APA, 2013). Research has provided evidence that there are comorbid associations between depression and stroke, Huntington's disease, Parkinson's disease, traumatic brain injury, Cushing's disease, and hypothyroidism (Jorge, Robinson, Moser, et al., 2004; Paulsen, Nehl, Hoth et al., 2005; Robinson, 1997). Another condition that is thought to be associated with depression is multiple sclerosis (Sadovnick, Remick, Allen et al., 1996).

Other Specified Depressive Disorder

This diagnosis is characterized by symptoms that are characteristic of a depressive disorder but they do not meet the full criteria for any of the disorders in the diagnostic class (APA, 2013). Some of the examples of disorders that will receive this designation include recurrent brief depression, short-duration depressive episodes (4-13 days), and depressive episodes with insufficient symptoms (APA, 2013).

Unspecified Depressive Disorder

Similar to other specified depressive disorders, unspecified depressive disorder is marked by presentation of characteristic depressive symptoms but individuals do not meet any full criteria for any of the depressive disorders. Subsequently, this category is used

when clinicians choose not to specify the reason that the criteria were not met, including when there is insufficient information to make a specific diagnosis (APA, 2013).

Prevalence of Depression

Depression is a common worldwide mental illness which, according to the World Health Organization, affects more than 300 million individuals (WHO, 2017). Major Depressive Disorder is one of the leading causes of disability in the world. In an epidemiological study of 10 high-income nations, it was found that depression had a lifetime prevalence rate of 14.6% (Bromet et al., 2011). There are many factors that affect the prevalence of depression - age, gender, nationality, ethnicity, and culture have all been implicated. According to the WHO, depression can lead to a decrease in an individual's ability to function at work, school, and other aspects of life (WHO, 2017). Although the current prevalence of depression is high, the burden of the disorder is expected to increase over time. As of 2002, depression ranked as the fourth disorder with highest burden of disease,but is projected to become the second-highest worldwide, and highest in high-income countries, by 2030 (Mathers & Loncar, 2006).

The prevalence of depression varies depending on a variety of variables, including sex, age, and clinical diagnosis. The 12 month prevalence of MDD in the U.S has been measured at approximately 7% (Kessler et al., 2003). A systematic review in 2012 showed the global prevalence of MDD to be 4.7% (Ferrari, Somerville, Baxter, & Norman, 2012). Again, gender is one variable that has been shown to affect the reported prevalence of depression. Across a lifetime, prevalence rates are approximately 20-25% for women and 9-12% for men (Craighead, Klein, Gillespie, et al., 2008). The rest of the DSM-5 diagnoses

are not nearly as prevalent as MDD. The prevalence of PMDD falls between 2-5% (Brotman, 2006). Other studies have determined that prevalence rate for PMDD to be estimated at 1.8% (Gehkert et al., 2009). Lastly, the prevalence of PDD, formerly dysthymia, in the United States is approximately 0.5% (Blanco et al., 2010). The prevalence rate for depression due to another medical condition cannot be pinpointed due to the variability of types of medical conditions. Epidemiological estimates have suggested that between 25-40% of individuals with certain neurological conditions (e.g., Parkinson's disease, Huntington's disease, and multiple sclerosis) can suffer from depressive symptoms during the course of the disease (Lack, 2018). For other diseases, the rates can be far more variable. The prevalence can range from 8% in end-stage renal disease patients to over 60% in Cushing's syndrome.

Theoretical Models of Depression

There are currently several models that have been theorized to possibly explain the etiology and pathology of depression. Although there is no consensus on a single mechanism by which depression occurs, it is possible that the pathology leading to its development is multi-factorial, including a combination of many of the theories discussed here. These theories include behavioral, cognitive, and biological models. In order for clinicians to best treat depression, and for clinical researchers to develop new therapies, it is important for the possible mechanisms by which depression occur to be studied.

Behavioral Models

Behavioral theories explain the development and persistence of depression and depressive symptoms as a result of decreased environmental reward, reinforcement of depressive behaviors, and punishment of healthy behaviors (Ferster, 1973; Lewinsohn, 1985; Martell, Addis, & Jacobson, 2001). Skinner (1953) proposed that depression is related to a reduction in behaviors that elicit positive reinforcement from the environment (Skinner, 1953). These ideas were further extrapolated upon by Ferster. Ferster proposed three causes that were likely to cause a shift toward depressive affect; these included, 1) infrequent positive reinforcement, 2) behaviors that are further inhibited by anxiety, and 3) unexpected changes in environmental stimuli which will decrease frequency of behaviors (Craighead, et al., 2008).

Three behavioral symptoms that are classically found in depression are anhedonia, lack of motivation, and avoidance. In addition to these classic behavioral deficits, a behaviorist theory has been proposed to explain other depressive symptomatology. The feelings of low self-esteem, pessimism, and guilt are due to being secondary elaborations of the feeling of dysphoria (Lewinsohn, 1985). Initially, individuals who are depressed begin to lose pleasure and interest in activities (anhedonia) (Craighead et al., 2008).The development of anhedonia can lead to individuals having difficulty mobilizing themselves to perform daily tasks (amotivation) (Coyne, 1986). The lack of motivation leads many depressed individuals to procrastinate and avoid work (Coyne, 1986). Avoidance serves as an attempt to prevent, escap, or reduce contact with adverse or minimally rewarding stimuli (Carvalho & Hopko, 2011).

One of the most common symptoms reported with depression is loss of motivation. Individuals suffering from depression typically recognize what they have to do but lack the motivation or energy to complete such tasks. Individuals may begin neglecting activities at home, socially, and at work or school. The cessation of completing small tasks has the ability to decrease individuals' self-efficacy. Initially developed by Albert Bandura, self-efficacy is defined as an individual's beliefs about their capabilities to produced designated levels of performance that influence events that affect their lives (Bandura, 1994). Individuals with low self-efficacy tend to dwell on their personal deficiencies when faced with a difficult task, which contributes to adverse outcomes (Bandura, 1994). Beats, Shakian, and Levy (1996) asked a depressed and non-depressed group to perform the Tower of London Planning task. The depressed group required more steps to complete the difficult problems. In addition, once participants made an error on a trial, their performance deteriorated rapidly (Beats et al., 1996). Therefore, a decrease in self-efficacy will increase a depressed individual's chances of receiving negative reinforcement and feedback (Craighead et al., 2008).

Positive reinforcement of maladaptive behaviors in individuals with depression can lead to the maintenance of depressive symptoms. Several studies have provided consistent evidence that there is an association between positive reinforcement and the intensity of depression (Coyne, 1986). Ferster (1973) first proposed that lowered frequency of positive reinforcement and an increase in negative reinforcement are reasons for depressive symptomology (Ferster, 1973). Lewinsohn's model, similar to Ferster's, recognized that symptoms of depression, specifically feelings of dysphoria, were a result of a reduction in positively reinforced behaviors (Lewinsohn et al., 1976). In addition to a decrease in

positive reinforcement, an increase in negative reinforcement may occur. Negative reinforcement refers to an increase in the frequency of avoidant and escaping behaviors (Abreu & Santos, 2008).

Research has confirmed that depressed subjects have an abnormal response to negative feedback (Elliott et al, 1996; Elliott et al, 1997; Steffens et al., 2001). Elliott et al. (1996) subjected individuals with unipolar depression to the CANTAB battery of neuropsychological tests. Researchers found that depressed patients were far more likely to fail a subsequent problem following a mistake (Elliott et al., 1996). The combination of motivational deficit, oversensitivity to negative feedback, and specific neuropsychological deficits were found to be correlated with the severity of depression (Elliott et al., 1996). In addition, individuals with remitted depression continue to show abnormal responses to negative feedback, even if their task performance improved (Elliott et al., 1997).

For individuals suffering from depression, avoidance functions to minimize distress, therefore becoming a negative reinforcer (Craighead et al., 2008). Avoidance is defined as attempts to prevent, escape, or reduce contact with aversive internal or external stimuli (Carvalho & Hopko, 2011). Cognitive avoidance coping involves minimizing, denying, or ruminating that unpleasant situations are unchangeable, while behavioral avoidance coping occurs when a problem is avoided through alternative activities or participation in temporary maladaptive behaviors (Cronkite & Moos, 1995). There are two main consequences of avoidant behavior: 1) avoidance is a short-term strategy that results in long-term difficulties and 2) avoidance reduces the ability of depressed individuals to encounter positive reinforcement in their environment (Dimidjian, Matell, Addis, &

Herman-Dunn, 2008). Longitudinal evidence has indicated that avoidance coping contributes to the etiology and maintenance of depressive symptoms (Cronkite, Moos, Twohey, Cohen, & Swindle, 1998)

Depression seems to be characterized by changes in behavior and behavioral responses. Evidence suggests that a relationship exists between depression and a decrease in, or abnormal response to, positive feedback, in addition to an increase in negative feedback. Abnormal responses to feedback lead to increases in avoidance behaviors and amotivation, which are classic symptoms of depression. These observations support behavioral theories of depression which argue that depressive symptoms are a result of decreased environmental reward, reinforcement of depressive behaviors, and punishment of healthy behaviors.

Cognitive Models

Although individuals suffering from depression can experience different combinations of symptoms, most individuals who are suffering from depression experience some type of cognitive disturbance (Craighead et al., 2008). Cognitive theories of depression originated over 40 years ago with the work of Beck and colleagues. Beck theorized that individuals who are vulnerable to depression have schemas that lead them to view their environment in negative ways (Beck, 1976). Beck's model has three main components: negative cognitive errors, self-statements, and underlying schemas or beliefs. In his model, Beck postulates that the combination of information processing deficits and negative cognitive patterns (schemas/beliefs) contribute to the development and maintenance of depression. Since Beck's initial theory and findings, researchers have been

examining cognition and emotion in major depression disorder and have expanded and updated the cognitive theories of depression (Ingram, 1984; William, Watts, MacLeod et al., 1988).

Cognitive Deficits in Depression

Cognitive theories of depression theorize that depression is associated with disturbances in cognitive processes. Congruently, the diagnostic criteria for MDD include cognitive deficits (APA, 2013); therefore, researchers have examined difficulties in cognitive function associated with depression. When compared to non-depressed individuals, studies have observed the effect of negative bias on memory processes (Hamilton & Gotlib, 2008; Joormann, Teachman, & Gotlib, 2009), attentional processes (Gotlib et al., 2004), and many aspects of executive functioning (Snyder, 2013). In addition, data indicate that depressed individuals have higher negative thoughts about self, the world, the future, and life in general (Blackburn, Jones, & Lewin, 2011).

Many of the cognitive hypotheses surrounding depression focus on cognitive deficits within the individual. The resource allocation hypothesis suggests that depression uses cognitive resources which lead to a reduction in cognitive capacity, therefore leading to difficulties in cognitive tasks (Ellis & Ashbrook, 1988). The affective interference hypothesis hypothesizes that, because depression involves a preoccupation with emotion, performance on cognitive tasks that require an individual to ignore emotional information may decline (Siegle, Ingram, & Matt, 2002). Research by Hertel supported this hypothesis (Hertel, 2004). Hertel (2004) observed that both depressed and non-depressed individuals

performed similarly on structured cognitive tasks, but depressed individuals exhibited greater memory and attention impairment on unconstrained tasks.

Multiple studies have shown that memory processes are affected over the course of depression (Austin, Mitchell, & Goodwin, 2001). Research has shown that depressed individuals frequently show deficits in episodic and learning memory (McDermott & Ebmerier, 2009).This finding seems to be consistent across research. Episodic memory and learning seem to be affected in individuals with both melancholic and non-melancholic depression (Austin et al., 1999). On the other hand, research has shown that implicit memory tasks are unaffected (Hertel & Hardin, 1990; Ilsley et al., 1995). In addition to deficits in memory, studies have indicated that depressed individuals show negative bias in recognition memory, event recall, and autobiographical memory (Joormann & Gotlib, 2007; Williams et al., 2007). This means that individuals suffering from depression are more likely to recall bad experiences rather than good ones.

Depressive disorders seem to be characterized by impairments in cognitive functioning. Systematic reviews have shown that, regardless of age, those suffering from depression are at increased risk of cognitive dysfunction (Austin et al., 2001; Castaneda, Tuulio-Henriksson, Marttunen et al., 2008; Kindermann & Brown, 1997). Joormann et al. (2010) showed that memory functioning is imperative for the regulation of negative affect.

Core Beliefs or Schemas

One of the central principles of Beck's cognitive theory of depression is the importance of underlying schemas or core beliefs. Core beliefs are defined as

"fundamental, inflexible, absolute, and generalizable beliefs that people hold about themselves, other, the world, and/or the future" (Wenzel, 2012). A core belief can have a profound impact on a person's self-concept, sense of self-efficacy, and vulnerability to depression when they are inaccurate, unhelpful, or maladaptive. Beck postulates that these enduring cognitive patterns contribute to the development and maintenance of depression (Craighead et al., 2008). In Beck's cognitive theory, core beliefs are just a larger construct of the schema. Beck and Clark (1999) define a schema as a "relatively enduring internal structure of stored generic or prototypical features of stimuli, ideas, or experience that are used to organize new information in a meaningful way thereby determining how phenomena are perceived and conceptualized." (Beck & Clark, 1999, pp. 79).

Core beliefs are cognitive contents that are indicative of a schema (Wenzel, 2012). Individuals tend to process information in a biased matter in line with their schema or core beliefs. Thus they tend to assign importance to encoding and retrieving information that is consistent with that schema, and ignoring information that is inconsistent (Wenzel, 2012). Sacco and Beck (1995) note that depressogenic schemas can begin to develop early in life and these beliefs will remain latent until they are activated by negative or stressful life events (Sacco & Beck, 1995). After these schemas are activated, they serve as a filter for incoming information. Therefore, depressogenic schemas predispose individuals to depression because they increase the likelihood of negative self-statements and thoughts ultimately resulting in negative emotional states (Craighead et al., 2008).

Cognitive Distortions

Another one of the central tenets of Beck's cognitive theory is that an individual with depression suffers from cognitive errors or distortions. According to Beck, individuals suffer in deviations from logical thinking and these distortions are activated by continuous negative self-statements (Beck, 1963, 1995). An example of a cognitive distortion includes, "My swim coach never gives me any feedback. I must be a terrible swimmer." This individual unreasonably magnified the negative aspects of a situation and minimized any positive aspects. These kinds of cognitive errors and distortions can function to screen out positive beliefs and manipulate information in a negative way (Craighead et al., 2008). Distortions may lead to the development of depression but predisposed cognitive bias can lead to distortions.

Cognitive models of depression hypothesize that depression is associated with biases across several cognitive domains (Mathews & MacLeod, 2005). Automatic biases in attention and perception have been associated with depressed mood. McCabe and Gotlib (1993) subjected depressed individuals to a listening task and a secondary task responding to a light probe. They found that depressed individuals took longer to respond to the probe when negative words were presented than when positive words were presented (McCabe & Gotlib, 1993). Research has shown that depressed individuals have difficulties disengaging from negative information once it captures their attention (Kircanski, Joormann, & Gotlib, 2012).

In addition to attentional bias, memory bias has been implicated as being associated with depression. Memory biases in depression are one of the most well established phenomena in the cognitive model (Mathews & MacLeod, 2005). Negative

events are better recalled by individuals suffering from depression than their nondepressed counterparts. This is consistent with research showing the habit of rumination about negative events related to self (Lyubormirsky, Caldwell, & Nolen-Hoeksema, 1998). Negative memory bias has been observed in studies about recall of actual life events (Clark & Teasdale, 1982), and affectively toned material presented in a laboratory (Finkel, Glass, & Merluzzi, 1982).

Learned Helplessness Theory

The learned helplessness theory originally developed within a behavioral learning framework. This theory proposes that individuals become depressed because they view their current situations as futile and themselves as unable to bring changes to their situations (Peterson, Maier, & Seligman, 1993). Therefore, individuals give up trying when they believe a bad situation is unlikely to change no matter what they do (Craighead et al., 2008). Seligman hypothesized that helplessness was related to motivational, cognitive, and emotional deficits that are often seen in depression (Maier & Seligman, 1976). In a study examining learned helplessness theory, Miller and Seligman found that there are parallel effects between helplessness and depression. In the study, they observed that non-depressed subjects given helplessness training exhibited a performance impairment similar to that shown by the depressed participants given no pretreatment (Miller & Seligman, 1975).

Abramson et al. (1989) developed a revised model of learned helplessness. They proposed three belief dimensions that are considered to be involved in the majority of depressive symptoms; these include internal-external, global-specific, and stable-unstable

(Abramson et al., 1989). Abramson observed that most depressed individuals have explanatory styles that are internal, global, and stable for negative events. For example, internal style is if a student fails an exam and states "I am so stupid." Subsequently, if the same student then concludes "I am terrible at everything," then they use a global style. Lastly, an example of a stable style is if an individual experienced a relationship break up and believes "I will be alone for the rest of my life" (Craighead et al., 2008). Although depressed individuals tend to attribute negative events to internal, global, and stable causes, the opposite is true for positive events. Individuals with depression tend to attribute positive events to external, unstable, and specific causes (Seligman et al., 1979). If a depressed student did well on an exam, he may say, "I passed the test, but that's only because the teacher made this one so easy. It is only one test, and I will not be so successful the next time" (Craighead, et al., 2008, p. 276).

Hopelessness Theory

In 1989, Abramson and colleagues published an updated version of the learned helplessness theory of depression called the hopelessness theory. This theory was developed as a response to the limitation of the learned helplessness theory (Liu, Kleiman, Nestor, & Cheek, 2015). The learned helplessness theory was limited in the fact that it was unable to explain why some individuals become depressed, and other individuals do not, when confronted with an uncontrollable stressor (Abramson, Seligman, & Teasdale, 1978). In order to address this limitation, Abramson incorporated attribution theory. They theorized that causal attribution formed by individuals following a negative life event influenced their risk for depression (Abramson et al., 1978).

The hopelessness theory of depression reduces the importance of causal attributions and instead characterizes negative inferential styles, in responding to a negative event, as involving three forms of inferential tendencies. This theory - suggests that depressive symptoms are more likely to occur and maintain when 1) important negative events are attributed to global and stable causes, 2) negative events are predicted to lead to additional negative consequences, and 3) an individual draws a causal attribution about the association between their inherent deficiencies and the negative event, or, more simplistically, inferring negative self-characteristics (Abramson et al., 2002; Liu, Kleiman, Nestor, & Cheek, 2015).

Overall, the hopelessness theory predicts that the interaction between negative cognitive styles and life events can cause a sense of hopelessness. The development of hopelessness can be sufficient enough alone to be about depression. Observations made by some researchers have shown that there is substantial conceptual overlap between the hopelessness theory and other cognitive theories of depression (Possel & Thomas, 2011).

Biological Models

Genetics

Family and twin studies have provided evidence that MDD is a familial disorder and 30-40% of susceptibility to MDD can be explained by genetic factors (Sullivan, Neale, & Kendler, 2000). The rest of the susceptibility to MDD can be explained by environmental effects. MDD is considered a complex genetic disorder. This term aids in distinguishing depression from Mendelian disorders, like Huntington's disease (Craighead et al., 2008).

Researchers have focused on a small subset of functional polymorphisms while examining genetic susceptibility to depression. These genetic polymorphisms affect monoaminergic neurotransmission as well as neurotrophic processes and the over-activation of the hypothalamic-pituitary axis (HPA) (Levinson, 2005). Kato (2007) identified as many as 32 potential candidate genes that may be implicated in genetically predisposing an individual to depression (Elder& Mosack, 2011). Current pharmacological approaches to treating depression involve the monoamines, serotonin and norepinephrine. Since many of these drugs are helpful in the treatment of depression, the pathways involved with serotonin and norepinephrine serve as targets, and therefore candidate genes to research (Elder & Mosack, 2011). As stated by Craighead, Klein, Gillespie, Ritschel, and Phillips (2008), there are multiple and complex genes and alleles that may increase an individual's susceptibility to depression.

The rest of susceptibility is explained due to the environmental effects and genetic interactions. Environmental effects include stress-evoking events that may be caused by psychosocial variables including low perceived social support, trauma, marital problems, or school and work related issues (Hasler, 2010). The overwhelming evidence supporting the idea that depression can be caused by psychosocial variables is supported by the fact that CCDAN currently lists 87 different psychotherapeutic approaches to treatment (CCDAN, 2013). In addition, research has shown that, although both women and men have similar depressive reactions to stressful episodes, there is a gender specific difference depending on the type of stressor. Men are more likely to have depressive episodes about marital and work issues. On the other hand, women typically react to events that occur within their social network, such as illness or death (Hasler, 2010). Although it has been

theorized that genetic factors account for up to 40% of an individual's susceptibility to depression, there has not been any evidence for specific genes that lead to the pathogenesis of MDD (Hasler, 2010).

Hypothalamic-Pituitary- Adrenal Axis (HPA) Dysfunction

The first neurochemical theory for depression involves dysfunction within the endocrine system and the HPA axis. The hypothalamic-pituitary-adrenal axis plays an important role in regulating the stress response through the use of negative feedback loops and the release of hormones. During a stressor, the HPA axis is activated, which causes a series of neurochemical releases which eventually lead to the release of cortisol from the adrenal cortex. An analysis of depression studies found that individuals with mood disorders have an excess of cortisol (Varghese & Brown, 2001). An excess of cortisol and its metabolites was first seen in depressed patients over 50 years ago (Carpenter & Bunney, 1971). In animal studies, when CRH (an upstream hormone regulating ACTH and cortisol) is administered, animals developed several symptoms of depression (Arborelius, Owens, & Plotsky, 1999). The observations of excess cortisol in depressed patients and the high prevalence rate of depression in individuals with disorders affecting the HPA (e.g., Cushing's disease) lead to the formation of the diathesis-stress model of depression (Craighead et al., 2008). This model theorizes that individual excess reactivity of endocrine and neural stress response systems plays a key role in susceptibility to depression. This model provides a comprehensive theory by which stressful events, cognition, and biology can cause depression.

The dexamethasone suppression test (DST) was first developed to aid in the diagnosis of Cushing's disease (al-Saadi, Diederich, & Oelkers, 1998). Dexamethasone works on the anterior pituitary to decrease secretion of ACTH (adrenocorticotropic hormone), thus decreasing the release of cortisol from the adrenal cortex. An individual with impaired feedback regulation or HPA hyperactivity will be unable to suppress cortisol levels following dexamethasone administration (Craighead et al., 2008). Studies have shown that a large percentage of patients with major depression fail to suppress secretion of cortisol following the DST. Fountoulakis, Gonda, Rihmerm Fokas, and Lacovides (2008) found that 32% of people with diagnosed depression were non-suppressors to DST. They determined that these non-reducers had higher melancholic features, worse sleep and more suicidal thoughts (Fountoulakis et al., 2008). Therefore, the DST test may be a better indication of the severity of depression. In addition, research has shown that following a resolution of depressive symptoms, levels of cortisol, blunting of the ACTH response to CRF, hypersecretion of CRF, and adrenal hypertrophy all normalize (Craighead et al., 2008).

Uncontrollable stressful activities have been shown to activate the HPA, but animal models of stress- induced depression have shown that depressive-like behaviors are accompanied by atrophy of neurons in the hippocampus, a reduction in development of new hippocampal neurons, and a deficit in in hippocampal brain-derived neurotrophic factor (BDNF) levels (Masi & Brovedani, 2012). In addition to animal studies, post-mortem human studies have observed low BNDF levels in individuals with depression (Takahashi, 2014). BDNF is implicated in the survival of neurons and the facilitation of

neurogenesis. Therefore, stress-induced depression may lead to HPA dysfunction, as well as deficits in neurogenesis and BDNF levels.

Monoamine Hypothesis

One of the most heavily studied theories for depression and mood disorders is the monoamine theory. The monoamine system is involved with many cognitive functions that include mood, attention, sleep, and appetite. The monoamine theory postulates that the underlying pathological basis for depression is due to a depletion of the central nervous system neurotransmitters serotonin, norepinephrine or dopamine (Hasler, 2010). This theory was developed in part from pharmacological interventions that act on this system and clinical observations of their effects on mood (Craighead et al., 2008). The monoamine theory is the basis for the development of most antidepressant medication, such as selective- serotonin reuptake inhibitors, and serotonin and norepinephrine reuptake inhibitors. The vast majority of well established, approved pharmacological antidepressants target the monoamine system (Hasler, 2010).

Serotonin

Serotonin (5-HT) is an idoleamine neurotransmitter that is synthesized from L-tryptophan in the neurons of the rostral and caudal raphe nuclei within the brain (Craighead et al., 2008). The majority of serotonin within the central nervous system (CNS) is produced by neurons in the brainstem. The production of serotonin in the caudal raphe, rostral raphe, dorsal raphe and medial raphe allows for the projection of serotogenic fibers to most cells in the brain (Berger, Gray, & Roth, 2009). Serotonin has been implicated in

the regulation of nearly all behaviors, including mood, memory, stress response, appetite and aggression, as well as other CNS effects (e.g., motor control, circadian rhythms, respiratory drive, and body temperature).

Serotonin is the most heavily study neurotransmitter, due to its implications in depression, but there is still controversy surrounding the extent to which this mechanism contributes to depression (Cowen, 2008; Healy, 2005; Lacasse & Leo, 2005). Scientists hypothesize that 5-HT plays a role in the pathophysiology of depression. The most compelling evidence to support the importance of serotonin comes from studies that reduce central serotonin synthesis. The reduction in serotonin synthesis leads to the development of depressive symptoms (Hasler, 2010). In addition, the implications of serotonin in depression developed from the observation that tricyclic antidepressants inhibit the reuptake of 5-HT, thus enhancing 5-HT in depressed patients (Cowen, 2008).

Serotonin has been implicated to regulate endocrine and metabolic functions. Not surprisingly, serotonin has been implicated as an important regulator of the HPA axis (Berger, et al., 2009; Pompili, Serafini, Innamorati et al., 2010). Scientists suggest that serotonin plays an excitatory role in the release of corticotropic releasing hormone (CRH) (Pompili, Serafini, Innamorati et al., 2010). CRH is the precursor hormone to the release of ACTH and thus cortisol. CRH neurons in the amygdala are connected to the major serotonergic projections, like the raphe nuclei. Pharmacological studies of fenfluramine, a 5-HT releasing agent, showed that this precursor can significantly enhanced cortisol concentrations in manic and depressed individuals (Dinan, 1996).

Several evidence bases, including scientific studies, observational studies, and pharmacological studies, suggest the role of 5-HT signaling in depression. Low CSF concentrations of the main 5-HT metabolite, 5-hydroxyindoleacetic acid (5-HIAA), have been observed in patients with MDD. In conjunction with increased CSF levels, imaging studies have shown reduced levels of serotonin transporters in the raphe nuclei of MDD patients (Craighead et al., 2008). In addition, depletion of the serotonin precursor, tryptophan, triggers the recurrence of depression in patients who were treated with SSRIs. A recently published network meta-analysis compared the efficacy of 21 different pharmacological interventions for MDD; medications included SSRI's, SNRI's, and TCIs. The study found that all 21 medications were more effective than a placebo at reducing depression. The most effective medication was the TCI amitriptyline (OR=2.13). The most effective SSRI was Paroxetine (OR=1.75) (Capriani, Furukawa, Salanti et al., 2018). The efficacy of medications that act on serotonin transporters and receptors supports the hypothesis and research data that suggests serotonin plays an important role in the modulation of mood, specifically depression.

Norepinephrine

Norepinephrine (NE) is a catecholamine neurotransmitter synthesized from tyrosine by neurons of the locus coeruleus and neurons in the midbrain (Craighead et al., 2008). Noradrenergic pathways project to frontal cortex and to the limbic system, including the amygdala, hippocampus, and hypothalamus. Therefore, NE pathways are implicated in emotion, cognition, appetite, pleasure, and aggressive behavior (Moret & Briley, 2011).

Moret and Briley (2011) suggest several lines of evidence that NE plays a role in the pathophysiology of depressive disorder, these lines include:

> 1. NE projections from the locus coeruleus innervate the limbic system, which is implicated in the regulation of emotions.
>
> 2. Numerous differences have been found in elements of the NE system in postmortem brains from depressed patients and healthy controls.
>
> 3. Genetic studies show that mice with genetically engineered functional enhancement of the NE system are protected from stress-induced depression-like behaviors.
>
> 4. Experimental depletion of NE in the brain results in a return of depressive symptoms after successful treatment with NE antidepressant drugs.
>
> 5. Therapeutic agents which specifically increase NE activity are effective antidepressants. (Moret & Briley, 2011)

Key observations that corroborate this evidence includes increased and decreased NE metabolism in depressed patients, increased density of alpha-2 adrenergic receptors in the locus coeruleus in suicidal patients with a history of MDD, increased tyrosine hydroxylase activity ,and decreased density of the NE transporter in the locus coeruleus (Charney & Manji, 2004). These effects, and development of depressive symptoms, can be reproduced through depletion of brain norepinephrine (Cubells et al., 1995; Lee, Javitch, & Snyder, 1983). Similarly to the clinical evidence provided by SSRI's to support the serotonin theory, selective serotonin and norepinephrine reuptake inhibitors (SNRI's) have been proved to mitigate depressive symptomology. Meta-analytic comparisons have shown that SNRI's are more effective then placebos at increasing depression remission rate (Capriani, Furukawa, Salanti et al., 2018; Machado & Einarson, 2010).

Dopamine

The role of dopamine in depression was first implicated in the late 1970s. Dopamine is a naturally occurring monoamine formed by the same precursor of norepinephrine, tyrosine (PubChem, 2018). There are four dopaminergic pathways identified within the central nervous system (Dailly, Chenu, Renard et al., 2004). These pathways originate at the ventral tegmental area, the hypothalamus, and the substantia nigra and they project to the limbic area, the pituitary gland, and striatum (Dailly et al., 2004). Dopamine had widespread effects within the central nervous system. It plays a key role in the control of movement, learning, working, cognition, memory, and emotion (Drozak & Bryla, 2005).

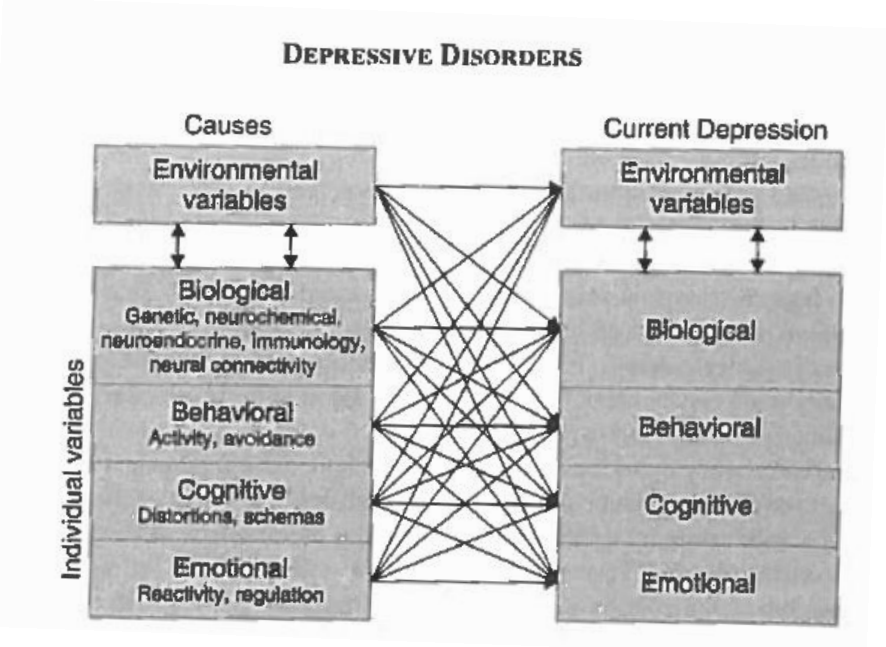
Evidence from both human and animal studies have suggested a relationship between dopaminergic pathways and depression. The first dopamine hypothesis of depression was theorized in 1975 (Randrup et al. 1975). D'haenen and Bossuyt (1992) found that up-regulation of dopamine D_2 receptor density was found in the basal ganglia of depressed patients whereas none was found in healthy subjects (D'haenen & Bossuyt, 1992). As previously discussed, genetic factors are implicated to account for 30-40% of susceptibility of depression. Some of the genes implicated in the pathophysiology of depression include polymorphisms of the D_4 receptor, one of the most polymorphic dopamine receptors (Dunlop & Nemeroff, 2007). A 2007 meta-analysis found that, in 12 studies, there was a significant association between the D_4 allele polymorphism and depression (Lopez et al., 2005).

Animal models have also demonstrated the role of dopamine in depression. Rodent models of depression have shown altered mesolimbic dopamine system function (Dunlop & Nemeroff, 2007). In addition, impaired dopamine release had been proposed to contribute to the pathophysiology of depression. A study by Salamone et al. (1999) observed reduced dopamine concentrations in the nucleus accumbens correlated with reduced efforts by rodents to work for specific reward (Salamone, Aberman, Sokolowski & Cousins, 1999). Loss of interest or pleasure is one of the classic symptoms of depression.

An integrative model

These models provide a pathological framework by which depression may be developed. Due to the nature of the disease and the variability in response to treatment, it is possible that the etiology of depression is multidimensional and comprised of many of these theories. It is important to understand the biological, psychological, and sociological research within the construct of depression. Implications of current research suggest that an integrative, biopsychosocial model may be the best option in trying to theorize a model by which the pathogenesis of depression occurs. Craighead, et al. (2008) provided an integrative model through which depression may develop.

Figure 1: An Integrative Model



This model incorporates various dynamic and interacting variables across several domains. Each of these variables has been implicated in the development of depression. Within this conceptual framework, predisposition to depression would be due to an imbalance between cognitions and emotions, as well as neuronal groups at a biological level. An external, environmental factor, such as stress, could initiate this imbalance, which would lead to an imbalance and depressive symptoms (Garcia-Toto & Aguirre, 2007).

The importance of an integrated model of depression stems from the implications that it has in the treatment of the disorder. In order to develop new treatment modalities, the mechanisms by which depression occurs must continue to be researched. The clinical implications of a multifactorial pathology of depression may mean that a multifaceted treatment approach, including both pharmacological and psychotherapeutic approaches, may be justified in order to result in significant symptom reduction.

Interventions

In general, a psychological intervention is defined as a method of inducing changes in a person's thoughts, feelings, or behavior implemented in the context of a professional relationship (Trull & Prinstein, 2012). J. D. Frank (1982) defined psychotherapy as:

> …a planned, emotionally charged, confiding interaction between a trained, socially sanctioned healer and a sufferer. During this interaction the healer seeks to relieve the sufferers distress and disability through symbolic communication, primarily words but also sometimes bodily activities. The healer may or may not involve the patient's relatives and others in healing rituals. Psychotherapy also often includes helping the patient to accept and endure further suffering as an inevitable aspect of life that can be used as an opportunity for personal growth. (Frank, 1982, p. 10)

It is paramount for clinicians to use treatments that have been shown to work better than no treatment or other psychotherapies. These evidence based treatments are more effective and efficacious then other therapies (Kazdin, 2008). Chambless and colleagues developed criteria for determining evidence based treatments. In order to be a well-established evidence based treatment, a treatment must have two good group design

RCT's that demonstrate its efficacy by being superior to another treatment or a placebo (Chambless et al., 1998).

There are many psychological treatments indicated for depression. Psychologists have suggested several common factors result in most of the therapeutic change resulting from psychotherapy (Wampold, 2011). Lambert and Ogles (2004) categorized common features of psychotherapy into three groups: supportive factors, learning factors, and action factors. They theorized that supportive factors lay the groundwork for changing attitudes and beliefs (learning factors) which lead to change (action factors) (Lambert & Ogles, 2004). Some examples of common factors include the therapeutic alliance (supportive factor), cognitive learning and advice (learning factors), and behavioral regulation and mastery efforts (action factors).

There are many types of psychotherapeutic interventions that it is impossible to describe a common sequence of therapy for all. Typically, psychotherapeutic interventions will involve initial patient contact, clinician assessment, goals of treatment, implementing treatment, and then termination and follow–up (Trull & Prinstein, 2012). Throughout the course of this literature review, the development and basic concepts of four different interventions will be discussed and analyzed. These interventions include cognitive behavioral therapy, behavioral activation therapy, non-directive supportive therapy, and physical activity.

Cognitive- Behavioral Therapy

Cognitive therapy is a form of psychotherapy based on an underlying theoretical rationale that an individual's behavior and affect are largely determined by her/his cognitions and the way she/he structures the world (Beck, 1979). Cognitions are based on schemas, or assumptions, developed from previous experience. Specific therapeutic techniques are developed from the cognitive therapy of depression. A cognitive therapist helps a patient think and act more realistically about his/her psychological problems, thus reducing symptoms. The focus of cognitive therapy includes 1) monitoring negative, automatic thoughts, 2) recognizing the connection between cognition and affect, 3) reviewing evidence that supports or refutes distorted automatic thoughts, and 4) learning to identify and alter dysfunctional thoughts (Beck, 1979).

Origin

Cognitive therapy is now interchangeably used with the term cognitive behavioral therapy (Beck, 2011). Cognitive behavioral therapy (CBT) refers to interventions that are based on the premise that mental disorders and other forms of psychological distress are maintained by cognitive factors. CBT was pioneered by Dr. Aaron Beck and Dr. Albert Ellis in the 1960s, and the treatment approach suggests that maladaptive cognitions may contribute to emotional and behavioral issues (Hofmann, 2013). Dr. Beck initially wanted to test the premise that depression results from an inward hostility towards oneself (Beck, 2011). In analyzing the dreams, as well as thought patterns while awake, of depressed patients, Beck concluded that psychoanalysis may be wrong (Beck, 1967). Dr. Beck then began to listen to his patients and he realized his depressed patients had two streams of thoughts: free association and quick, evaluative thoughts (Beck, 2011). In order to

demonstrate the efficacy of CBT to others, Dr. Beck and colleagues conducted an RCT analyzing the efficacy of CBT versus an antidepressant for individuals suffering from depression. The study found that CBT was just as effective as pharmacotherapy (Beck, Rush, Shaw, & Emery, 1979).

The focus of CBT is to uncover a patient's unhealthy thoughts as well as analyze how these thoughts may be causing self-destructive behavior (NAMI, 2017). This model states that therapeutic strategies, such as cognitive, behavioral, and emotion- focused techniques, will intervene by changing any maladaptive cognitions in order to decrease self-deprecating thoughts and actions (Hofmann, 2013). The focus of CBT treatment is to change harmful thinking and behavioral patterns in patients. There are many different strategies cognitive therapists use in order to treat patients. Typically, treatment interventions combine a number of cognitive, behavioral, and emotion-focused techniques. Components of CBT for depression often include a focus on helping patients solve problems, become behaviorally activated, and identify, evaluate, and respond to negative or harmful thought patterns about themselves (Beck, 2011). The goal of cognitive interventions is to identify thoughts that may trigger emotional and behavioral reactions. A therapist will help patients rationally analyze harmful beliefs and help patients develop more adaptive beliefs (Flynn & Warren, 2014). The behavioral component of CBT is meant to help the patient increase behaviors that are rewarding and decrease behaviors that help maintain symptoms (Flynn & Warren, 2014).

Typical CBT Intervention

Typically, CBT consists of 15-25 sessions on a weekly basis, although individuals suffering from moderate to severe depression may require sessions bi-weekly (Beck, 1979). The structure of a typical session, and interventions used, can vary from patient to patient (Beck, 2011). At the beginning of a session, a therapist typically reestablishes the therapeutic alliance and checks on the patient's thoughts, mood, and experiences in the past week. In addition, a therapist will review activities that a patient engaged in during the previous week. After asking about a problem a patient wants help in addressing this week, a therapist will then collect data, conceptualize the patient's difficulties, and plan a strategy for negative thought patterns and/or behavioral change (Beck, 2011). Some techniques used to help patients include problem solving and skills training, mindfulness and relaxation, exposure, role-playing, and imagery (Beck, 2011).

Therapeutic Evidence for CBT

Cognitive Behavioral Therapy has been extensively studied as an intervention for a wide range of disorders. It has been shown to be efficacious for many psychiatric and somatic disorders, some of which include (but not limited too): affective disorders, personality disorders, schizophrenia, phobic disorders, somatoform disorders, irritable bowel syndrome (IBS) and disease (IBD), obesity, insomnia, cancer pain, and tinnitus (Beck, 2011). Rector and Beck (2001) found that CBT provided a beneficial effect on positive symptoms for individuals suffering from schizophrenia. In addition to schizophrenia, meta-analyses have shown the efficacy of CBT for insomnia. When compared to behavioral techniques and relaxation, CBT was found to be more effective in improving subjective sleep outcomes (Irwin, Cole, & Nicassio, 2006). As previously

stated, CBT has been shown to decrease distress that occurs due to other medical conditions, such as cancer or multiple sclerosis. For individuals suffering from certain forms of cancer, CBT has been shown to moderately improve quality of life, psychological distress, and pain when compared to a patient education control (Luckett, Britton, Clover, & Rankin, 2011).

Cognitive behavioral therapy is one of the best known evidence based, empirically supported treatments for depression (Drissen & Hollon, 2010). The efficacy of CBT for depression is shown across different depression subtypes (e.g., MDD, PDD, antenatal depression), therapy delivery type (Internet or face to face) and therapy frequency. Andersson et al. (2005) found that an internet administered CBT program resulted in a greater reduction of symptomology then a discussion only group (Andersson, Bergstrom, Hollandare et al., 2005). In addition to RCTs showing the effectiveness of CBT across delivery types, trials have also provided evidence that CBT is just as effective as pharmacotherapy. DeRubeis and colleagues (2005) found that CBT can be as effective as antidepressants in the initial treatment of depression, but moderators, like the therapist's level of experiences, may affect how beneficial CBT is (DeRubeis et al., 2005). Lastly, when given the choice between antidepressants and CBT, an RCT found that 49 individuals chose drugs while 33 choose psychotherapy. Although fewer individuals chose CBT, researchers found that CBT was more effective at reducing symptomatology then a guided self-help control.

RCTs, meta-analyses, and systematic reviews have shown the efficacy of CBT therapy. One of the most notable findings is that CBT produces similar or superior

antidepressant effects then tricyclic antidepressants (TCAs)(Beck, Hollon, Young et al., 1985; Murphy, Simons, Wetzel, & Lustman, 1984). In a recent meta-analysis, researchers found that CBT resulted with a number needed to treat of 2.6 (Cuijpers, Berking, Andersson et al., 2013). This means that 2.6 patients would have to be treated in order for one to benefit, compared to a control. CBT is the most studied form of psychotherapy for depression. RCTs and meta-analysis leave no doubt that CBT is an effective form of treatment for depression, but the overall benefit when compared to other therapies warrants further examination.

Strengths and Weaknesses

There is general agreement in the literature that CBT is effective in treating depression. Elkin (1994) ran a large multi-site RCT examining the effects of multiple treatments for depression. Researchers found that CBT is effective at reducing depressive symptomatology and is equivalent to other forms of therapy, such as interpersonal therapy or antidepressant medication. A more recent network meta-analysis found that CBT, along with six other psychotherapeutic interventions, provided benefits for those suffering from depression when compared to a waitlist (Barth et al., 2013). Overall, some researchers have concluded that CBT is about as effective as pharmacotherapy (Hollon & Beck, 1994). Another strength of CBT, like many forms of psychotherapy, is that the use of CBT is not contraindicated by the prescription of medication. Actually, research has shown that the use of antidepressants with CBT may have a synergistic, reinforcing effect (Evans et al., 1992).

When compared to other forms of psychotherapy, CBT has been shown to be effective in a shorter duration. Studies have found that a variety of treatment durations can positively affect depressive symptomology; durations range from one day (Brown et al., 2008), six sessions (Scott et al., 1997), to multiple months (Lustman, Griffith, Freedlan et al., 1998). When compared to psychoanalysis, the shorter therapeutic time may be due to the emphasis on symptom management rather than insight (Spinelli, 1994). In addition, when compared to more humanistic or supportive approaches, therapist skills are valued over therapist traits (Newell & Dryden, 1991). This makes some researchers draw the conclusion that CBT approaches can cause symptom reduction beyond the effects of more general therapeutic factors such as empathy and compassion (Robins & Hayes, 1993).

Another major strength of CBT is that it has been shown to work across social classes, cultures, and treatment delivery. Williams (1989) reports that CBT approaches work across a range of social classes (Williams & Moorey, 1989). In addition to social classes, CBT has been adapted to work for diverse populations. Many of the psychotherapeutic approaches were developed based on Euro-American social values (Henrick, Heine, & Norenzayan, 2010). Studies have suggested that culturally adapted CBT can be effective within a multicultural context (Miranda et al., 2003). Research has shown that adapted CBT was effective at resolving psychological issues experienced by a Venezuelan women (Diaz-Martinez et al., 2010), and was effectively adapted to Chinese culture (Guo & Hanley, 2015). RCTs have demonstrated the effectiveness of CBT delivery through multiple methods. Group CBT has been shown to provide a more cost-effective and beneficial therapy for multiple conditions (Stravynski et al., 1994; Wilhelm

et al., 1999). In addition, computer-delivered CBT and minimal contact cognitive bibliotherapy have proven to be just as an effective as therapist delivered CBT (Selmi et al., 1990; Stevens, 1996).

As with many psychotherapies, one of the limitations of CBT is the methodological issues seen in RCTs (Abrahman, Neese, & Westerman, 1991). Within the scope of CBT research, there are some issues that are problematic to the claim of being an evidence based treatment. One such issue is the large deficit in research measuring treatment integrity. There have been few studies examining the degree to which how poorly or well CBT interventions are being implemented (Gresham, 2005). There are many treatment manuals for CBT but these may not be sufficient to decrease variability and ensure treatment integrity.

One suggested weakness of CBT is that the approach views emotions as something to be controlled rather than be experienced and that therapists may over-emphasize rationality (Emery & Tracy, 1987). Lastly, a drawback of CBT is that it failed to explain the physical symptoms that accompany depression. These include sleep disturbances, poor appetite, and aches and pains. In addition, CBT fails to explain the success of biologically based antidepressant medication (Beech, 2001). Some researchers have pointed to the large amount of evidence suggesting that depression is a biopsychosocial event (Calarco & Krone, 1991).

Behavioral Activation Therapy

Behavioral Activation (BA) has been indicated as a treatment for depression since the 1970s (Kanter et al., 2010). The goal of behavioral activation (BA) is to increase patients' contact with sources of reward by helping them become more active (Hershenberg, 2015). Both Ferster (1973) and Lewinsohn (1974) identified the link between avoidant behavior and depression and recommended activation strategies to increase positive reinforcement. The efficacy of BA treatments are well documented. Mazzucchelli et al. (2009) concluded that BA is a "well-established empirically validated treatment" (Mazzucchelli et al., 2009). Due to the large amount of empirical support, the APA notes that one of the four core aspects of depression is to help patients "gradually incorporate enjoyable, fulfilling activities back into their lives" (APA, 2009). This definition is the primary goal of BA.

Origins

The behavioral theory of depression was first described by Lewinsohn in 1974 (Lewinsohn, 1985). A couple of years after this theory was described, Lewinsohn and colleagues developed a comprehensive treatment manual based on pervious intervention studies (Lewinsohn, Biglan, &Zeiss, 1976). The main therapeutic component of this manual was the encouragement of activity scheduling in order to address deficits in positive reinforcement. In addition to activity scheduling, the manual suggested social skills training to address behavioral deficits and contingency management strategies (Lewinsohn et al., 1976). The development of Lewinsohn's manual spurred the development of many interventions that incorporated various behavioral approaches (Gardner & Oei, 1981; Rehm, 1977; Wilson, 1982). For example, McLean (1976)

developed a variant that included training in interpersonal, behavioral, and cognitive skills which outperformed medication in a RCT (McLean & Hakstain, 1970).

Throughout the late 1970s and 1980s, there was a decrease in use of behavioral therapies. One study that led to this decrease was performed by Zeiss and his colleagues. A component analysis found that there was no difference in the effectiveness of activity scheduling, cognitive techniques, or skills training (Zeiss, Lewinsohn, & Munoz, 1979). As the popularity of CBT grew, the empirical support of its effectiveness began to grow (DeRubeis & Crits-Christoph, 1998). Behavioral therapies were again emphasized in the 1990's. The renewed emphasis was in part due to another component analysis of CT. Jacobson et al. (1996) found that when cognitive techniques were added to behavioral techniques there was no difference (Jacobson et al., 1996). . This lead to the conclusion that the addition of cognitive techniques to behavioral therapy did nothing to improve the outcome. The renewed emphasis on BA lead to the development of a full behavioral treatment model. This model employed activity scheduling to overcome deficits in positive reinforcement and emphasized the need to block avoidance behaviors (Martell, Addis, & Jacobson, 2001). In addition, this treatment model was developed to be flexible, rather than a structured session-by-session format. In addition to a full behavioral treatment model, a specific behavioral treatment for depression was developed. Lejuez et al. (2001) developed a brief BA treatment for depression which included similar behavioral techniques in the framework of treating depression (Lejuez, Hopko, & Hopko, 2001). See Lejuez et al. for the updated BATD manual.

Therapeutic Techniques

Over the course of the past 40 years, seven treatment manuals outlining behavioral activation treatment and techniques have been formed (Beck et al., 1979; Gallagher et al., 1981; Lejuez, Hopko & Hopko, 2001; Lewinsohn et al., 1976; Martell et al, 2001; McLean, 1976; Rehm, 1977). All seven of the treatment manuals included activity scheduling and monitoring as therapeutic techniques. In addition, five of the manuals included skills training (excluding Rehm (1977) and Lejuex et al.(2001)), contingency management (excluding Beck et al.(1979) and Gallagher et al.(1981)), and procedures targeting verbal behaviors (excluding Beck et al.(1979) and Lejuez et al. (2001)). Overall, some of the other techniques described in a few manuals included values assessment, relaxation, and procedures targeting avoidance. For a more in-depth review of BA therapeutic techniques see Kanter et al. (2010).

Therapeutic Evidence for BA

The majority of behavioral activation interventions have been exclusively studied in the context of treating depression. One study examined a case of an individual suffering from co-morbid depression and anxiety. Researchers found that BA treatment was effective at improving both anxiety and depressive symptoms (Hopko, Robertson, & Lejuez, 2006). Several other case studies have shown the effectiveness of BA in reducing symptoms in various types of depression. Some of these include improvement in a suicidal client with borderline personality disorder (Hopko, Sanchez, Hopko et al., 2004) and depressed cancer patients (Hopko, Bell, Armento et al., 2005). A recent RCT comparing BA treatment to usual care for depression found that participants undergoing

BA experienced significant decrease in depressive symptomatology when they adhered to treatment (Kanter et al., 2015).

Studies have shown the effectiveness of BA as compared to other treatment modalities. In 2006, researchers examined the effects of cognitive therapy, behavioral activation, and antidepressant medication as a treatment for MDD. The results of this study found that BA is comparable in efficacy to psychotropic medication and is more efficacious than cognitive therapy (Dimidjian, 2006). In a network meta-analysis comparing the efficacy of seven different psychotherapeutic interventions, researchers found that BA reduced depressive symptomatology by a moderate to large effect (Barth et al., 2014). In addition, meta-analysis have shown the overall efficacy of BA when compared to controls. Cuijpers et al. (2007) found that there was a large effect size across the 16 included studies (Cuijpers, van Straten, & Warmerdam, 2007).

Strengths and Weaknesses

One of the strengths of BA therapy is that it is a relatively simple intervention; therefore it is easy for depressed patients to understand and it does not require difficult skills (Lejuez et al., 2001). This can also be viewed as a weakness due to the fact it lacks the complexity that other psychotherapies have (e.g. CBT) (Veale, 2008). Due to the fact that it is so simplistic, many individuals believe simple therapies are only suitable for mild illness. Likewise, the simplicity of the intervention allows for staff to be trained much more easily (Veale, 2008). One common limitation or obstacle with BA is overcoming an individual's beliefs about avoidance: individuals will tell themselves that they will engage in an activity when they feel like it. Individuals suffering from

depression typically suffer from amotiviation to begin with; therefore, getting clients to engage in activities may be difficult. In order to overcome this, individuals should act according to the plan or schedule and not how they feel in the moment (Veale, 2008).

Non-Directive Supportive Therapy

Non- directive supportive therapy (NDST) is typically referred to as supportive counseling, counseling, supportive therapy, or person-centered therapy in the literature. It is typically conducted as unstructured therapy without specific psychological techniques other than aspects such as helping people vent their emotions (Barth et al., 2013). The aim of supportive counseling is to help patients feel understood and supported so that their ability to heal and find solutions to their problems may work more effectively, thus decreasing their overall inability to cope with depressive thoughts (Cuijper, 2012). In previous research, this intervention has been defined as a "psychological treatment in which therapists do not engage in any therapeutic strategies other than active listening and offering support, and focusing on participant's problems and concerns." (Arean et al., 2010, p.1394).

Origin of NDST

NDST or client centered therapy (CCT) was first developed by Carl Rogers in the early 1940s (Trull & Prinstein, 2012). The basis of NDST lies within the theory of phenomenology, or the idea that to understand an individual's behavior, you must understand what their phenomenal field is (or what the world is like for them) (Greenberg, Elliott, & Lietaer, 2003). Rogers (1959) named three important therapist

characteristics when practicing CCT: empathic understanding, unconditional positive regard, and genuineness (Rogers, 1959). Empathy is one central tenet of NDST or CCT because it aids in conveying a sense of therapist sensitivity to clients' needs and feelings. Therapist use of empathy helps to provide a sense to clients that they are being understood (Trull & Prinstein, 2012). Another important feature of CCT is unconditional positive regard, or respect for a client as a human being. A therapist must put aside all biases or judgments of a client, in order to be accepting and to convey the feeling that the clients have the ability to achieve their inner potential. The last feature important to NDST is genuineness or congruence. Rogers believed that clients would respond to honesty and trust the therapist is dedicated to their wellbeing (Rogers, 1961).

As stated in the NDST definition by Arean et al (2010), one of the main aspects of the therapeutic process is active listening and offing support (Arean et al., 2010). Greenberg and colleagues (1994) reported that about 75% of all CCT therapists' responses were reflections of what the client had said (Greenberg, et al., 1994). Typically, techniques of reassurance or interpretation (Trull & Prinstein, 2012) and giving advice or providing solutions (Cuijper, 2012) are not used. The general process of CCT or NDST has been described by Rogers in a sequence of seven stages (Meador & Rogers, 1984). The initial stages focus on the clients as they begin to their feelings. As the stages progress, the therapist aids in helping the client freely express emotions, accept their feelings and become comfortable with experiencing self (Meador & Rogers, 1984).

Therapeutic evidence of NDST

In NDST or CCT, diagnosis or assessment is usually deemphasized or avoided. Many client centered therapists believe this puts the therapist in a superior role and can hinder the development of autonomy (Trull & Prinstein, 2012). Studies have shown that NDST is efficacious for a number of conditions. Case studies have described the usefulness of supportive therapy for the management of patients suffering from diabetes (Berlin & Wise, 1980), coronary artery disease (Razin, 1982), acute leukemia (Foerster, 1984), and herpes simplex viral infection (Evans, Fishman, Spielman et al., 2003). In addition to somatic disorders, studies have shown the benefits of NDST with patients diagnosed with psychiatric disorders, including personality disorders, eating disorders, addiction disorders, schizophrenia, and affective disorders (Conte, 1994). Although there have been many case studies involving supportive therapy for medical conditions, there have been few randomized control trials, especially high quality trials. One study conducted by Sjodin et al. (1986), compared the effect of usual care with and without supportive therapy for individuals suffering from peptic ulcer disease. After 15 months, researchers found that the supportive therapy group showed significant improvement compared to the usual care control (Sjodin, Swedlund, Otlosson et al., 1986).

Although suffering from methodological issues, there have been more RCTs examining the effect of NDST on types of depression. Freedland and colleagues (2009) examined the efficacy of cognitive behavioral therapy and supportive counseling in reducing depression after coronary artery bypass surgery. The results suggest that both psychotherapies were effective at reducing depressive scores when compared to the usual care group (Freedland, Skala, Carney et al., 2009). Another study, found that both CBT

and supportive psychotherapy are equally effective in reducing symptoms in depressed patients (Bright, Baker, & Neimeyer, 1999).

Although many studies show the effectiveness of NDST at reducing depressive symptomology, not all studies have found a significant benefit over usual care. In the Edinburgh primary care depression study, researchers determined that there were only small clinical advantages to the use of counseling or CBT when compared to routine care. In addition, researchers concluded that the small benefits were outweighed by the higher costs of time and treatment (Scott & Freeman, 1992). In a recent meta-analysis of RCTs, researchers found that NDST (Supportive Counseling) is an effective treatment for depression but may be less effective than other psychological treatments (Cuijper, 2012).

Strengths and Weaknesses

The supportive therapy or CCT approach has many positive benefits. The NDST approach provides a psychotherapeutic approach that focuses on self-determination and inner directedness. Another benefit of supportive therapy is that it is a shorter form of psychotherapy as compared to other forms. Again, Rogers described the process of client centered therapy as a series of seven stages (Meador & Rogers, 1984). For example, when compared to psychoanalysis, supportive therapy is much shorter due to a lack of emphasis on resolutions of transference relationships, detailed reconstruction of the past, and cathartic experiences (Trull & Prinstein, 2012). Given the current mental health needs of the nation, and the current projections showing an increasing occurrence of disorders like depression, the need for more mental health personnel exists. Supportive therapy requires a therapist to play a less active role which means a therapist needs less

training (Trull & Prinstein, 2012). Therefore, a therapeutic discipline like supportive therapy that can produce personnel faster may be beneficial.

A major strength of client centered therapy or supportive therapy is the focus on research, both by Rogers and other psychologists. Rogers focused on researching the therapeutic process (Trull & Prinstein, 2012). Rogers was the first to employ recordings in therapy sessions in order to study the process and its effectiveness. In addition to examining the processes, Rogers also studied the outcome of therapy (Trull & Prinstein, 2012). Rogers and colleagues developed guides of therapeutic outcomes, as well as indicators of improvement, like the ratio of client-to-therapist talk (Rogers & Dymond, 1954; Rogers, Gendlin, Kiesler, & Truax, 1967). In addition to research performed by Rogers, meta-analyses performed over the past 30 years have indicated the therapeutic benefits of NDST. Greenberg et al. (1994) found a mean effect size, with eight included studies, to be .88. In addition, an adult client in the included studies was functioning better than 81% of individuals not receiving treatment (Greenberg et al., 1994). Another meta-analysis performed in 2010 found that, across 200 studies, clients who underwent person-centered therapy reported significant positive change (Elliott & Freire, 2010). In addition, aspects of NDST, specifically the therapist alliance, empathy and positive regard, have been shown to be important for a positive outcome (Trull & Prinstein, 2012). Overall, the extensive research by Rogers and others is one of the primary strengths of NDST or CCT.

Although there are many strengths to NDST, there are some limitations to it. Several limitations to supportive therapy are evident by claims made by client centered

therapists. First, they claim that to understand their clients, one must experience the same view point. This is a non-specific statement without methodology to guide therapists in the process (Trull & Prinstein, 2012). In addition, CCT therapists claim that they do not change clients but they just aid in releasing the clients inner potential for growth. Therapy is a stimulus for change and the outcome of change seems to be largely affected by the therapists and their methods (Trull & Prinstein, 2012).

Another limitation to CCT or NDST is that it seems to involve a single attitude set: empathy, unconditional positive regard, and acceptance (Trull & Prinstein, 2012). Due to this, every client is treated the same. Therapists have no need to assess the client to see what would be the most effective therapy or a specific technique to meet the client's needs. In order to combat the one-size fits all approach to therapy, some therapists have developed specific techniques and methods for certain client issues (Greenberg et al., 2003). A central aspect of CCT or NDST is an unwavering faith that the client knows best. Due to the emphasis on the client's inner potential and freedom, there is a condemnation of therapist interventions, whether it would be through advice, suggestions, or interpretations (Trull & Prinstein, 2012). In some cases, the severity of a client's issue could dictate that a therapist use a more active approach, thus leading to a limitation in this approach.

Lastly, NDST may have limited applicability to certain populations. CCT or NDST was developed in the 1940s and 50s on college campuses from work with college students (Trull & Prinstein, 2012). When compared to individuals in the general population, college students tend to be intelligent, better educated, have more coping

methods, and be less maladjusted when they do develop problems (Trull & Prinstein, 2012). A non-directive therapeutic method would most likely be more effective with a population like college students, rather than those with severe psychosis, low verbal functioning, or low intelligence. Although there are some limitations or weaknesses to NDST, the indications for its ability to decrease depressive symptomology are strong.

Physical Activity

Physical activity has been suggested and shown in research to be a potential treatment for depression, and it has been incorporated into guidelines as a complementary treatment for those in the mild to moderate severe category (Cleare et al., 2015; NICE, 2013). Since the early 1900s, scientists have been interested in the effect of exercise on depression. Early studies concluded that, for some, exercise is beneficial for depression and will result in a happier mood (Franz & Hamilton, 1905; Vaux, 1926). Since the early case studies in the 1900s, researchers have recently begun to examine the relationship through experimental designs.

The overwhelming majority of randomized control trials (RCTs) have shown that exercise provides a positive benefit in reducing symptoms of depression. For example, a study of moderately depressed men and women found that an exercise intervention, walking for 20 to 40 minutes for 3 times per week for 6 weeks, alleviated overall symptoms of depression more effectively than a support or control group (McNeil, LeBlanc, & Joyner, 1991). A recent RCT compared the efficacy of exercise to a control for individuals suffering from mild to moderate depression. Researchers found that the aerobic exercise group had a significant reduction in depressive scores, as compared to

the control (Ho, Chan, & Wong, 2014). Overall, RCTs suggest that exercise does result in a reduction of depressive symptomatology.

In 2013, the National Institute for Health and Care Excellence developed guidelines for depression that included a physical activity program as a treatment for mild to moderate depression (NICE, 2013). There have been several reviews and meta-analyses analyzing the effects of physical activity on depression. In a 2016 meta-analysis, researchers adjusted for publication bias and found that exercise had a large and significant diminishing effect on depression. The largest effects were found in interventions that implemented activities such as aerobic exercise at a moderate or vigorous intensity (Schuch et al., 2016). Another recent meta-analysis confirmed the results of Schuch et al. Kvam et al. (2016) found that exercise had a moderate to large effect size on depression when compared to control conditions and no interventions. When compared to usual care, exercise still yielded a moderate and significant effect on depression (Kvam, Kleppe, Nordhus et al., 2016).

In addition, research has shown that the benefits of exercise as a treatment for depression may be long lasting (DiLorenzo, 1999). This study showed that individuals who took part in a 12-week physical activity program had significant decreases in depressive scores and improvements in self-concept as compared to a control group (DiLorenzo, 1999). Researchers have examined the effects of exercise on depression in comparison to psychotropic medication. In a 1999 study, Blumenthal and colleagues found, when comparing running and psychotropic medication, that medication would work faster to reduce depressive symptoms, but at 16 weeks there were no significant

differences (Blumenthal et al., 1999). Physical activity has been shown to reduce depressive symptoms and improve quality of life to the same extent as CBT or antidepressant medication for mild to moderate depression (Cooney et al., 2013).

Types of Physical Activity

The majority of RCTs and literature surrounding the association between physical activity and depression focus on aerobic exercise. These studies have included interventions such as walking programs, running, swimming, and cycling. The mood enhancement aspects of aerobic physical activity were first noted in the mid-1900s. Morgan and colleagues observed that more participation in aerobic exercise is accompanied by lower levels of depressed mood (Morgan, 1969; Morgan, Roberts, Brand, & Feinerman, 1970). Greist et al. (1979) found a 10-week running therapy program to be just as effective as psychotherapy for patients with MDD (Greist et al., 1979). In a three-arm RCT, researchers found that 10 weeks of endurance training reduced depressive scores significantly more than relaxation or a control group (McCann & Holmes, 1984). In a more recent study, researchers at Duke found that participants in the aerobic exercise intervention group and sertraline group showed no difference in levels of depressive symptoms. This suggests that exercise and usual antidepressant treatment are equally effective (Blumenthal et al., 2007).

Although the bulk of research has focused on the effect of aerobic physical activity on depressive disorders, some research has been conducted on the effects of nonaerobic exercise interventions. In 1987, Doyne compared the efficacy of running to weightlifting (Doyne, Ossip-Klein, & Bowman, 1987). They found that there were no

significant differences among the two treatment groups and that both treatment modalities were effective at reducing symptoms of depression (Doyne et al., 1987). In addition, the latest Cochran report shows that weight training greatly affects depressive symptoms when compared with no treatment or a placebo (Cooney et al., 2013).

In addition to aerobic and anaerobic exercise, mindful based forms of exercise (e.g., yoga and tai chi) have been found to significantly improve depressive symptoms. Multiple studies have shown that yoga, and individual components of yoga, can improve depressive symptomatology. Khumar et al. (1993) found that shavasana, comprised of rhythmic breathing and relaxation, significantly decreased depression scores when compared to a control (Humar, Kaur, & Kaur, 1993). A triple arm RCT compared Sudarshan Kriya Yoga (SKY), electroconvulsive therapy, and drug therapy for depression. After the 4-week trial, researchers found that the response to SKY was comparable to the response found in the drug therapy arm (Janakiramaiah, 2000). Overall, yoga and other mindful-based forms of physical activity have demonstrated potentially beneficial effects for individuals suffering from depression.

Intensity of Exercise

It is important to analyze the effect of exercise intensity and dose on depressive symptomology. Several reviews purpose recommendations for optimal dose and intensity of exercise. One article suggests moderate or self-selected intensity, another review suggests 60-80% maximum HR, while a third review found that 61-74% of maximum heart rate was less effective than higher and lower intensity exercise (Perraton, Kumar & Machotka, 2010; Rethorst, Wipfli, & Landers,2009; Stanton & Reaburn, 2014). These

recommendations are based on the levels of exercise used in RCTs. There have only been a few studies examining the effect of different exercise intensities on depression.

One study examined the effects of high and low intensity weight lifting and found that the high intensity group achieved a larger remission of depressive symptoms (Singh, Stavrinos, Scarbek et al., 2005). Dunn et al. (2005) found that an exercise dose equivalent to public health recommendations was more efficacious then exercise below this level, and that exercise frequency did not matter (Dunn, Trivedi, Kampert et al., 2005). Finally, the most recent RCT comparing multiple intensities of exercise and a usual care control found that the light intensity exercise group had significantly lower depression scores then both usual care and moderate exercise. In addition, the vigorous intensity had significantly lower scores then the moderate intensity group. (Helgadottir, Forsell, Hallgren et al., 2017).

Therapeutic Mechanisms

Although the effect of exercise on depression has been observed in the literature, the mechanisms by which it does so remain unclear. There are several hypotheses that attempt to explain physiological and psychological mechanisms that regulate this relationship. These hypotheses include: the thermogenic hypothesis, the endorphin hypothesis, the monoamine hypothesis, the distraction hypothesis, and the enhancement of self-efficacy. The thermogenic hypothesis states that the rise in body temperature, due to exercise, is responsible for depression symptom reduction (DeVries, 1981). DeVries states that an increase in blood flow and heat specific brain regions can lead to overall feelings of relaxation. The endorphin hypothesis focuses on biological responses during

exercise that increase the amount of B-endorphins. Endorphins are related to a positive mood and enhanced sense of well-being (Craft & Perna, 2004). Depression is associated with low levels of BDNF, and studies have observed that physical activity causes increases in levels of BDNF in individuals with depression (Szuhany, Buggatti, & Otto, 2015). The monoamine hypothesis states that exercise leads to an increased availability of neurotransmitters, which have been implicated as having decreased levels in individuals with depression. These neurotransmitters include serotonin, dopamine, and norepinephrine (Craft & Perna, 2004).

The last two hypotheses are more psychological in nature; these include the distraction and self-efficacy hypothesis. The distraction hypothesis states that physical activity serves as a mechanism of distraction, and therefore serves as a coping mechanism for those with depression (Leith, 1994). Exercise distracts individuals from worries and depressive thoughts, which helps individuals cope with the depressive symptomatology (Craft & Perna, 2004). Lastly, exercise has been proposed to help increase an individual's self-efficacy, which is the belief that one possesses the necessary skills to complete a task (Craft & Perna, 2004). A study reported that involvement in an exercise program was associated with enhanced feelings of self-efficacy, which were inversely related to feelings of depression (Craft, 2005). Overall, the mechanisms by which exercise affects depression are not well understood, but there are hypotheses about how exercise may be mediate depressive symptoms. It is highly likely that many of these biological and psychological factors that occur while exercising have an impact on feelings of depression.

Strengths and Weaknesses

There are some weaknesses to the use of physical activity as a treatment for depression. One of the classic symptoms of depression is amotivation. Therefore, patients who are suffering from depression typically are sedentary and may lack the motivation to begin an exercise program (Craft & Perna, 2004). Current physical activity recommendations for adults may seem overwhelming for individuals suffering from depression, thus possibly impacting their feelings of self-efficacy. It may be difficult to motivate individuals who are experiencing medical problems or life stressors to become physically active.

Although research has suggested an association between exercise and reduction in depression symptomatology, issues with RCTs and poor methodological integrity raise criticism surrounding the true effect size (Rethorst, Wipfli & Landers, 2009). Lawlor and Hopker's (2001) meta-analysis concluded that the evidence does not support the use of exercise in the treatment of depression, due to methodological weaknesses; these methodological weaknesses include lack of treatment concealment, lack of intent to treat, and lack of a clinical interview to confirm the diagnosis in included studies.

Another issue with the use of exercise for the treatment of depression is the costs and health risks associated with it. These risks and costs include time, cost of gym memberships, muscle soreness and fatigue, and effort expenditure (Rethorst et al., 2009). Although there are some risks involved with exercise, the costs and risks associated with psychotherapies and drugs can be far greater. These costs can include high monetary costs and side effects of medication (e.g., changes in sleep patterns, weight loss, suicidal

ideations, and seizures)(Rethorst et al., 2009). Exercise can have many additional benefits beyond mood improvement. These benefits include 1) reduced risk of cardiovascular disease, high blood pressure, and certain cancers, 2) improved mortality rates and cognitive function, and 3) maintenance of normal strength and peak bone mass (US Department of Health, 1996; Warburton, Nichol, & Bredin, 2006).

In addition to fewer side effects and increased health benefits in using exercise for the treatment of depression, studies have established the efficacy of exercise in decreasing symptoms of depression. Although lacking the highest methodological quality, prior data and meta-analysis have concluded that exercise does result in mood improvement. The extent to which exercise improves depressive symptomology, as compared to other forms of therapy, is yet to be significantly examined.

Meta-Analysis

Meta-analysis, a subset of systematic reviews, has been previously described as the pinnacle of evidence based research design (Hippokraqtia, 2010). In 1979, Glass defined a meta-analysis as “The statistical analysis of a large collection of analysis results from individual studies for the purpose of integrating the findings" (Glass, 1979). In medicine, it is important to integrate clinical evidence from multiple studies into the decision-making process (Haidich, 2010). Meta-analytic statistics allow for clinicians to draw stronger conclusions about particular interventions, thus assisting them as they decide on clinical interventions.

According to Rousseau and Evans (2017), there are two scenarios in which meta-analysis can be useful. Meta-analysis may be useful when there is a need to resolve disagreement regarding the true effect size of a particular treatment or intervention and/or in order to determine the assumptions that will be used when designing a study hypothesis (Rousseau & Evans, 2017). The purpose of this network meta-analysis is to resolve inconsistencies surrounding the precise effect size of aerobic physical activity, behavioral activation therapy, cognitive behavioral therapy, and non-directive supportive therapy on depression. Meta-analyses have been done on each of these four interventions using a population suffering from depression. This study provides an up to date analysis and inclusion of new RCTs, as well as the incorporation of indirect statistics based upon a network meta-analysis framework.

Several statistical and methodological considerations must be made when performing meta-analysis. One of the most important considerations that must be made is statistical heterogeneity (Haidich, 2010). Because physical activity and psychotherapeutic research are highly variable in patient characteristics and treatment protocol, some heterogeneity is likely expected. Subsequently, due to expected heterogeneity, the random effects model will be used. The random effects model assumes that the observed estimates of treatment effects can vary across studies because of differences in treatment effect in each study, as well as by chance (Riley, Higgins, & Deeks, 2011). In order to examine heterogeneity across studies, the I^s statistic will be used. I^s is a statistic developed by Higgins and Thompson, which quantifies the percentage of variability in point estimates that is due to heterogeneity rather than sampling error (Haidich, 2010). In order to investigate and mediate sources of potential heterogeneity, this author intends to

run a meta-regression analysis. Meta-regressions allow for an outcome variable to be predicted according to values of one or more explanatory variables (i.e., sex or age) (Cochrane, n.d).

The other major methodological and statistical consideration that must be made when performing a meta-analysis is bias detection (Haidich, 2010). The most significant source of potential bias in meta-analyses results from the selection criteria used to identify the publications for inclusion (Haidich, 2010; Rousseau & Evans, 2017). Due to the assumptions that must be met for a network meta-analysis, the inclusion criteria for this systematic review will be strong enough to reduce likelihood of bias. Several methods have been developed to reduce the risk of publication bias or, at the very least, to account for it. The most commonly used method is the funnel plot (Haidich, 2010; Rousseau & Evans, 2017). Developed by Light and Pillemer (1984), the funnel plot provides a graphical representation (i.e., a scatterplot) of each included study's effect estimates against its sample size (Egger, Smith, Schneider, & Minder, 1997). If publication bias is not detected, the plot is expected to have a symmetric inverted funnel shape (Egger et al., 1997). To evaluate evidence of publication bias in this meta-analysis, funnel plots will be used.

Network Meta-Analysis

Network meta-analysis, or multiple treatment comparison meta-analysis, expands the scope of a traditional meta-analysis by integrating direct and indirect comparisons across trials due to the presence of a common comparator. The basic example is when a researcher is interested in comparing two interventions, A and C. Direct evidence can be

obtained from RCTs of either A or C versus a common comparator B. Then indirect comparisons can be made between A and C due to the common comparator B (Li, Puhan, Vedula, Singh, & Dickersin, 2011). The usefulness of network meta-analyses occurs, according to Lu and Ades (2004), when the following issues arise:

> 1) There is no direct evidence that relates interventions to health outcome.
>
> 2) Direct evidence does exist for a specific treatment comparison but the evidence does not provide enough information for statistical analysis. Therefore, indirect comparisons can add to the strength of direct comparisons so statistical analysis can be performed.
>
> 3) No single treatment comparisons are of interest, therefore researchers want to simultaneously compare multiple treatment options.

There are a number of underlying assumptions that must be met to perform a network meta-analysis. These assumptions are underlying indirect and mixed comparisons, and they include transitivity and consistency (Salanti, 2013). In order to conduct a comparison between studies, it is important that treatments and studies are similar in clinical and methodological characteristics (Cipriani et al., 2013). Transitivity is defined as when "Treatment A is similar when it appears in AB and AC trials." (Salanti, 2013, Slide 7). Due to its definition, transitivity is also commonly referred to as

similarity. In order to conduct a network meta-analysis, this assumption should hold true for all cases where indirect or mixed estimates are derived (Cipriani et al., 2013). The plausibility of this assumption lies with a researcher's judgment to decide whether the distribution of effect modifiers is consistent enough across studies to make a network meta-analysis valid. If an inconsistent distribution of effect modifiers across studies is identified, it is possible to improve transitivity through a network meta-regression (Cooper, Sutton, Morris, Ades, & Welton, 2009).

The second assumption when performing a network meta-analysis is consistency. Consistency is the idea that direct and indirect evidence agree (Salanti, 2013). Consistency is the statistical manifestation of transitivity and can only be evaluated when a loop in the network exists, meaning there are direct and indirect comparisons of interventions (Cipriani et al., 2013).Inconsistency refers to the degree to which there is disagreement between specific treatment effects. Inconsistency is measured by examining the differences between direct and indirect estimates and analyzing whether the difference is beyond that which could be explained by chance (Salanti, 2012). Within a meta-analysis, heterogeneity is typically evaluated through the Cochran Q test or the I2 test. Consistency in a network meta-analysis will be evaluated statistically by comparing the direct and indirect summary effects in loops (Cipriani et al., 2013).

In analyzing network meta-analysis, it is important to recognize the type of evidence contributing to the comparisons. Arguments in literature suggest that priority should be given to direct evidence since it does not rely on the transitivity assumption (Cipriani et al., 2013). If it is deemed by researchers that the transitivity assumption holds

true, then the argument could be raised that mixed evidence is preferable due to the fact the inclusion of indirect comparisons can lead to improvement in precision for the estimated effect sizes. Conversely, a study in 2008 found that, in some situations, indirect evidence may be more reliable than either mixed or direct evidence (Song, Harvey, & Lilford, 2008). One case where this may be true is if all the direct evidence used for analyses is subject to the same or similar types of bias. If this is the case, then these biases can be theoretically cancelled out when indirect comparisons are made. Although the distinction between evidence is important, it is more important to note that if there are inconsistencies between the types of evidence then, instead of choosing between types of evidence, the possible sources of inconsistency should be examined (Cipriani et al., 2013).

A conceptual question that may be asked when conducting a network meta-analysis is 'How many studies are needed to conduct one?' Ideally, the more treatments included in a network meta-analysis the more informative and strong the results of the network will be (Cipriani et al., 2013). As seen in previous studies, the minimum requirement for a network meta-analysis is that each study of interest must be represented by at least one study and the network needs to be connected. It is also possible that data sets that are too large may lead to increased variability across comparisons and therefore make the transitivity argument difficult to hold true (Cipriani et al., 2013). Therefore, when conducting a network meta-analysis, having strict inclusion criteria may decrease the number of studies included, possibly leading to imprecise estimates; less strict inclusion criteria may include more studies that may increase confidence in the results, but might cause the transitivity argument to become difficult to defend.

CHAPTER 3

METHODOLOGY

The objective of this thesis was to systematically review and meta-analyze RCTs evaluating the effects of CBT, BA, NDST, and PA on depressive severity in patients with depressive disorders. In addition, it was the goal of this study to expand upon the four pairwise meta-analytic comparisons using a network meta-analytic framework. This chapter includes: (1) Research Design; (2) Inclusion of Studies; (3) Procedures; and (4) Statistical Analyses.

Research Design

This thesis will be conducted as a systematic review and will be reported in line with PRISMA guidelines. The protocol is registered through PROSPERO, registration number CRD42018089067. The PRISMA statement is a 27-item checklist that aims to help improve reporting of systematic reviews and meta-analyses (See Appendix A) (Moher, Liberati, Telzlaff, & Altman, 2009). A detailed literature search was conducted by a medical librarian, Stephanie Roth. Inclusion criteria will be defined a priori using the PICOS components (participants, interventions, comparators, outcomes, and study design) as defined by the PRISMA statement on systematic reviews (Moher et al., 2009). Articles identified underwent a three-step process. First, studies retrieved using the search strategy were screened in a blinded process by two independent authors, myself included, using Rayyan QCRI software, a tool designed to expedite the initial screening of abstracts and titles (Ouzzani, Hammady, Fedorowicz, & Elmagarmid, 2016), and to identify

studies that potentially satisfied the inclusion criteria. Any discrepancies over the inclusion of particular studies will be resolved by three independent conflict resolvers. Following resolution of conflicts, two independent authors will extract data using a data extraction form created a priori. Lastly, prior to beginning data analysis, two authors assessed the studies for risk of bias using the Cochrane Risk of Bias Tool (RoB 2.0) for assessing the risk of bias in randomized trials (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). The risk was assessed by analyzing the following factors: random sequence generation, allocation concealment, blinding of participants, blinding of those delivering the intervention, blinding of outcome assessors, incomplete data outcome, and selective reporting of others (Schuch et al., 2016). Risk of bias was assessed for each criteria as low risk of bias, unclear, or high risk of bias (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). Discrepancies, with both data extraction and risk of bias, were discussed with a third reviewer until consensus was reached.

Inclusion Criteria

Inclusion criteria was defined a priori using the PICOS components (participants, interventions, comparators, outcomes, and study design) as defined by the PRISMA statement on systematic reviews (Moher et al., 2009).

Participants

Patient populations with diagnosed depression, as well as elevated depressive symptoms, were eligible for inclusion. Studies that included individuals with seasonal

depressive disorder or bipolar disorder were excluded. Studies involving patients suffering from psychosis, such as schizophrenia, were excluded. Studies that involved other forms of depression, including post-partum depression, were included. No restrictions involving patient gender were made. Patients must have been 18 years or older in order to be considered for inclusion. No other restrictions regarding population characteristics were applied. Studies involving participants with comorbid disorders were eligible for inclusion, whether they suffered from comorbid general medical or psychiatric disorders.

Interventions

Due to the nature of this review, there were multiple experimental interventions. The different inclusion criteria for each intervention included:

Physical Activity-Studies on physical activity included aerobic exercise interventions or mixed exercise interventions. Mixed exercise interventions included aspects of aerobic exercise as well as anaerobic activity such as weightlifting. RCTs including mindfulness based exercise programs (e.g. yoga or tai chi) were excluded.

Cognitive Behavioral Therapy-CBT or CT was defined as a therapy in which the therapist focuses on the impact that a patient's present dysfunctional thoughts affect current behavior and functioning. The goal of CBT is to help patients evaluate, challenge, and modify dysfunctional beliefs, in order to promote behavioral change and improve overall functioning. Therapies that could be part of CBT, Psychological Skills Training, Behavioral Activation, or Social Skills Training were not included if there was no

mention of cognitive restructuring. CBT must be described as it was originally defined by Beck. Second and third generation CBT therapies, like acceptance and commitment therapy, were excluded.

Behavioral Activation Therapy- Studies were included when the effects of activity scheduling on adults with depression were compared to a control condition. An intervention was considered to be activity scheduling when the registration of pleasant activities and the increase of positive interactions between persons and their environment were the core elements of treatment.

Non-Directive Supportive Therapy (**NDST**)- Studies were included if they compared NDST to usual care or waitlist control in a population suffering from depression as their main problem. NDST is defined as any unstructured therapy that used only psychological techniques common to all psychotherapeutic approaches, such as empathy and compassion. Trials in which the intervention was not intended to be therapeutic were excluded.

For all interventions, no restrictions were made regarding treatment length, frequency, or duration of the intervention program. Psychotherapeutic interventions, as defined by a previous meta-analysis, were defined as interventions with a focus on language-based communications between a therapist and a patient, or as therapist supported bibliotherapy (Barth et al., 2013). No restrictions were made based on the treatment setting (online or face-to-face) and treatment format (individual or group). Comparisons of a psychotherapeutic intervention with pharmacotherapy or other non-psychotherapeutic interventions were excluded. Studies that included participants on

stable doses of pharmaceuticals were included. Studies were excluded if the psychological interventions could not be distinguished from other elements of the intervention. Excluded were studies on relapse prevention and maintenance treatment, as well as studies that included anxious, but not depressed, individuals at the time of inclusion. All studies comparing the experimental interventions to usual care, waitlist control, or placebo control interventions were included. Comparisons of psychotherapeutic interventions with pharmacotherapy or other non-psychotherapeutic interventions were excluded. Again, studies that use treatment as usual (TAU) or usual care (UC) for controls are included, even if TAU or UC includes pharmacotherapy. If the comparison group was a single drug comparison, then those studies were excluded.

Outcome Measures

The outcome measure for the pairwise meta-analytic portion of this study was the overall effect size of CBT, BA, NDST and PA on depression as computed by standardized mean difference (SMD). The outcome for the network meta-analytic portion was also the SMD statistic. To be eligible, RCTs must have assessed depression symptomatology through the use of any validated depression scale. Studies that did not include a validated screening measurement scale for depression, such as the Hamilton Rating Scale for Depression (HAM-D) (Hamilton, 1967) or the Beck Depression Inventory (BDI) (Beck et al., 1961), were excluded. Additional measurement scales that were included are the Center for Epidemiologic Studies Depression Scale (CES-D), the Patient Health Questionnaire-9 (PHQ-9), the Minnesota Multiphasic Personality Inventory (MMPA-D), or any other validated scale for depression. In addition to the use

of a measurement scale, studies must have reported statistical data through which SMD can be computed; this includes, but is not limited to, pre-and post- intervention scores, or reported mean change and standard deviation, and p-value statistics.

Secondary Outcomes included:

1) A sub-group analysis exploring the effect of several potential moderator variables. These variables included: type of control, treatment format, depression severity, intervention length, and number of treatment sessions.

Types of Studies

Only RCTs (published and peer-reviewed) were considered for inclusion. No language restrictions or publication date restrictions were imposed on the initial search. Studies without available data or without English translation were excluded.

Search Methods for Identification of Studies

Procedures

For the identification of studies included or considered for this network meta-analysis, the reviewers worked with a medical librarian with expertise in systematic reviews to develop detailed search strategies for each database. The search included seven searches developed for PubMed (NLM) for seven distinct categories (See Appendix B). The search strategies were a combination of controlled vocabulary and free text terms. There were no date restrictions. The search period was from January 22, 2018 until March 8, 2018 and the seven searches were translated and replicated in each of the

additional databases as listed below. The following electronic databases and grey literature sources were searched: (1) PubMed (NLM) (Appendix B); (2) Embase (Elsevier); (3) Scopus (Elsevier); (4) Cochrane Central (Wiley); (5) PsycInfo (EbscoHost); (6) ClinicalTrials.gov; (7) PsychiatryOnline.org. A search filter was implemented for human studies (reference for humans filter: http://aub.edu.lb.libguides.com/c.php?g=329862&p=3023731) and the search was limited to randomized controlled trials using the Therapy Broad filter from Clinical Queries.

Additional Search

The author crossed – checked the reference lists of all included RCTs, and the most recent systematic reviews and meta-analysis for each intervention. In addition, Google Scholar was checked in order locate any unpublished grey literature, on-going studies, studies that were not catalogued, and relevant dissertations.

Data Collection and Analysis

Study Selection

After studies were identified, duplicate studies were omitted from the results. Endnote was used for the deduplication of records. Included studies were screened by title and abstract by two independent reviewers based on inclusion criteria. Rayyan QCRI was used to expedite the initial blinded screening of abstracts and titles by two independent reviewers, including myself (NH) and AS (Ouzzani et al., 2016). If a

decision could not be made regarding an article's eligibility, three independent reviewers (CL, FA, JS) resolved any discrepancies.

Data Extraction

Data were extracted using a data extraction form created a priori. The data extraction form made by the Cochrane Collaboration was modified and converted into a Microsoft Excel™ file to extract data from selected articles. The form captured: (1) general information, (2) research design, (3) participant characteristics, (4) outcome measures, (5) statistical data, and (6) details about type and nature of each interventions. Data extraction was completed by three independent outcome extractors (LT, TJ, AB).

Assessment of Study Quality and Risk of Bias

The same two reviewers (NH, AS) conducted a risk of bias assessment on included studies using the Cochrane Risk of Bias Tool (RoB 2.0) for assessing the risk of bias in randomized trials (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). This assessment evaluated the following: bias arising from the randomization process; bias due to deviations from intended interventions; bias due to missing outcome data; bias in measurement of the outcomes; and bias in selection of the reported result (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). Risk of bias was assessed for each criterion as low risk of bias, some concerns for bias, or high risk of bias (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). The overall judgement of each item for each study was judged as 'low', 'high' and 'unclear' according to the levels of bias. Discrepancies between reviewers were resolved by the third reviewer (TJ).

Statistical Analysis

Measure of Treatment Effect

All outcome data were processed as continuous variable to calculate the SMD with 95% confidence intervals. In addition, all extracted data was presented as OR with 95% confidence intervals for the network meta-analysis.

Assessment of Heterogeneity

The I^2 statistic was used to evaluate heterogeneity of the pooled data. This is a statistical tool for reporting heterogeneity by estimating the percentage of variation across trials (Higgins & Thompson, 2002). Heterogeneity results were interpreted based on the guidelines proposed by Higgins and Thompson. Heterogeneity was considered 'low', 'medium', and 'high', when corresponding to 25%, 50%, and 75% respectively (Higgins & Thompson, 2002).

Data Synthesis

All pairwise meta-analytic procedures were performed in the software Comprehensive Meta-Analysis (CMA) version 3 (CMA: Version 3, Biostat, Englewood, NJ). Due to expected heterogeneity, a random effects meta-analysis will be conducted. Unlike the fixed effects model, the random effects model states that studies may differ on certain factors and therefore, different effect sizes among studies may be found (Borenstein et al., 2009). The standardized mean difference (SMD) and 95% confidence intervals will be used as the effect size (ES) measure. For the individual pairwise meta-analysis, all between-group effect sizes were computed. In addition, CMA will be used to

produce a forest plot to visually inspect for publication bias and Egger's test confirmed visual inspection by yielding a significant p-value (Borenstein et al., 2009, Chapter 30).

The network meta-analytic extension was run through the program Stata version 15 (StataCorp, 2018). The network meta-analysis was performed using Stata routines described elsewhere (Chaimani, Higgins, Mavridis et al., 2013). All within-group effect sizes were computed in order to run the network meta-analysis through Stata. A network plot was produced in order to visually represent the interventions and the evidence base for each. The amount of available information for each treatment arm was presented by weighing the nodes and using different node sizes or line thickness (Chaimani et al., 2013). In addition to a network plot, a contribution plot will be produced. This outcome showed the influence of each direct piece of information, RCT, on their neighboring comparisons (Chaimani et al., 2013).

In order to evaluate the basic assumptions of a NMA, an inconsistency plot and a predictive interval plot will be produced (Chaimani et al., 2013). Inconsistency refers to any differences between direct and indirect effect estimates for the same comparison (Chaimani et al., 2013). Inconsistency threatens the validity of the results and the basic assumptions that the NMA were performed on. The inconsistency plot produces inconsistency factors (IF) for each closed loop (Chaimani et al., 2013). Stata produces predicative intervals (PrL) which is an interval in which the estimate of a future study is expected to be. Within the NMA framework, tests to assess multivariate heterogeneity have yet to been applied to NMA. Therefore, the presentation of summary effects with

PrL can help facilitate the interpretation of the results even with heterogeneity (Chaimani et al., 2013).

Lastly, surface under the cumulative ranking (SUCRA) probabilities were produced in order to rank the treatments based on the outcome measure (Chaimani et al., 2013). SUCRA curves express, as a percentage, the efficacy of every intervention relative to an imaginary intervention that is always the best (Salanti, Ades, & Ioannidis, 2011). Therefore, large SUCRA scores indicate a more effective intervention.

CHAPTER 4

RESULTS OF META-ANALYSES

Cognitive Behavioral Therapy

Description of Studies

Results of the Search

The electronic search of 5 databases, grey literature, and hand searching identified 20, 745 studies for consideration. Only a fraction of the 20,745 studies examined the effects of cognitive behavioral therapy as an intervention for treating depression. Two reviewers (NH, AS) examined the literature results and excluded obviously irrelevant records based on the title using the Rayyan QCRI software (Ouzzani, et al., 2016). After applying the inclusion and exclusion criteria, as specified in the previous chapter, 123 studies were included across all treatment arms. Out of the 123 studies, only 80 met the inclusion criteria for examining CBT as an intervention for depression. Some of the studies involved multiple CBT treatment arms, thus 85 total treatment arms were included in the pooled meta-analysis. As a result, 80 studies including a total of 8,890 participants were included in this meta-analysis. The actual number of participants analyzed varied according to the study design and type of intervention.

Characteristics of Included Studies

General Characteristics

The final sample consisted of 55 2-arm parallel, 10 3-arm parallel, and two 4-arm parallel RCTs. The studies were conducted all over the world, but most frequently in Asia, Europe, Australia, and North America. Only a few studies were from the Middle East and South America. Table 1 lists all the countries and regions for the included studies. All but two of the trials were reported in English. Two studies that met the inclusion criteria were in German (Ayen & Hautzinger, 2004; Hautzinger & Welz, 2004). The English translation of these studies was obtained and used to obtain study characteristics and outcome data.

Table1:

Region and Country of Included Trials

Region	# of Studies	Country
Asia	7	China, Malaysia, Japan, Thailand
Europe	24	England, Sweden, Netherlands, Switzerland, Italy, Germany, Ireland
Middle East	7	Iran, Jordan, Romania, UAE, Pakistan, Sudan
North America	25	United States, Canada
Oceania	8	Australia
South America	1	Brazil

Characteristics of Participants

Patients were recruited through a variety of methods. The most common ways participants were recruited to the trials included media recruitment, recruitment from

primary care, from a hospital, and from a university. Some of the studies directly studied the effects of CBT in a primary care setting (Eriksson et al., 2017; Williams et al., 2013). One RCT stated "Participants were recruited nationally from community and clinical settings…" (Fann et al., 2015). Many of the studies stated similar recruitment strategies, using both primary care referrals and media outlets in the community to recruit participants. As a whole, 11 studies directly stated that they used some form of media (e.g. newspaper, internet, radio, etc.) to recruit participants. In addition, 18 studies reported that they recruited participants through primary care referrals.

Types of depression examined varied greatly across the studies. The majority of studies examined the effect of CBT on depression or increased depressive symptomology. A few studies examined specific populations of individuals; these included the elderly (Hautzinger & Ward, 2004), college students (Peden et al., 2000; Saravanan et al., 2015), an a Latino population (Dwight-Johnson et al., 2011), religious individuals (Propst et al., 1992), an Asian population (Choi et al., 2012; Mukhter et al., 2011; Wong et al., 2008; Zu et al., 2014), and a Pakistani population (Naeem et al., 2014; Rahman et al., 2008). Out of the 80 studies, only five examined the effects of cognitive behavioral therapy on individuals with major depressive disorder (Fann et al., 2015; Omidi et al., 2013; Qiu et al., 2013; Scott et al., 1997; Teasdale et al.). Lastly, 16 studies examined depression due to another medical condition, these conditions include: diabetes (Lustman et al., 1998; Newby et al., 2017; Noroozi et al., 2017), multiple sclerosis (Larcombe et al., 1984; Mohr et al., 2000), alcoholism (Thapinta et al., 2014), parkingsons disease (Dobkin et al., 2011), cancer (Qiu et al., 2013; Savard et al., 2006), cardiac patients (Doering et al., 2016; Doering et al., 2013), traumatic brain injury (Fann

et al., 2015), stroke (Lincoln et al., 2003), substance abuse (Hunter et al., 2012), migraine (Martin et al., 2015), and hemodialysis patients (Duarte et al., 2009). Lastly, several studies examined depression in female populations caused by a variety of difficulties. These studies examined depression in females suffering from infertility (Farmazari et al., 2008), postnatal depression (Milgrom et al., 2011; Milgrom et al., 2016; Ngai et al., 2015; Prenderast et al., 2001) , and perinatal depression (O'Mahen et al., 2013).

All included studies reported clear diagnostic, inclusion, and exclusion criteria for their participants. Each study varied when considering the minimum degree of depression required in order to be included in the study. As stated previously, five studies examined the effects of CBT on individuals with major depressive disorder. Overall, the inclusion criteria for each study varied greatly. This is evident by the fact that 22 studies stated that their inclusion of participants required a DSM or ICD-10 diagnosis of major depressive disorder, persistent depressive disorder, or another form of depression. The majority of studies did require some minimum score on a depression measurement scale necessary to be included in the RCT. The scales used to determine inclusion and exclusion of participants were the BDI, PHQ-9, EPDS, HAMD, GDS, CES-D, MASDS, and the 9Q.

In addition to the variety of scales used for inclusion, RCTs used a large range of minimum scores necessary to include participants in their study. The most common measure used to include participants was the BDI, but the minimum score needed to be achieved ranged from a nine to above 20. A number of studies provided a maximum score as well, stating that participants must score between a 10 and a 47 on the BDI in

order to participate in the study. Another commonly used scale for inclusion was the HAMD. A majority of the studies that used this inventory stated that participants must score above 14 in order to be included, but one study stated that individuals must score between 10 and 24. Lastly, other commonly stated inclusion scores include above 9 on the PHQ-9, above 12 on the EPDS, and above 16 on the CES-D. In summary, the inclusion scores indicate that most studies were evaluating, at minimum, mild to moderate depression. Only a few studies indicated inclusion scores that would indicate individuals were, at minimum, suffering from severe depression.

Intervention Characteristics

The protocol used to administer cognitive behavioral therapy was dissimilar across studies. Studies were included regardless of intervention delivery method, therefore studies that examined the effects of telephone administered CBT, internet administered CBT, bibliotherapy and face-to-face CBT were all included. The majority of studies examined the effects of face-to-face CBT on depression (n = 43). Of the remaining studies, 16 examined the effects of internet administered CBT on depression and the rest were evenly split between examining bibliotherapy and telephone administered therapy. Another important consideration when examining CBT protocol across studies is whether the CBT was individual or group led. Most of the studies examined the effects of individual group counseling (n = 24) on depression, while 16 studies examined the effects of group counseling. Overall, two studies used different protocol for administering individual or group therapy sessions. Ross et al (1985) examined the comparative effects of group CBT and individual CBT to a treatment as

usual control (Ross et al., 1985). The second study allowed participants to use either group or individual therapy, without any specification within the study protocol (Miranda et al., 2008). Most of the face-to-face delivered CBT interventions were delivered by a masters or doctoral level therapist. The few exceptions to this were a couple of studies involving trained nurse delivered therapy (Doering et al., 2016; Pendergast et al., 2001).

The procedures of many studies directly stated that CBT therapy was delivered as described by Beck. Even when studies did not state that techniques implemented were based on Beck, the description of the methods used provided evidence of proper CBT interventions. Embling et al. (2002) stated that the intervention "involved activity scheduling focusing on 'mastery and pleasure', behavioral assignments and identification and monitoring of negative automatic thoughts and emotions, rational appraisal of these and of dysfunctional attitudes using dysfunctional thought record" (p. 37). Other studies reported similar techniques, such as social skills training, challenging dysfunction al beliefs, and pleasant activity scheduling (Martin et al., 2015). In addition, an important element to most of the interventions included homework assignments.

In addition to inconsistencies in cognitive behavioral therapy protocol, studies varied dramatically surrounding the length and frequency of the intervention. The length of treatment varied from one day (Harrell et al., 2014) to one year (Wiersmia et al., 2014), with the majority of treatment durations being between 8 and 12 weeks. The number of sessions completed within each week during the intervention also greatly varied. The majority of studies had participants undergo therapy once a week. Other studies had participants undergo therapy biweekly (Jarrett et al., 1999; Lustman et al.,

1998; Mukhter et al., 2011; Thapinta et al., 2014), and once every other week (Carta et al., 2012). Overall, the session durations lasted anywhere from 30 minutes (Scott et al., 1997) to 3 hours (Mukhter et al., 2011). The majority of studies had session lengths between 1-2 hours.

Of the 80 studies included, all of them compared cognitive behavioral therapy to a non-active control. A majority of the studies (n = 38) compared CBT to a treatment as usual control. A total of 36 studies compared CBT to a waitlist control, and the remaing six studies compared the experimental group to a placebo group. Although the vast majority of studies were two-arm designs, there were some multiarm designs as well. There were a total of 55 studies that compared CBT to a control and all of the other studies compared CBT to a control and another active group. Many of the multiarm designs compared multiple forms of CBT to each other (e.g. internet-delivered CBT to therapist delivered CBT) and CBT to medication, as well as a control group. One multiarm trial compared CBT to supportive counseling (NDST), as well as to a control (Freedland et al., 2009). The remaining three multiarm trials all compared CBT to physical activity as well as a control group (Huang et al., 2015; Hallgren et al., 2015; Hess-Homeier, 1981).

Outcome Measures

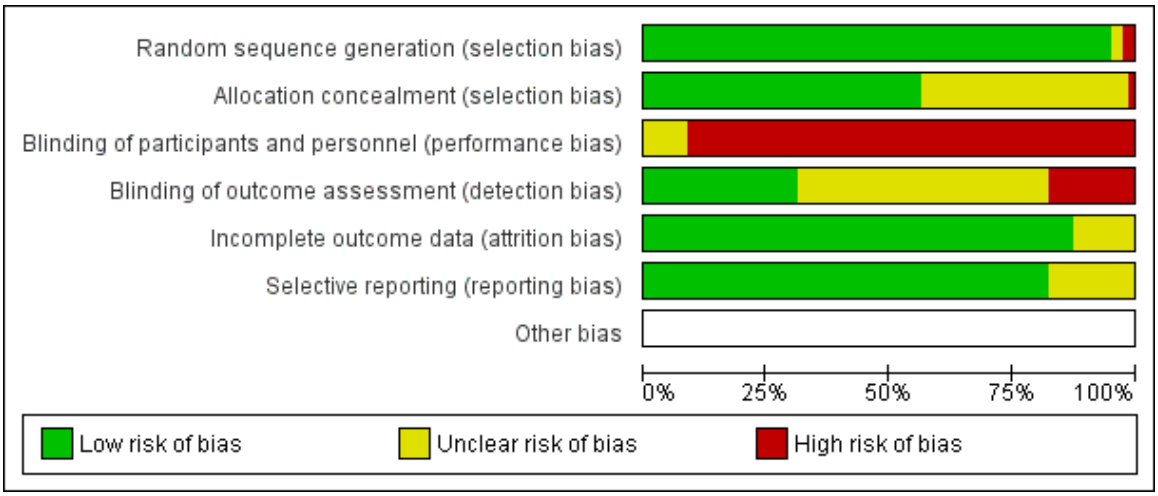
The primary outcome of the review was change in depression scores. In order to quantify this measure, all of the included studies used a validated depression scale. All of the included studies used many different measurement inventories to measure depression. The majority of studies (n = 37) used Becks Depression Inventory (BDI) or some version

of the BDI (e.g. BDI-2) in as the primary outcome measure of depressive symptoms. The next most frequently used outcome measure for the included studies was Hamilton's Rating Scale for Depression (HAMD) (n=8). Some studies (n=7) used both the HAMD and the BDI in order to quantify change in depression. The rest of the studies used a variety of different outcome measures; three studies used the CES-D (Christensen et al., 2004; Haringsma et al., 2006; van Bastelaar et al., 2011), three used the EPDS (Ngai et al., 2015; O' Mahen et al., 2013; Prendergast et al., 2001), two studies used the PHQ-9 (Dwight-Johnson et al., 2011; Smith et al., 2017), two studies used both the CES-D and BDI (Peden et al., 2000; Brown et al., 1984). Finally, there was a variety of outcome measures that only one study used; these outcome measures included: the 9Q (Thapinta et al, 2014), HAD (Naeem et al., 2014), GDS (Hautzinger et al., 2004), IDS (Wiersma et al., 2014), the combined GDS and BDI (Landreville et al., 1997), the combined BDI and MARDS (Andersson et al., 2005), the SCID-1 (Omidi et al., 2013), and the combined BDI and PHQ-9 (Titov et al., 2010).

Risk of Bias Assessment

Figures 2 and 3 provides a summary of the risk of bias of the included studies.

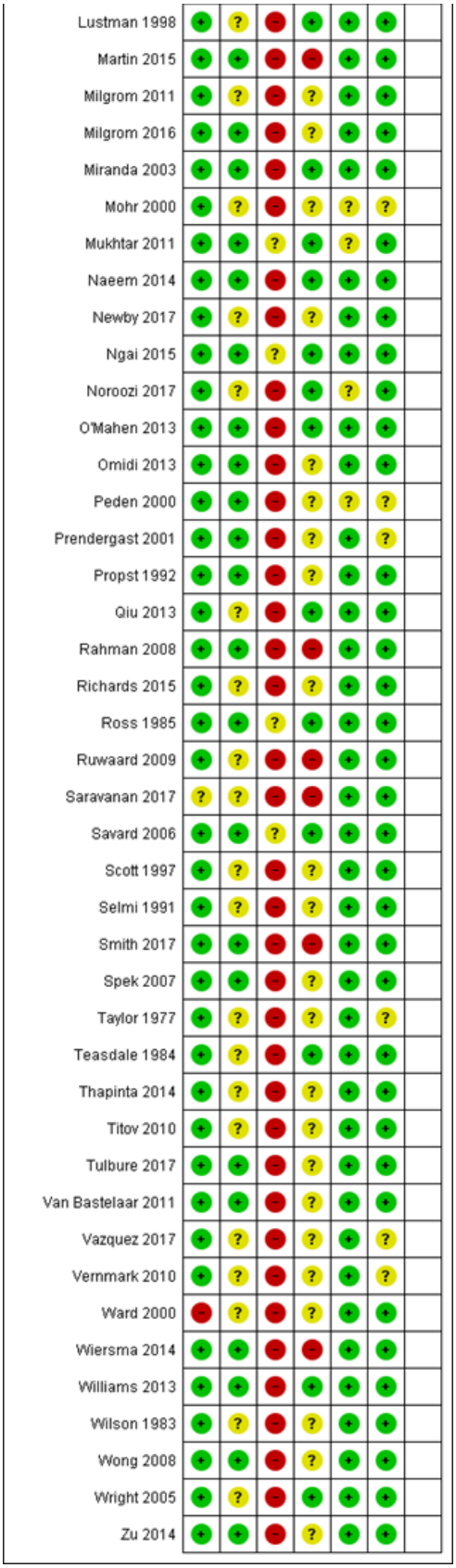
Figure 2: Risk of Bias Graph



Randomization

In order to determine if the studies were randomized, it was assessed whether the authors clearly described the method by which randomization was achieved. All included studies reported that the groups were randomized. Almost all of the studies were deemed to have low risk of bias due to randomization procedure. Ward et al. (2000) was rated a high risk of bias because the participants were only partially randomized. Ward et al. described the process as follows: "We encouraged participants to accept randomisation. Those who continued to express a strong preference were allowed to choose their treatment" (Ward et al., 2000, p. 1384). Studies used a variety of different ways to achieve randomization. Hallgren and colleagues, for instance, did not use a computer generated list in order to preform randomizations. Researchers randomized the participants through an independent clinical research organization (Hallgren et al., 2015).

Figure 3: Risk of Bias Summary


Lustman 1998
Martin 2015
Milgrom 2011
Milgrom 2016
Miranda 2003
Mohr 2000
Mukhtar 2011
Naeem 2014
Newby 2017
Ngai 2015
Noroozi 2017
O'Mahen 2013
Omidi 2013
Peden 2000
Prendergast 2001
Propst 1992
Qiu 2013
Rahman 2008
Richards 2015
Ross 1985
Ruwaard 2009
Saravanan 2017
Savard 2006
Scott 1997
Selmi 1991
Smith 2017
Spek 2007
Taylor 1977
Teasdale 1984
Thapinta 2014
Titov 2010
Tulbure 2017
Van Bastelaar 2011
Vazquez 2017
Vernmark 2010
Ward 2000
Wiersma 2014
Williams 2013
Wilson 1983
Wong 2008
Wright 2005
Zu 2014

Allocation Concealment

Only a few of the studies reported on allocation concealment. The majority of studies had an unclear risk of allocation concealment bias. One study that reported on allocation concealment was performed by Freedland. This study described the procedure as "Group assignments were concealed in sealed envelopes and revealed to the study coordinator immediately after the participant completed all of the baseline assessments" (Freedland et al., 2009, p. 2009). Another study stated that "The randomization process was performed with all study patients in one group, which concealed the allocation to be from both the PCC personnel and the researchers" (Eriksson et al., 2017, p. 129). The majority of the studies did not report on allocation concealment, which is evident by the majority of studies have unclear risk of allocation concealment bias.

Blinding Interventions

Blinding of the participants was not possible because of the nature of the interventions. As evidenced in Figures 2 and 3, the risk of potential performance bias was high for almost all included studies due to the nature of the behavioral interventions assessed; it was impossible to blind participants to the status of their intervention, and difficult to blind personnel and staff (e.g. counselors or psychologists). Out of the 80 included studies, only seven received an unclear level of performance bias. The seven studies that received unclear performance bias ratings were able to blind assessors and researchers at each feasible point. Ngai (2015) blinded the therapists who delivered the intervention and the outcome assessors to the pretreatment scores, group, and the protocol of the participants. Some studies stated the nature of the blinding for the outcome

assessors but many of the studies did not. One study stated, "This was followed by the administration of the HDRS by an independent evaluator, a resident in psychiatry, who was blind to study objectives and procedures. At the posttreatment evaluation, as well as 3 and 6 months after the end of treatment, the participants again met the independent evaluator, who was blind to study objectives and procedures and the patients' group allocation, for the administration of the HDRS and to complete the battery of self-report scales." (Savard et al., 2006). Fann et al.(2015) also stated that all screening, baseline, and outcome assessments were conducted by trained staff blinded to randomization status. Because blinding is not possible with these types of interventions, blinding of outcome assessors would help decrease detection bias.

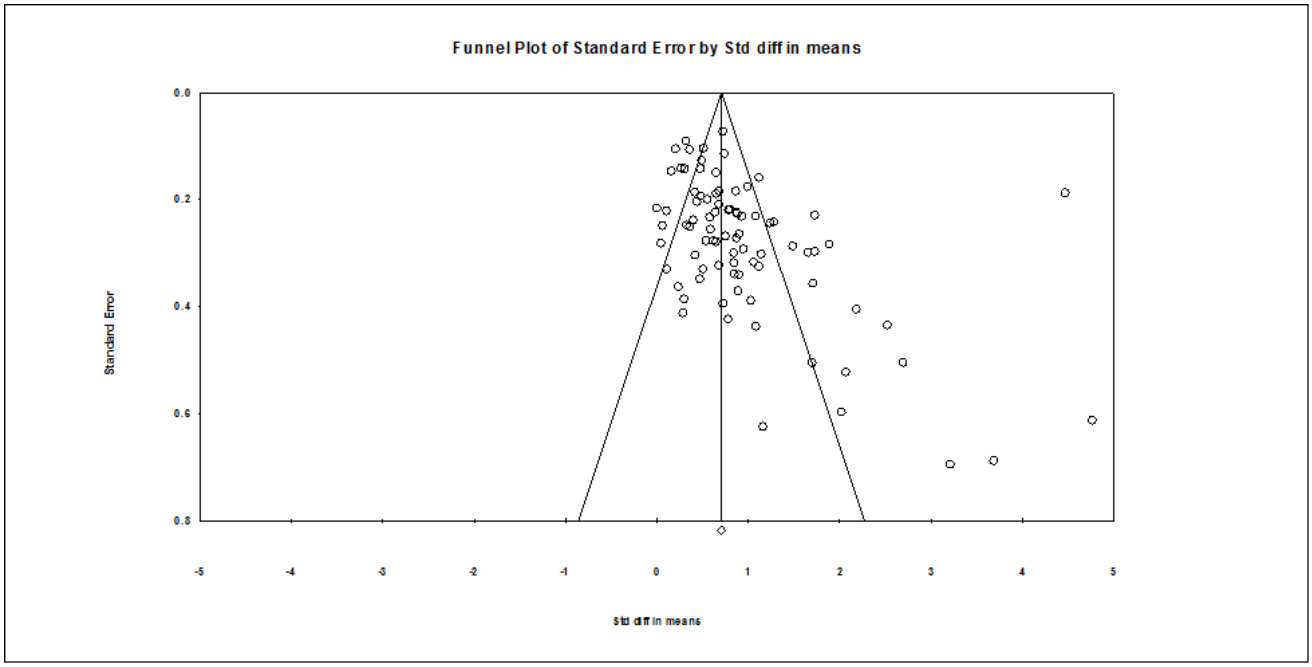
Reporting Bias

In order to assess reporting bias, the likelihood that information was chosen based off of multiple outcome measures or multiple analyses of data was examined. As a whole, there was evidence in multiple studies that selective outcome reporting or outcome reporting based off of multiple analyses of data may have occurred.

Assessment of Reporting Bias

P ublication bias was examined by visually inspecting a funnel plot according to the guidelines presented by Egger (Egger et al., 1997).

Figure 4: Funnel Plot for CBT



Following inspection of the funnel plot, it was clear that there is evidence of publication bias. The publication bias was judged as being moderate to high due to the asymmetry observed and the variation of where studies are plotted as compared to average (see Figure 4). The results of the funnel plot supported the results of the risk of bias assessment. Due to a variety of methodological issues, including reporting bias, selection bias, and performance bias, the risk of publication bias is moderate to high.

Effect of Cognitive Behavioral Theory

In the following section, the effects of Cognitive Behavioral Therapy on depression symptomology are presented. In addition to the overall effect of CBT on the primary outcome, the results of a series of meta-analysis moderating for specific a-prior defined variables are presented as well.

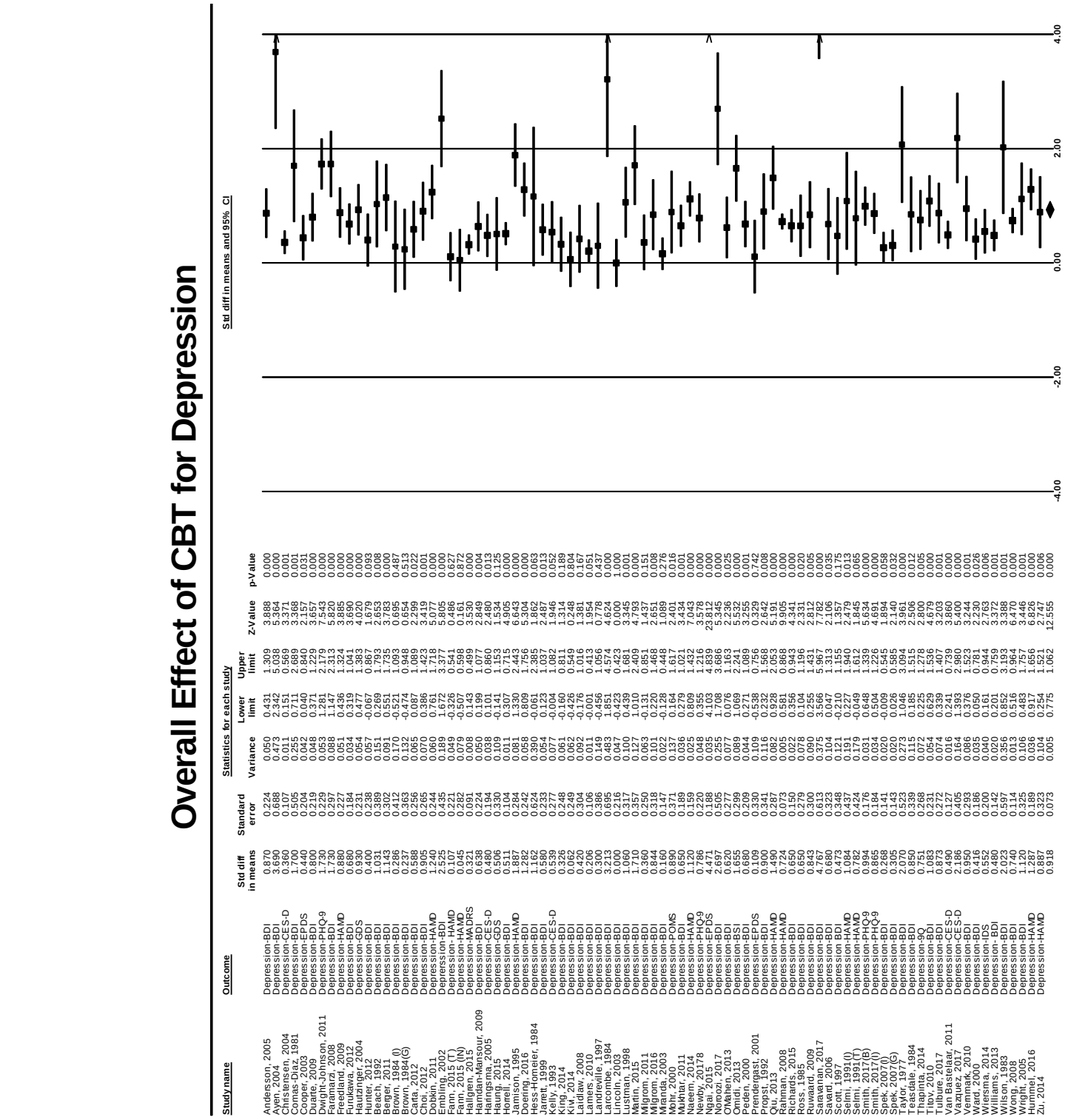
Overall Effect

In this analysis, data from 80 studies, and 85 treatment arms, were pooled together using the standardized mean difference (SMD). A large significant effect was found, SMD= .918 (SE=.073, 95% CL=.775-1.062, p=.000, I^2=30.420%; Figure 5). These results indicate that cognitive behavioral therapy significantly decreases depressive symptomology in individuals suffering from depression. The effect size of each study ranged from SMD=.000 (p=1.00) (Lincoln et al., 2003) to SMD=4.767 (p=.000) (Saravanan et al., 2017). Due to expected heterogeneity, the random effects model was used to conduct the meta-analysis. The I^2 statistic indicates that there was low to moderate heterogeneity and the results were slightly inconsistent across the studies analyzed. Subsequently, these findings must be interpreted cautiously due to potential publication bias and heterogeneity.

Effect due to Control Type

All of the included studies compared cognitive behavioral therapy to a non-active control. The three non-active controls used in the RCTs were treatment as usual (TAU), placebo control (PLC), and a waitlist control (WL). Out of the 80 included studies, only six used a placebo control design (Andersson et al., 2005; Christensen et al., 2004; Jarrett et al., 1999; Prendergast et al., 2001; Rahman et al., 2008; Saravanan et al., 2017). All of the remaining studies used either waitlist controls (n = 36) or treatment as usual (n = 38) as a control group. Overall, the treatment as usual trails found a

Figure 5: Overall Effect of CBT on Depression

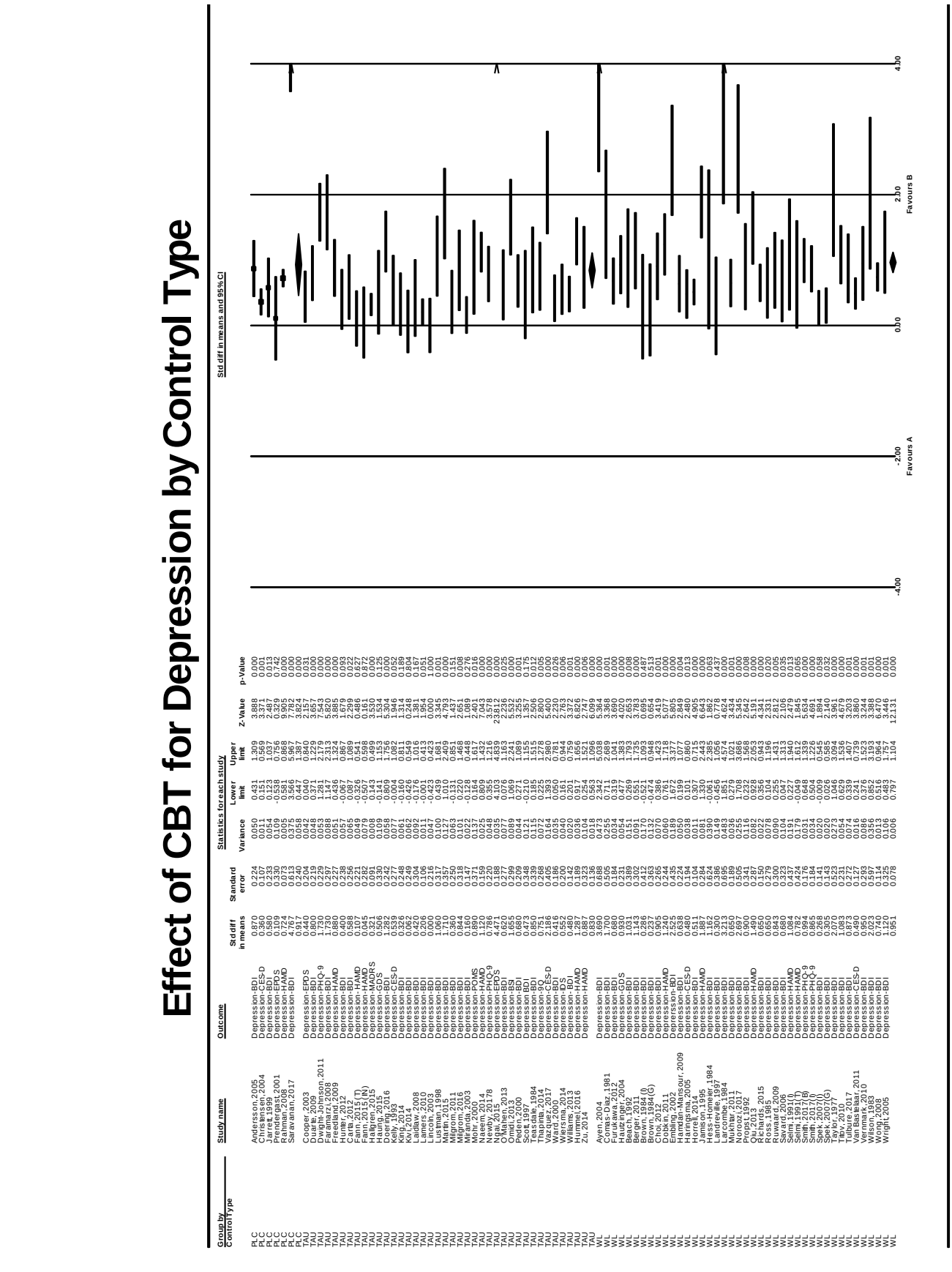


significant large effect, SMD= .830 (SE=.136, 95% CI=.563-1.096, p=.000, I^2=0.00; Figure 6). In addition, a significant large effect was found for the placebo control design study, SMD=.917 (SE=.240, 95% CI=.447-1.387, p=.031, I^2=80.857; Figure 6). Due to the fact only a few studies compared CBT to a placebo, the results of the PLC meta-analysis should be interpreted with caution. In addition, the placebo control studies displayed very high heterogeneity. Therefore, In order to strengthen the results of the PLC group, further research must be conducted. Overall, the largest significant effect was found when PA was compared to a waitlist control. A large significant effect was found (SMD=.951, SE=.078, 95% CI=.797-.1.104, p=.000, I^2=38.511; Figure 6). The heterogeneity in the waitlist control studies was low to moderate indicating some variability in study results.

Effect due to Treatment Intervention Length

The RCTs included used a variety of intention lengths to analyze the effectiveness of CBT for depression. The shortest study examined the effects of a one-day CBT workshop for depression (Horrell et al., 2014), while the longest intervention was one year in length (Rahman et al., 2015; Wiersma et al., 2014). The majority of the studies examined the effects of an 8 week intervention (n = 17), a 10 week intervention (n = 14), or a 12 week intervention (n = 15). The sub-group analysis found that all three interventions, 8 week, 10 week and 12 week, resulted in a large significant effect.

Figure 6: Effect of CBT on Depression due to Control Type

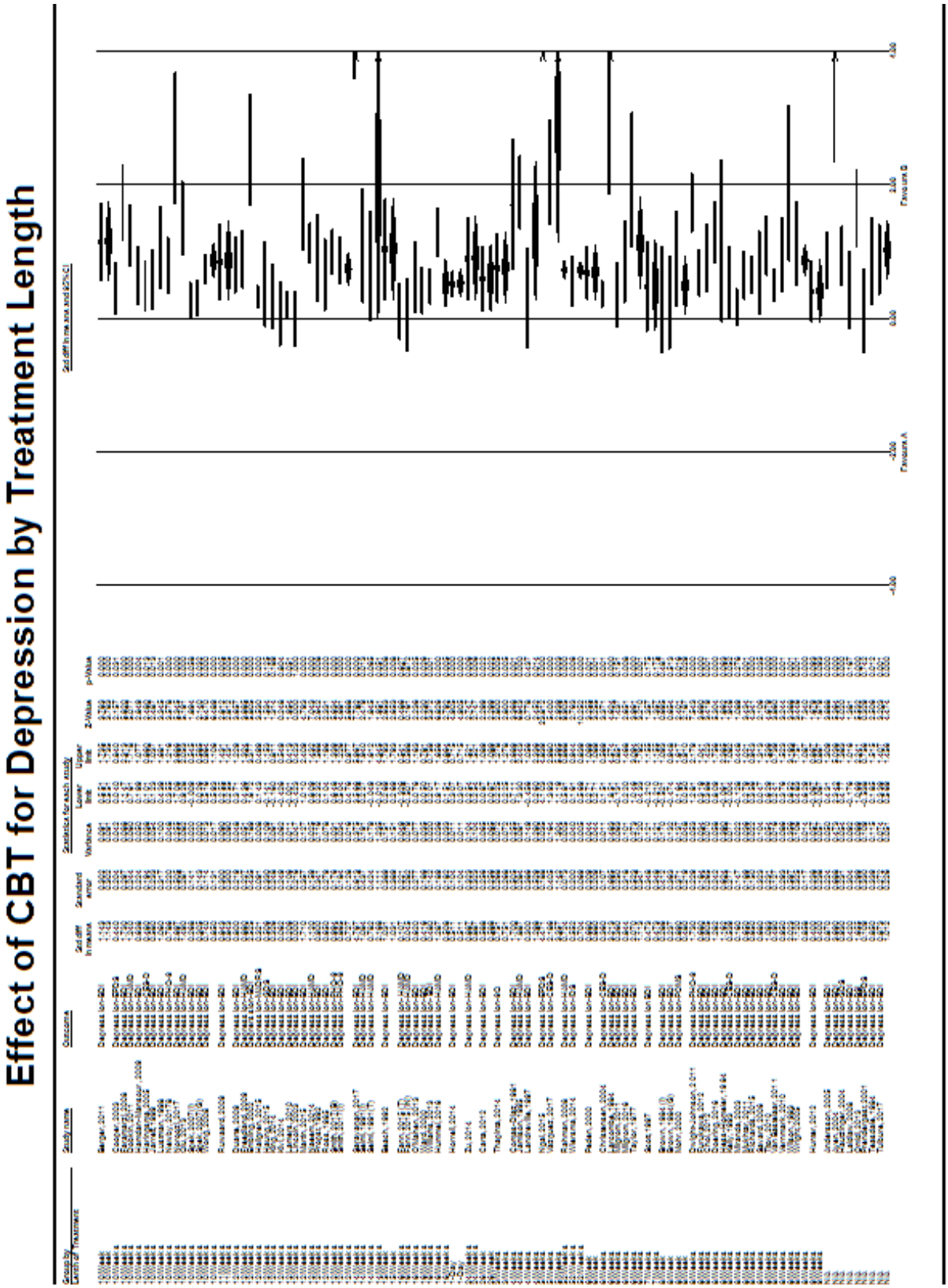


The pooled analysis of the 8 week intervention studies resulted in a SMD=.807 (SE=.107, 95% CI= .599-1.016, p=.000, I^2=0.000; Figure 7). The I^2 statistic for the 8 week long studies indicated that there was zero heterogeneity. Similarly, the pooled analysis of the 10 week intervention studies found a large significant effect, SMD= .864 (SE=.118, 95% CI= .631-1.096, p=.000, I^2=31.631; Figure 7). Lastly, the 12 week interventions resulted in a SMD= .815 (SE=.138, 95% CI= .544-1.087, p=.000, I^2=48.612; Figure 7). Both of the 10 and 12-week intervention sub-group analysis found a moderate level of heterogeneity. Therefore, there is some indication that there was moderate variation in the included RCTs. The result of the intervention time lengths had few studies included which suggests those results should be interpreted with caution. The shortest interventional time frame with multiple studies was 4 weeks (n=3). The analysis of these studies found a very large significant effect, SMD=1.298 (SE=.529, 95% CI= .260-2.336, p=.014, I^2=0.000; Figure 7).

Effect due to Treatment Format

The included studies used two main treatment format options to deliver cognitive behavioral therapy; these options were individual or group therapy. Miranda et al (2003) and Hummel et al. (2016) used both individual and group CBT. In addition, two studies compared the effects of both group and individual CBT for depression (Brown et al., 1984; Spek et al., 2007). These two studies had each treatment arm entered individually

Figure 7: Effect of CBT due to Treatment Length

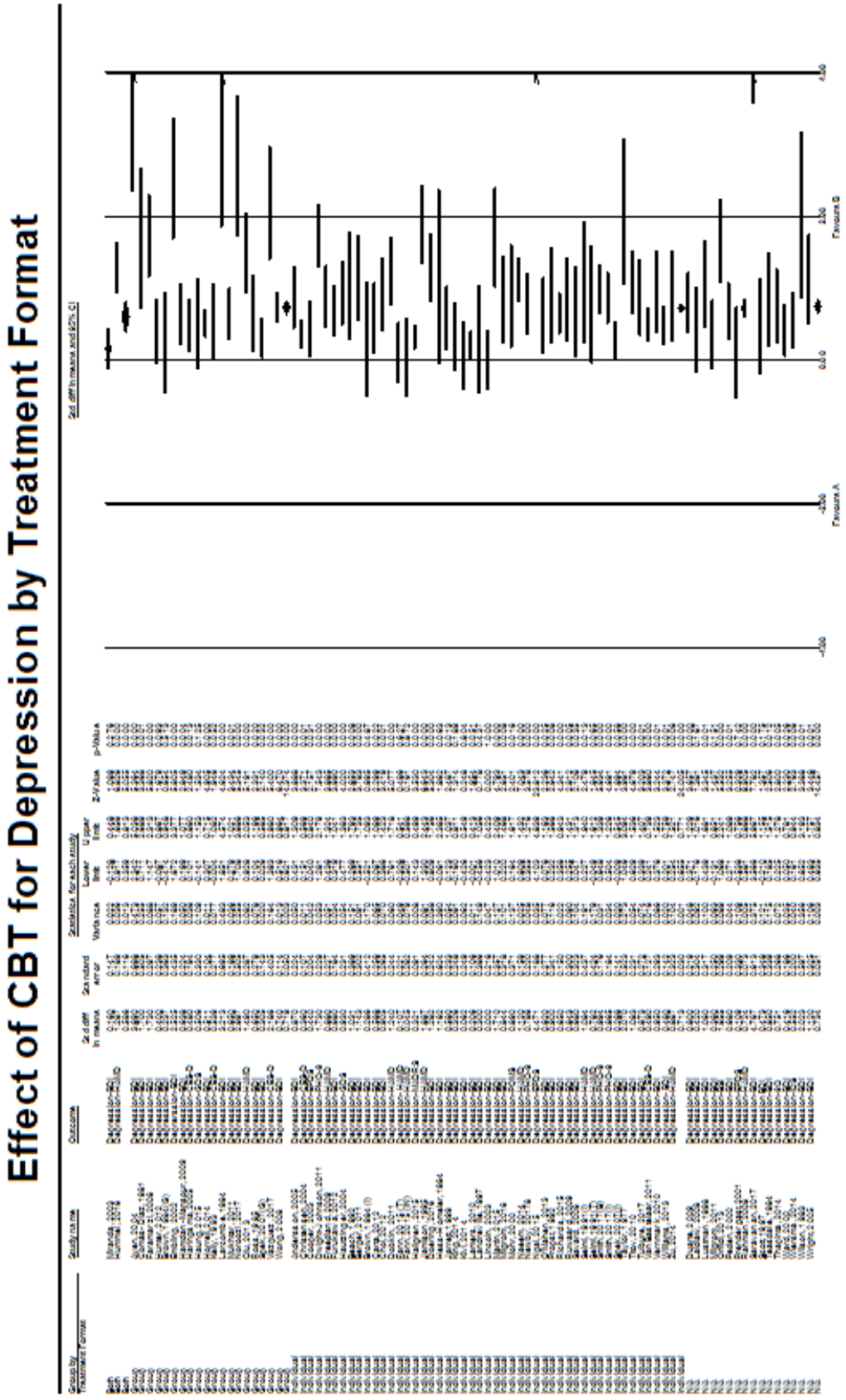


for the purpose of this subgroup analysis. Nineteen of the included studies compared group CBT to a control and the remaining 47 compared individual CBT to a control. The remaining studies did not indicate whether group or individual CBT was used. Overall, the results indicate that group CBT results in a significant large effect, SMD= 1.090 (SE=.144, 95% CI=.809-1.372, p=.000, I^2=54.915; Figure 8). The heterogeneity of the group therapy sub-group was found to be moderate. In addition, a significant large effect was found for individual CBT, SMD=.852 (SE=.112, 95% CI=.633-1.071, p=.000, I^2=0.000; Figure 8). These results indicate that both forms of CBT are efficacious at reducing depressive symptomology for individuals suffering from depression. In addition, the results indicate that group CBT is slightly more effective the individual CBT at improving symptomology. Due to the moderate amount of heterogeneity found in the group therapy analysis, the results should be interpreted with some caution.

Effect due to Treatment Delivery Method

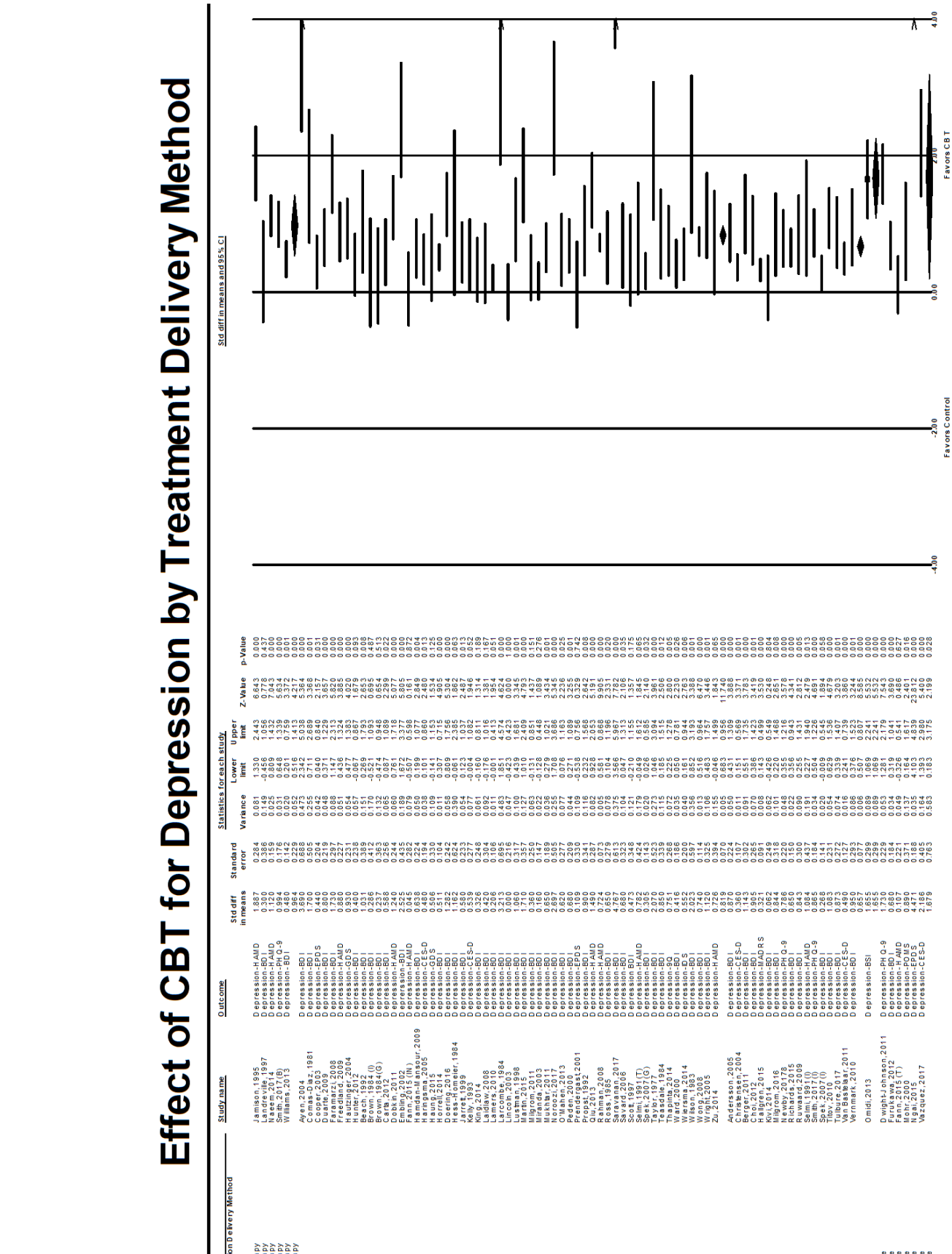
Due to extensive research performed on cognitive behavioral therapy throughout its history, several different means of delivering the therapy have been developed. There were four main therapy delivery methods examined in this meta-analysis; these included in-person, internet delivered, telephone delivered, or bibliotherapy. The overwhelming majority of RCTs examined the effects of in-person CBT on depression (n = 56). The pooled analysis of these studies showed that in-person CBT results in a large significant result (SMD=.819, SE=.070, 96% CI= .683-.956, p=.000, I^2=49.247; Figure 9).

Figure 8: Effect due to Treatment Format



The second heavily most researched treatment delivery method was through the internet (n = 17). These studies showed that internet delivered CBT for depression had moderate to large significant effect (SMD=.657, SE=.077, 95% CI= .507-.807, p=.000, I^2=0.000; Figure 9). Lastly, 6 studies examined the effect of telephone administered CBT and 5 studies examined the effect of bibliotherapy on depression symptomology. The subgroup analysis of bibliotherapy resulted in a large significant effect (SMD=.964, SE=.229, 95% CI= .516-1.413, p=.000, I^2=24.809; Figure 9). Finally, the subgroup analysis of telephone administered CBT resulted in a very large significant effect (SMD=1.679, SE=.763, 95% CI= .183-3.175, p=.028, I^2=0.000; Figure 9). Although the heterogeneity was low for the telephone administered sub-group, as indicated by the I^2 statistic, results of the group must be interpreted with caution due to a very large standard error and wide ranging confidence intervals.

Figure 9: Effect of Treatment Delivery Method on Depression



Behavioral Activation

Description of Studies

Results of the Search

The electronic search of five databases, grey literature, and hand searching identified 20,745 studies for consideration. Only a fraction of the 20,745 studies examined the effects of behavioral activation therapy (BA) as an intervention for treating depression. Two reviewers (NH, AS) examined the literature results and excluded obviously irrelevant records based on the title using the Rayyan QCRI software (Ouzzani, et al., 2016). After applying the inclusion and exclusion criteria, as specified in the previous chapter, 123 studies were included across all treatment arms. Out of the 123 studies, only 12 met the inclusion criteria for examining BA as an intervention for depression (Naik & Cully, 2017; Taylor & Marshall, 1977; Comas-Diaz, 1981; Wilson, Goldin, & Charbonneau-Powis, 1983; Vazquez, Torres, Otero et al., 2016; Nystrom et al., 2017; Bombardier et al., 2013; Kanter et al., 2015; McIndoo, File, Preddy et al., 2016; Cullen, 2002; Soucy, Provencher, Fortier & McFadden, 2017; Ross et al., 2016). One study that met the inclusion criteria only provided the study protocol (Ross et al., 2016). An unsuccessful attempt was made to receive the results from these researchers, therefore there is 11 studies were included in the meta-analysis. As a result, 11 studies including a total of 660 participants were included in this meta-analysis. The actual number of participants analyzed may vary according to the study design and type of intervention. More detailed information can be found later in this section under outcome evaluation.

Characteristics of Included Studies

The final sample consisted of five 2-arm parallel, four 3-arm parallel, one 4-arm parallel, and one 5-arm parallel RCTs. Overall the studies were conducted all over the world, but most were conducted in North America (Bombardier et al., 2013; Comas-Diaz, 1981; Cullen, 2002; Kanter et al., 2015; McIndoo et al., 2016; Naik & Cully, 2017; Soucy et al., 2017; Taylor & Marshall, 1977), Europe (Nystom et al., 2017; Vazquez et al., 2017), and Australia (Wilson, Goldin & Charbonneau-Powis, 1983). The majority of the studies occurred in the United States, while two of the North American studies occurred in Canada. The characteristics of the included studies are provided in Appendix D.

Types of depression that were examined varied greatly across the studies. The majority of the studies examined the effects of depression in specific populations. The different populations assessed included depression in caregivers (Vazquez et al., 2017), depression in college students (McIndoo et al., 2016), depression in Latinos (Kanter et al., 2015) and depression in Puerto Rican women (Comas-Diaz, 1981). In addition, a few studies examined depression in non-specific populations (Cullen, 2002; Nystom et al., 2017; Soucy et al., 2017; Taylor & Marshall, 1977; Wilson, Goldin & Charbonneau-Powis, 1983). Lastly, two studies examined depression due to another medical condition, specifically multiple sclerosis and diabetes (Bombardier et al., 2013; Naik & Cully, 2017).

All included studies reported clear diagnostic, inclusion, and exclusion criteria for their participants. Each study varied when considering the minimum severity of depression participants must be suffering from in order to be included in the study. Three

studies used the Patient Health Questionarrie-9 (PHQ-9) for inclusion, but the minimum scores needed to be included varied across the three studies. Two studies included participants with a PHQ-9 score greater than 10 (Bombardier et al., 2013; Naik & Cully, 2017). The other study that used the PHQ-9 included participants with score between 5 and 19 (Soucy et al., 2017). The majority of the studies used either the HAMD or the BDI as part of their inclusion criteria. The minimum scores participants needed in order to be included varied greatly, but were usually between 13-20 (Comas-Diaz, 1981; Cullen, 2002; Kanter et al., 2015; McIndoo et al., 2016; Taylor & Marshall, 1977; Wilson, Goldin & Charbonneau-Powis, 1983). Out of the 11 included studies, only two did not use the PHQ-9, HAMD, or BDI. One study included participants that scored above 16 on the Center for Epidemiological Studies-Depression (CES-D) scale (Vazquez et al., 2017) and the second included participants that scored between 15 and 35 on the Montgomery-Asberg Depression Rating Scale (Nystom et al., 2017). In addition to a wide variety of inclusion criteria, these studies all used many different measurement inventories to measure depression. The majority of the studies used either the Beck Depression Inventory (BDI) or the Hamilton's Rating Scale for Depression (HAMD) or a combination of the two. Of the studies that did not use the HAMD or BDI, three used the PHD-9 (Naik & Cully, 2017; Nystom et al., 2017; Soucy et al., 2017) and one used the CES-D (Vazquez et al., 2017).

The protocol used to administer BA was inconsistent across studies. The primary goal for most of these studies was defined as increasing the frequency, quality, and range of activities and social interactions of participants. In addition, the goal of the intervention for most of the studies was to restore behaviors in clients that were likely to

be positively reinforced. The mechanisms through which investigators achieved this was inconsistent. Many of the studies stated that they based their model off of work performed by Lewinsohn and colleagues (Comas-Diaz, 1981; Nystom et al., 2017; Taylor & Marshall, 1977; Wilson, Goldin & Charbonneau-Powis, 1983). In addition to examining the Lewinsohn model, Nystrom investigated the effects of Martell's model of behavioral activation as well (Nystom et al., 2017). One study based their model of treatment on Jacobson and colleague's 1997 treatment manual (Cullen, 2002). On the whole these various models of treatment included pleasant activity planning, and educating participants about the connection between behaviors and how it could relieve depression.

In addition to inconsistencies in BA protocol, studies varied dramatically surrounding the length and frequency of the intervention, and how the intervention was implemented. The length of treatment varied from four weeks (Comas-Diaz, 1981; McIndoo et al., 2016) to sx months (Naik & Cully, 2017) with the majority of treatment lengthing being 12 weeks (n=3). The number of sessions completed within the duration of the intervention also greatly varied. The longest intervention length lasted six months, but that intervention only consisted of six sessions and three booster sessions (Naik & Cully, 2017). In the majority of studies, participants completed one session once per week over the duration of the study. Lastly, the length of each session differed across the included studies. Multiple studies consisted of treatment sessions lasting 90 minutes (Vazquez et al., 2017; Comas-Diaz, 1981) or 60 minutes (Cullen, 2002; McIndoo et al., 2016). The length of each session for other studies typically was less than one hour.

There was considerable variation in the modality of treatment implementation. All of the studies had researchers trained in psychotherapy (e.g. counselors, psychologists, social workers, etc.) implement the intervention. The majority of behavioral activation interventions were implemented as face-to-face therapy (Taylor & Marshall, 1977; Comas-Diaz, 1981; Wilson, Goldin & Charbonneau-Powis, 1983; Cullen, 2002; McIndoo et al., 2016; Kanter et al., 2015). The remaining studies had interventions implemented in other ways, which included; guided self-help book (Soucy et al., 2017), over the internet (Nystom et al., 2017), or over the telephone (Naik & Cully, 2017; Vazquez et al., 2017). Lastly, of the 11 studies, only one implemented treatment in multiple ways. Bombardier et al. intervention included seven telephone sessions and one face-to-face sessions (2013).

Of the 11 studies included, all of them compared behavioral activation to a non-active control. A majority of the studies (n = 8) compared behavioral activation to a waitlist control (Bombardier et al., 2013; Comas-Diaz, 1981; Cullen, 2002; McIndoo, et al., 2016; Nystrom et al., 2017; Soucy, et al., 2017; Taylor & Marshall, 1977; Wilson, Goldin, & Charbonneau-Powis, 1983). The remaining three studies compared behavioral activation to a treatment as usual control group (Kanter et al., 2015; Naik & Cully, 2017; Vazquez et al., 2017). In addition there was an almost equal number of multiarm designs and 2-arm designs. There were a total of five studies that compared behavioral activation to a control (Bombardier et al., 2013; Cullen, 2002; Kanter et al., 2015; McIndoo, et al., 2016; Naik & Cully, 2017). All of the other studies compared behavioral activation to a control and another active group. Most of the remaining studies compared BA to cognitive behavioral therapy (Comas-Diaz, 1981; Taylor & Marshall, 1977; Vazquez et

al., 2017; Wilson, Goldin, & Charbonneau-Powis, 1983). The remaining studies compared behavioral activation to physical activity (Nystrom et al., 2017; Soucy, et al., 2017) or to mindfulness based therapy (McIndoo, et al., 2016).

Risk of Bias Assessment

Figures 10 and 11 provide a summary of the risk of bias of the included studies.

Figure 10: Risk of Bias Summary

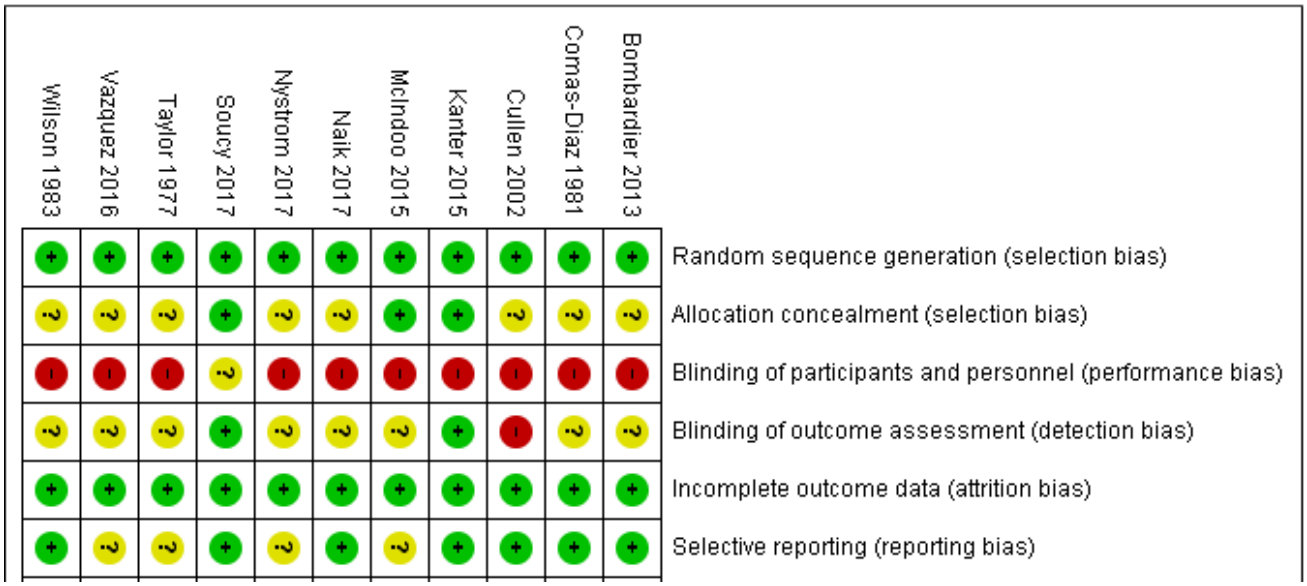
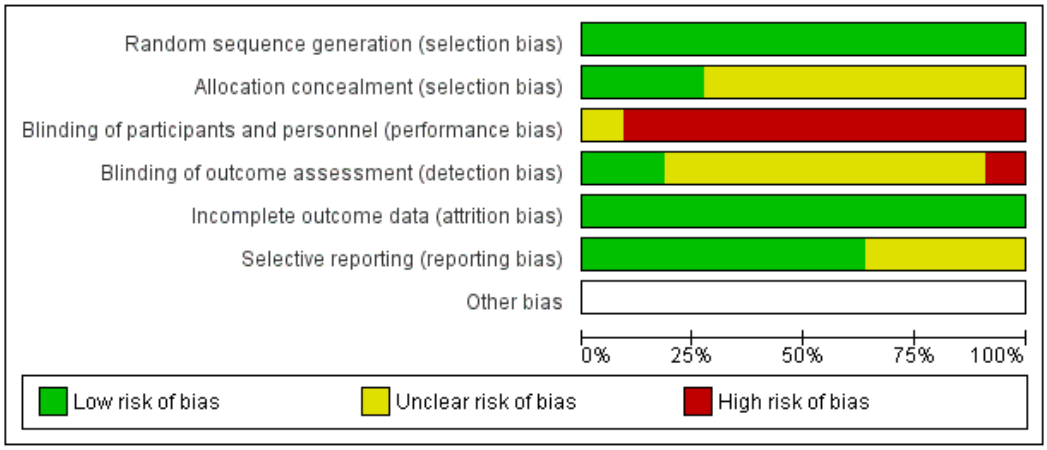


Figure 11: Risk of Bias Graph



Randomization

In order to determine if the studies were randomized, it was assessed whether the authors clearly described the method by which randomization was achieved. All included studies reported that the groups were randomized. All of the studies were deemed to have low risk of bias due to randomization procedure. Studies used a variety of different ways to achieve randomization. Vazquez et al. (2016) stated that "An independent statistician randomly assigned participants to groups using a table of random numbers" (p. 940). Another studied stated "The participant was randomly allocated to one of the three conditions following a double-blind procedure. The randomization sequence was determined prior to recruitment through a computer generated random number sequence (ratio 1:1:1, block size of 6 for the first randomization, block size of 9 for the second randomization)" (Soucy, 2017, p. 497). Other studies used a computer administered randomized block sequence generator (Bombardier et al., 2013) or a randomization table (McIndoo et al., 2016). A majority of the included studies stated that randomization occurred but did not provide means by which researchers performed it.

Allocation Concealment

Only a few of the studies reported on allocation concealment. Soucy et al. stated that, "Randomly assigned conditions were sealed in envelopes labelled with participant codes and opened following completion of the baseline questionnaire." (Soucy et al., 2017, p.497). Another study that reported on allocation concealment was conducted by Kanter. Researchers stated that all baseline measures were obtained prior to the allocation process. The majority of the studies did not report on allocation concealment, which is evident by the majority of studies have unclear risk of allocation concealment bias.

Blinding Interventions

Blinding of the participants was not possible due to the nature of the interventions. As evidenced in Figures 10 and 11, the risk of potential performance bias was high for almost all included studies due to the nature of the behavioral interventions assessed; it was impossible to blind participants to the status of their intervention and difficult to blind personnel and staff (e.g. counselors or psychologists). Out of the 11 included studies only one received unclear level of performance bias. Soucy and colleagues attempted to minimize performance bias by following a double blind procedure. Both allocation of conditions and randomization of participants were blinded to the researchers (Soucy et al., 2017). Although it was impossible to completely avoid performance bias while researching these types of interventions, Soucy et al. maximized their blinding procedures to the maximum extent.

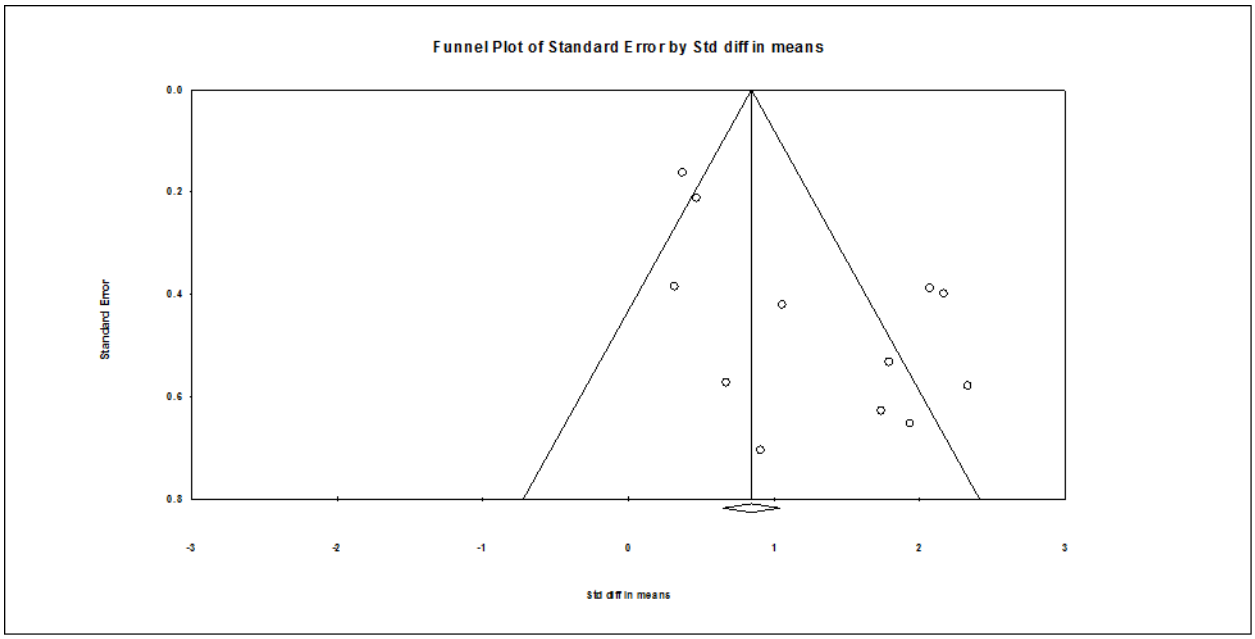
Reporting Bias

In order to assess reporting bias, the likelihood that information was chosen based on multiple outcome measures or multiple analyses of data was examined. As a whole, there was evidence in multiple studies that selective outcome reporting or outcome reporting based on multiple analysis of data may have occurred.

Assessment of Reporting Bias

Publication bias was examined by visually inspecting a funnel plot according to the guidelines presented by Egger (Egger et al., 1997).

Figure 12:



Following inspection of the funnel plot, it is clear that there is evidence of publication bias. The publication bias was judged as being moderate due to the asymmetry observed and the variation of where studies are plotted as compared to average (see Figure 12). The results of the funnel plot support the results of the risk of

bias assessment. Due to a variety of methodological issues, including reporting bias, selection bias, and performance bias, the risk of publication bias is moderate.

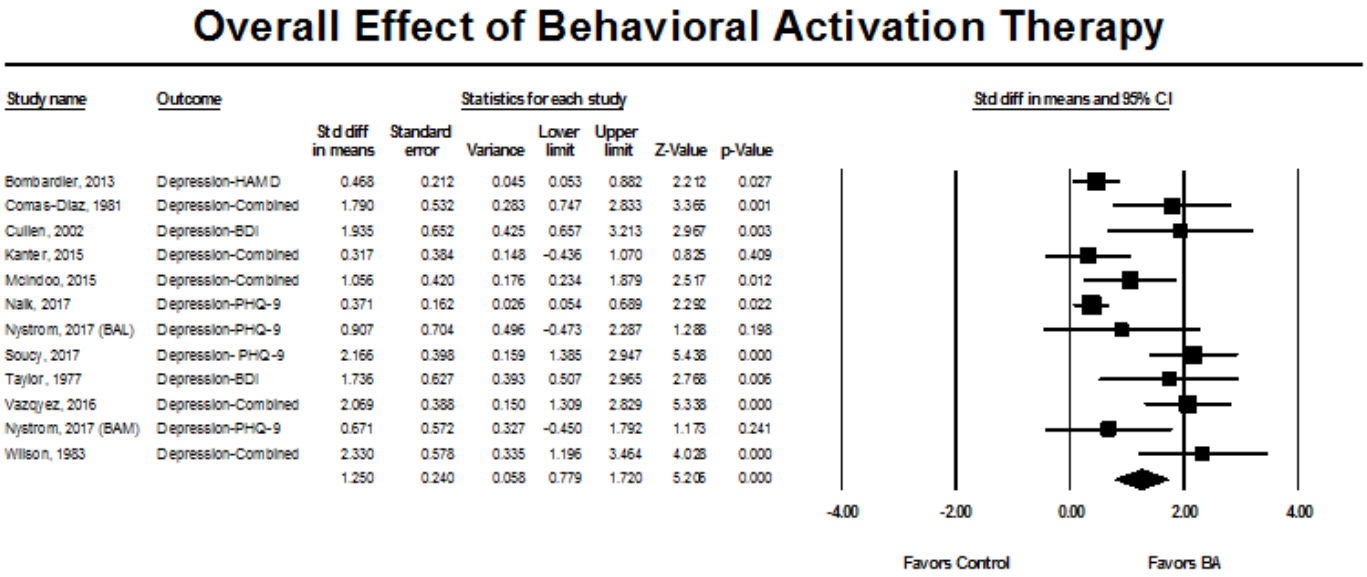
Effect of Behavioral Activation Therapy

In the following section, the effects of behavioral activation therapy on depression symptomology are presented. In addition to the overall effect of BA on the primary outcome, the results of a series of meta-analyses moderating for specific a-prior defined variables are presented as well.

Overall Effect

In this analysis, data from 11 studies and 12 treatment arms, were pooled together using the standardized mean difference (SMD). A large significant effect was found, SMD= 1.250 (SE=.240, 95% CL=.779-1.720, p=.000, I^2=0.000%; Figure 13). These results indicate that physical activity significantly decreases depressive symptomatology in individuals suffering from depression. The effect size of each study ranged from SMD=.371 (p=.022) (Naik et al., 2017) to SMD=2.166 (p=.000) (Soucy et al., 2017). Due to expected heterogeneity, the random effects model was used to conduct the meta-analysis. The I^2 statistic indicates that there was no heterogeneity and the results were highly consistent across the studies analyzed.

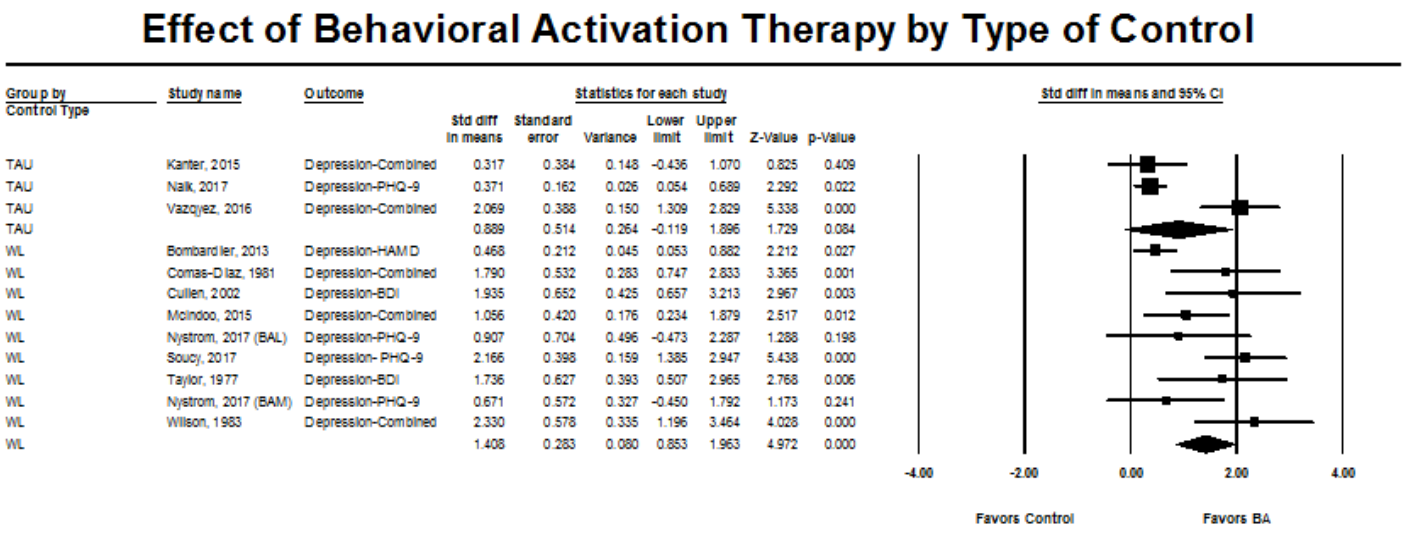
Figure 13: Overall Effect of Behavioral Activation for Depression



Effect due to Control Type

All of the included studies compared BA to a non-active control. The two non-active controls used in the RCTs were treatment as usual (TAU) and a waitlist control (WL). Out of the 11 included studies, only three used a treatment as usual control design (Kanter et al., 2015; Naik et al., 2017; Vazquez et al., 2017). All of the remaining studies used waitlist as a control group. Overall, the waitlist control trails found a significant large effect, SMD= 1.408 (SE=.283, 95% CI=..853-1.963, p=.000, I^2=0.000; Figure 14). In addition, a large but non-significant effect was found for the treatment as usual control design studies, SMD=.889 (SE=.514, 95% CI=-.119-1,896, p=.084, I^2=17.559; Figure 14). The I^2 statistic indicated that the heterogeneity of the TAU included studies was low. Because only a few studies compared BA to a treatment as usual control, the results of the TAU meta-analysis should be interpreted with caution. In order to strengthen the results of the TAU group, further research must be conducted.

Figure 14: Effect of BA due to Control Type

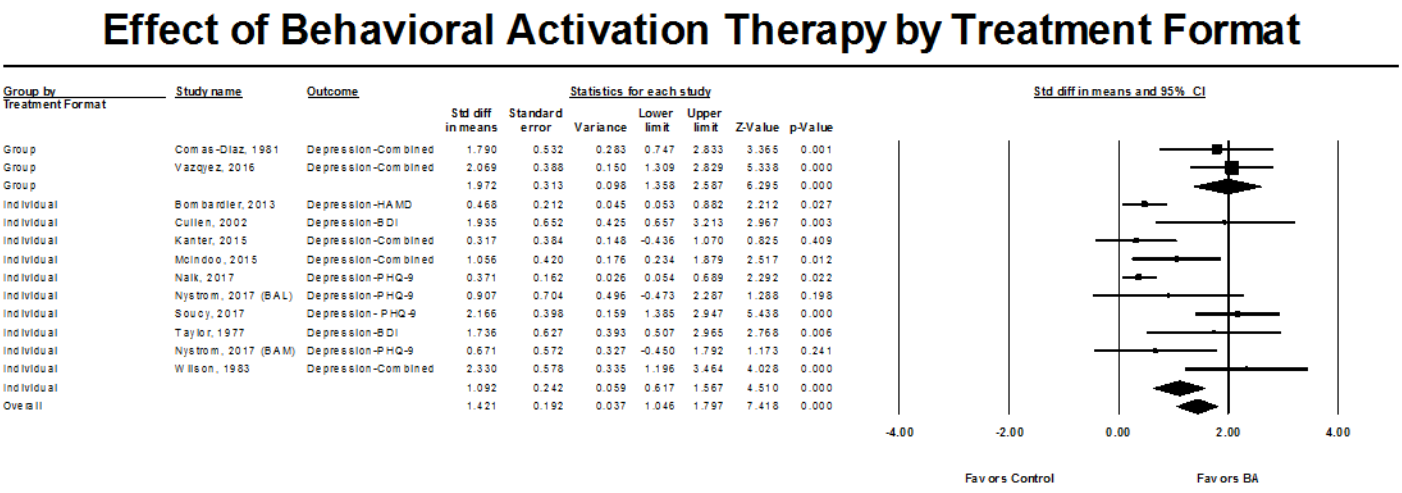


Effect due to Treatment Format

The included studies used two main treatment format options to deliver behavioral activation therapy; these options were individual therapy or group therapy. Only two of the included studies compared group behavioral activation to a control (Comas-Diaz et al., 1981; Vazquez et al., 2016) and the remaining nine compared individual behavioral activation to a control. Overall, the results indicate that group BA results in a significant large effect, SMD= 1.972 (SE=.313, 95% CI=.1.358-2.587, p=.000, I^2=0.000; Figure 15). In addition, a significant large was found for individual BA, SMD=1.092 (SE=.192, 95% CI=1.046-1.797, p=.000, I^2=4.670; Figure 15). These results indicate that both forms of BA are efficacious at reducing depressive symptomatology for individuals suffering from depression. In addition, the results indicate that group therapy was slightly more effective the individual therapy at improving symptomology. In addition, both sub-groups presented very low

heterogeneity. Due to the small number of RCTs included in the group therapy meta-analysis, the results must be interpreted with caution.

Figure 15: Effect of BA Treatment Format

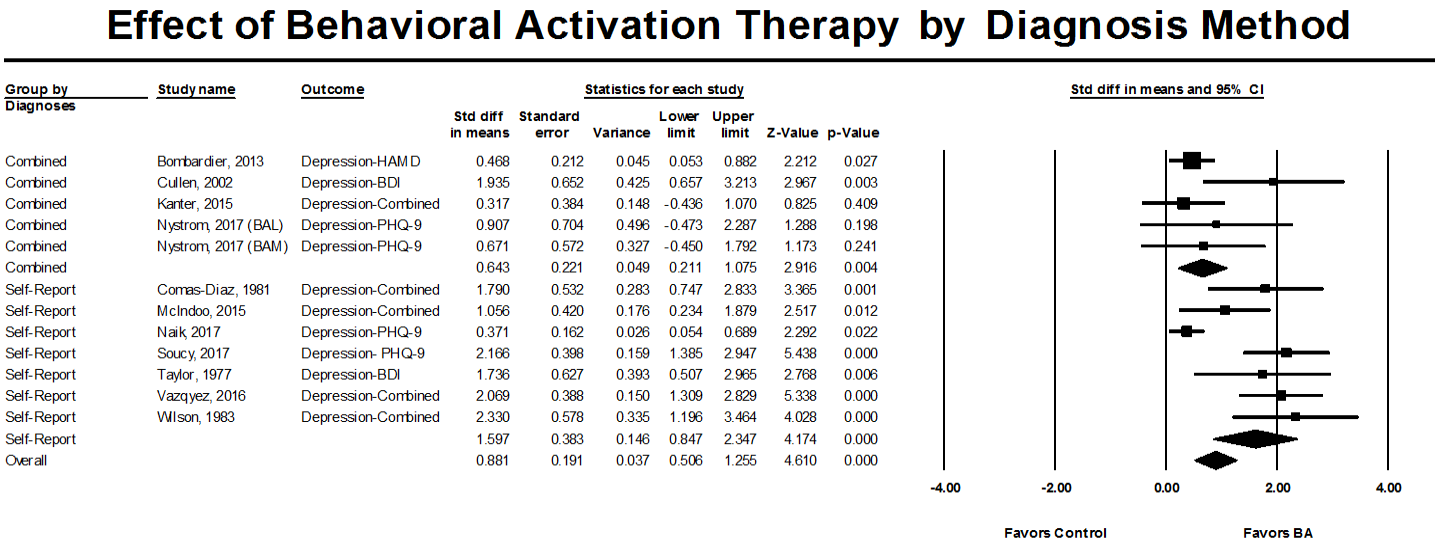


Effect due to Diagnosis Method

Researchers used a variety methods to measure and diagnose depression. Researchers either used a self-report measure or both a clinical interview and scale in order to diagnose depression and depression severity. Seven of the studies used self-report scales (e.g., BDI) in order to determine if participants met inclusion criteria (Comas-Diaz et al., 1981; McIndoo et al., 2015; Naik et al., 2017; Soucy et al., 2017; Taylor et al., 1977; Vazquez et al., 2016; Wilson et al., 1983) Only four studies used a combined method, both a self-report measure and clinical interview to diagnose depression (Bombardier et al. 2013, Cullen et al., 2003; Kanter et al., Nystrom et al., 2017). These studies used a clinical interview to determine if recruited participants met the criteria for a DSM or ICD-10 depressive episode. Overall, the results indicate that studies that used combined methods to diagnose depression result in a significant

moderate to large effect. (SMD= .643, SE=.221, 95% CI=.211-1.075, p=.004, I^2=8.001; Figure 16). The other means by which researchers diagnosed depression, through self-report measures, resulted in a much larger result. Studies that used self-report measures to diagnose depression result in a significant very large effect (SMD= 1.597, SE=.383, 95% CI=.847-2.347, p=.000, I^2=0.000; Figure 16). Both sub-groups presented very low heterogeneity, indicating consistency across the included studies.

Figure 16: Effect of BA due to Diagnosis Method

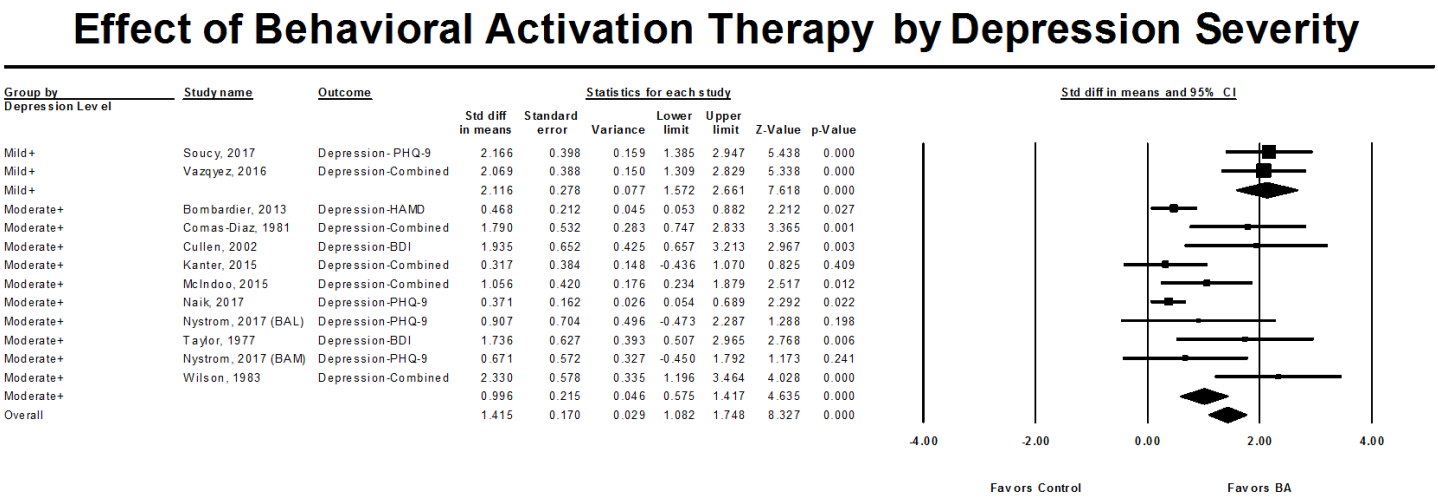


Effect due to Depression Severity

All of the included studies examined the effects of behavioral activation therapy on depression. The severity of depression that researchers studied varied in each RCT. None of the studies examined the effects of BA on individuals suffering from Major Depressive Disorder. In order to determine the level of depression severity for the remaining studies, the minimum scores on depression scales that researchers would allow

for their study was examined. The scoring criteria for each scale used, in order to determine if the minimum inclusion score related to mild, moderate or severe depression, was also reviewed. Two studies included all participants with at least mild depression (Soucy et al., 2017; Vazquez et al., 2016). The results indicate that BA significantly and to a large effect improves depression in individuals with mild depression (SMD=2.116, SE=.278, 95% CI=1.572-2.661, p=.000, I^2=0.000; Figure 17). The remaining nine studies examined the effects of BA on individuals suffering from at least moderate depression. BA largely and significantly improves depression in individuals suffering with, at minimum, moderate depression (SMD=.996, SE=.215, 95% CI=.575-1.417, p=.000, I^2=11.275; Figure 17).

Figure 17: Effect of BA due to Depression Severity



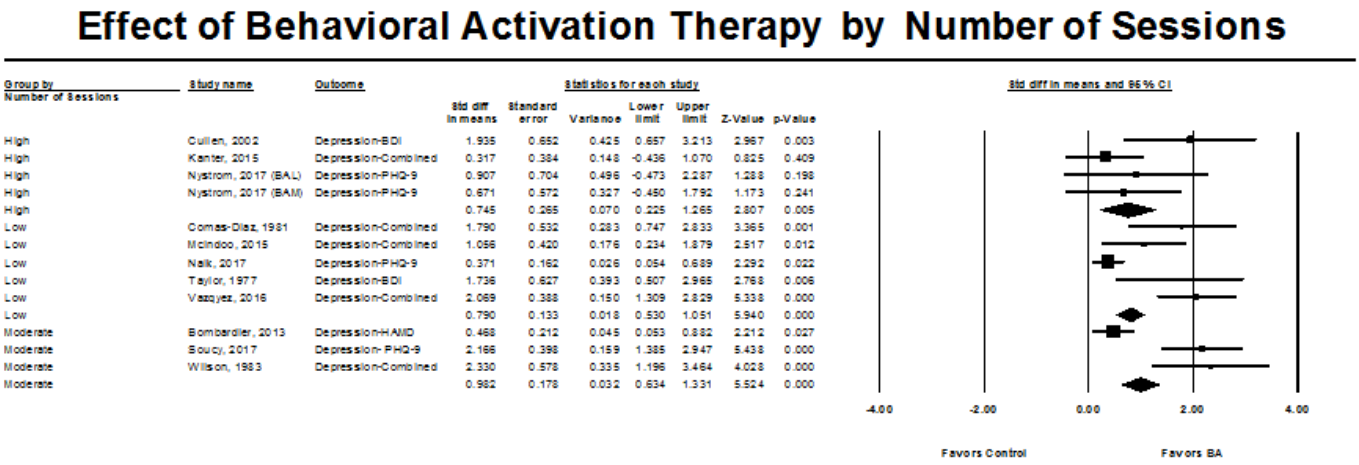
Effect due to Number of Treatment Sessions

All of the included RCTs used a variety of protocol in order to implement behavioral activation interventions. One aspect of the protocol that variety throughout

studies was the number of treatment sessions each RCT provided. For the purpose of this subgroup meta-analysis, the number of sessions were coded as “high”, “moderate”, or “low”. In order to be defined as low a study must have consisted of 4-6 treatment sessions, moderate consisted of 7-9 treatment sessions, and high consisted of 10-12 treatment sessions.

Overall, there were three studies that examined the effects of BA with a high number of treatment sessions (Cullen et al., 2002; Kanter et al., 2015; Nystrom et al., 2017). The pooled results of these studies showed that a high number of treatment sessions results in a moderate to large significant effect (SMD=.745, SE=.265, 95% CI=.225-1.265, p=.000, I^2=.000; Figure 18). In addition, there were also three studies examining the effect of BA with a moderate number of treatment sessions (Bombardeir et al., 2013; Soucy et al., 2017; Wilson et al., 1983). These studies also showed that a moderate number of treatment sessions result in a large significant effect (SMD=.982, SE=.178, 95% CI=.634-1.321, p=.000, I^2=.000; Figure 18). Lastly, the remaining five studies examined the effects of BA with a low number of treatment sessions (Comas-Diaz et al., 1981; Naik et al., 2017; Vazquez et al., 2016; McIndoo et al., 2015; Taylor et al., 1977). The pooled results of these studies showed that a high number of treatment sessions results in a moderate to large significant effect (SMD=.790, SE=.133, 95% CI=..530-1.051, p=.000, I^2=.000; Figure 18).All of the subgroups presented I^2 values of 0%, indicating that there was no heterogeneity across the subgroups.

Figure 18: Effect of BA due to Number of Treatment Sessions



Non-Directive Supportive Therapy

Description of Studies

Results of the Search

The electronic search of 5 databases, grey literature, and hand searching identified 20,745 studies for consideration. Only a fraction of the 20,745 studies examined the effects of non-directive supportive therapy as an intervention for treating depression. Two reviewers (NH, AS) examined the literature results and excluded obviously irrelevant records based on the title using the Rayyan QCRI software (Ouzzani, et al., 2016). After applying the inclusion and exclusion criteria, as specified in the previous chapter, 123 studies were included across all treatment arms. Out of the 123 studies, only 8 met the inclusion criteria for examining NDST as an intervention for depression (Ayen & Hautzinger, 2004; Chen, Tseng, Chou, & Wang, 2000; Cooper, Murray, Wilson, & Romaniuk, 2003; Freedland et al., 2009; Kelly et al., 1993; King, Marston, & Bower, 2014; Milgrom, Negri, Gemmill, McNeil & Martin, 2005; Ward et al., 2000). Milgrom

(2005) examined the effects of both a group and individual supportive counseling intervention, therefore both results were entered separately. As a result, 8 studies, and 9 treatment arms, including a total of 665 participants were included in this meta-analysis. The actual number of participants analyzed varied according to the study design and type of intervention. More detailed information can be found later in this section under outcome evaluation.

Characteristics of Included Studies

The final sample consisted of one 2-arm parallel and seven 3-arm parallel RCTs. The studies were conducted all over the world but, as a whole, they were conducted in Asia (Chen, et al., 2000), North America (Freedland et al., 2009; Kelly et al., 1993), Europe (Ayen & Hautzinger, 2004; Cooper et al., 2003; King, Marston, & Bower, 2014; Ward et al., 2000), and Australia (Milgrom et al., 2005). One study that met the inclusion criteria was in German (Ayen & Hautzinger, 2004). The English translation of this study was obtained and used to obtain study characteristics and outcome data.

Types of depression examined varied greatly across the studies. Three studies examined depression due to another medical condition; these conditions included multiple sclerosis and human immunodeficiency virus (HIV) (Freedland et al., 2009; Kelly et al., 1993). In addition, two studies examined the effectiveness of supportive counseling on individuals suffering from depression (King, Marston, & Bower, 2014; Ward et al., 2000). Lastly, the majority of studies examined depression in females. Three of the included studies examined the efficacy of NDST on individuals suffering from postpartum depression (Chen, et al., 2000; Cooper et al., 2003; Milgrom et al., 2005), and

one study examined the efficacy of NDST on females suffering from climacteric depression (Ayen & Hautzinger, 2004). All included studies reported clear diagnostic, inclusion, and exclusion criteria for their participants. Each study varied when considering the minimum degree of depression participants must be suffering from in order to be included in the study. Two studies only included participants who scored above 10 on Beck's Depression Inventory (BDI) (Chen, et al., 2000; Freedland et al., 2009). Multiple studies included participants who scored above 14 on the BDI (King, Marston, & Bower, 2014; Ward et al., 2000). Lastly, one study did not use the BDI as inclusion criteria, but instead used the Edinburgh Postnatal Depression Scale (EPDS) as an inclusion measure (Cooper et al., 2003).

The protocol used to administer NDST differed across studies. The primary goal of the researchers studying NDST was to provide a space for individuals to air their current concerns and feelings, and to provide support as they coped with life events. Two of the included studies stated that their supportive therapy intervention was implemented based on a treatment manual developed by Carl Rodgers (King, Marston, & Bower, 2014; Ward et al., 2000). Another study focused of supportive techniques to mitigate the effects of stress (Freedland et al., 2009). This intervention was delivered by a therapist and focused on a supportive therapeutic relationship in order to cope with stress and overcome depression. In addition, further variations occurred based on the cause of depression. Chen and colleagues developed a goal for each session that was directed towards a different aspect of motherhood in order to aid in diminishing post-partum depression symptoms (Chen et al., 2000). The goal of this approach ass to facilitate emotional expression. In addition to differences in NDST protocol, studies varied

dramatically surrounding the length and frequency of the intervention, and about who implemented the intervention. The length of interventions ranged from one month (Chen et al., 2000) to three months. The majority of interventions were about three months in length, with only two studies having intervention lengths shorter than two months. Overall, there was the same number of studies examining individual versus group supportive therapy. One study examined the effects of both group supportive therapy and individual supportive therapy on depression (Milgrom et al., 2005). The duration of treatments was mixed between studies. Chen et al. (2000) used one weekly session that was an hour and a half to two hours in length. Other studies protocol also outlined sessions as being once per week, but the sessions were shorter, ranging from 50 to 60 minutes (Freedland et al., 2009; Ward et al., 2000).

Of the seven studies included, all of them compared supportive therapy to a non-active control. A majority of the studies (n=5) compared supportive therapy to treatment as usual (Cooper, et al., 2003; Freedland et al., 2009; King, Marston, & Bower, 2014; Milgrom et al., 2005; Ward et al., 2000). The remaining three studies compared supportive therapy to a waitlist control group (Ayen & Hautzinger, 2004; Chen et al.,2000; Kelly et al., 1993). In addition, the majority of the studies were multiarm designs. Chen was the only study that compared supportive counseling to a control condition only (Chen et al., 2000). All of the other studies compared supportive counseling to a control and another active group. All of the remaining studies compared NDST to cognitive behavioral therapy. In addition to a wide variety of inclusion criteria, these studies all used many different measurement inventories to measure depression. The majority of the studies used either the Beck Depression Inventory (BDI) or the

Hamilton Rating Scale for Depression (HAMD) or a combination of the two. The one study that used neither was performed by Cooper (2003). This study used the Edinburgh Postnatal Depression Scale (EPDS) as the outcome measure.

Risk of Bias Assessment

Figures 19 and 20 provide a summary of the risk of bias of the included studies.

Figure 19: Risk of Bias Summary

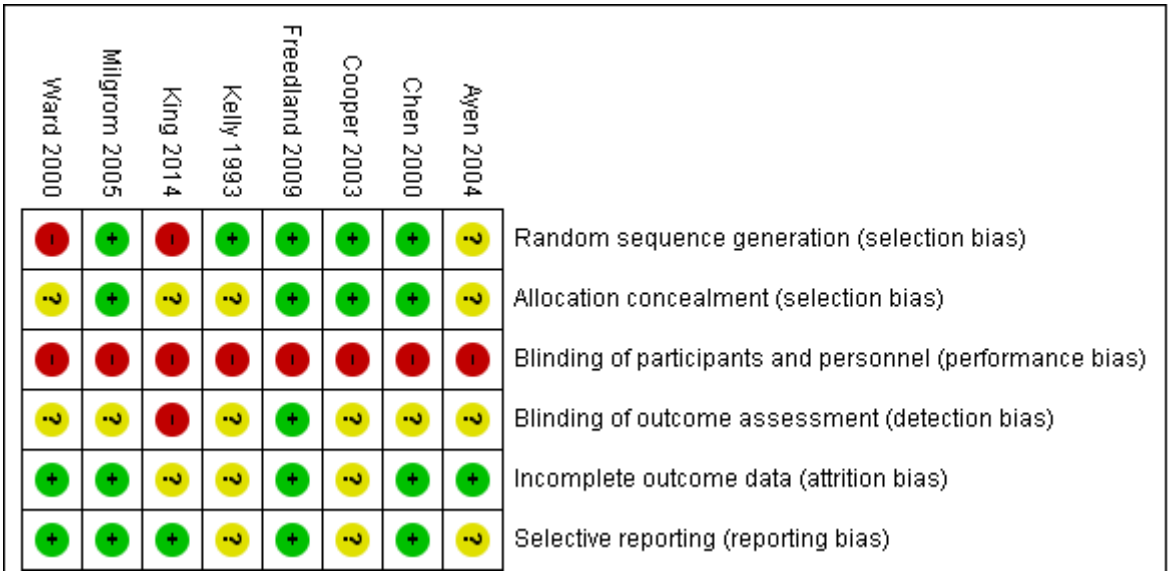
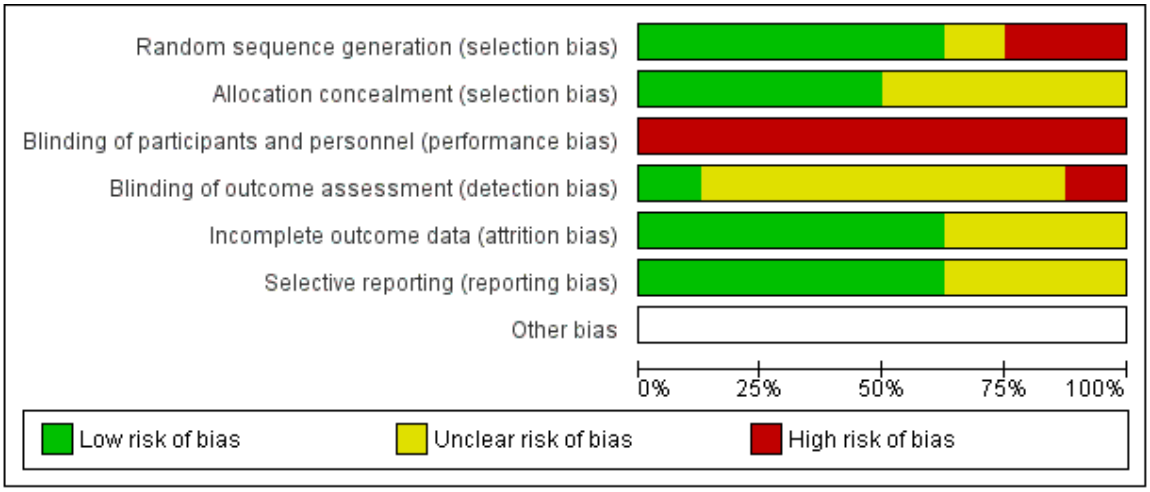


Figure 20: Risk of Bias Graph



Randomization

In order to determine if the studies were randomized, it was assessed whether the authors clearly described the method by which randomization was obtained. All included studies reported that the groups were randomized. Ward et al. (2000) was rated a high risk of bias because the participants were only partially randomized. Ward et al. described the process as follows: "We encouraged participants to accept randomisation. Those who continued to express a strong preference were allowed to choose their treatment" (Ward et al., 2000, p. 1384). All of the other studies were deemed to have low risk of bias due to randomization procedure. Studies used a variety of different ways to achieve randomization, which included four colored balls (Cooper et al., 2003) to statistical software (Freedland et al., 2009).

Allocation Concealment

Only a few of the studies reported on allocation concealment. Milgrom et al. stated that, "To preclude conscious or unconscious selection bias, all potential participants were kept blinded to treatments until the point of allocation" (Milgrom et al., 2005, p. 532). Another study that reported on allocation concealment was performed by Freedland. This study described the procedure as: "Group assignments were concealed in sealed envelopes and revealed to the study coordinator immediately after the participant completed all of the baseline assessments" (Freedland et al., 2009, p. 2009). The majority of the studies did not report on allocation concealment, which was evident by the majority of studies have unclear risk of allocation concealment bias.

Blinding Interventions

Blinding of the participants was not possible due to the nature of the interventions. As evidenced in Figures 19 and 20, the risk of potential performance bias was high for all included studies because of the nature of the behavioral interventions assessed; it was impossible to blind participants to the status of their intervention and difficult to blind personnel and staff (e.g. counselors or psychologists). Out of the nine included studies, only one was described as being blinded towards the researcher (Freedland et al., 2009).

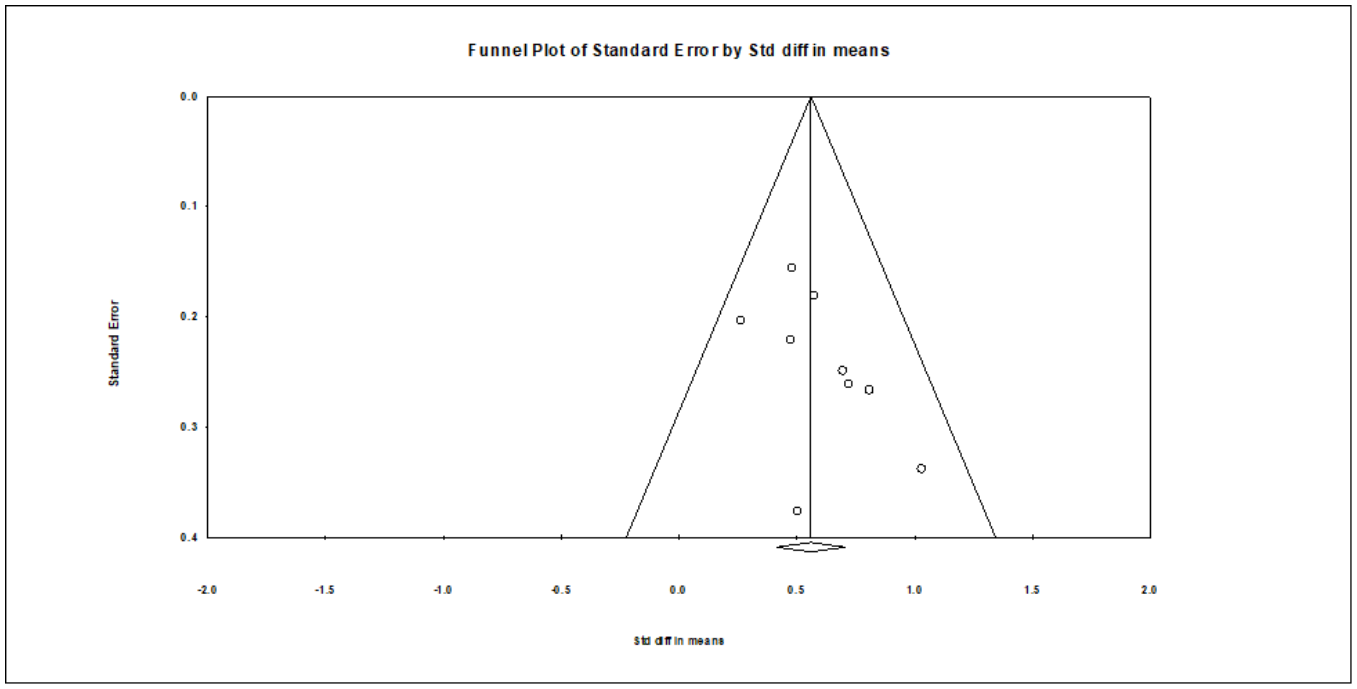
Reporting Bias

In order to assess reporting bias, the likelihood that information was chosen based on multiple outcome measures or multiple analysis of data was examined. As a whole, there was evidence in multiple studies that selective outcome reporting or outcome reporting based off of multiple analysis of data may have occurred.

Assessment of Reporting Bias

Publication bias was examined by visually inspecting a funnel plot according to the guidelines presented by Egger (Egger et al., 1997).

Figure 21:



Following inspection of the funnel plot, it was determined that there was a low risk of publication bias. Publication bias was judged as low due to symmetry of the funnel plot and the lack of extreme deviation from the average (see Figure 21). As previously noted, many of the included studies suffered from methodological issues, such as reporting bias, selection bias, and performance bias which can lead to an increase risk of publication bias. Therefore, the results of the funnel plot should be interpreted with caution.

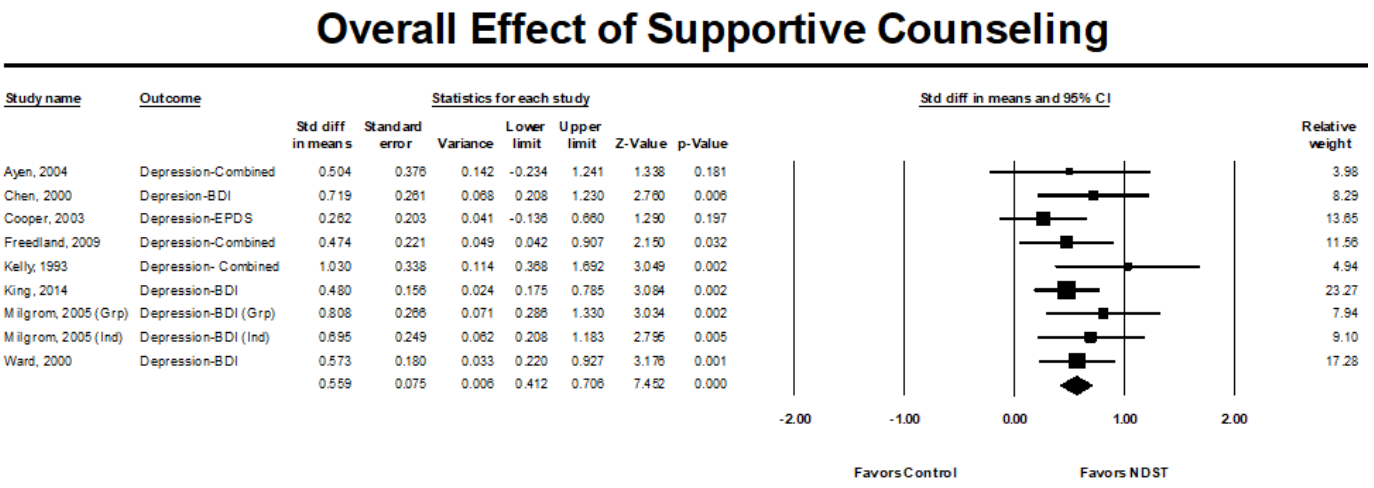
Effect of Non-Directive Supportive Therapy

In the following section, the effects of NDST on depression symptomatology are presented. In addition to the overall effect of NDST on the primary outcome, the results of a series of meta-analyses moderating for specific a-prior defined variables are presented as well.

Overall Effect

In this analysis, data from eight studies and nine treatment arms, were pooled together using the standardized mean difference (SMD). A significant moderate effect was found, SMD=.559 (SE=.075, 95% CL=.412-.706, p=.000, I^2=0.000; Figure 22). These results indicate that NDST has a significant and moderate effect on depressive symptomatology in individuals suffering from depression. The effect size of each study ranged from SMD=.262 (p=.197) (Cooper et al., 2003) to SMD=1.030 (p=.002) (Kelly et al., 1993) Due to expected heterogeneity, the random effects model was used to conduct the meta-analysis. Subsequently, these findings must be interpreted cautiously due to potential publication bias and heterogeneity.

Figure 22: Overall Effect of NDST on Depression

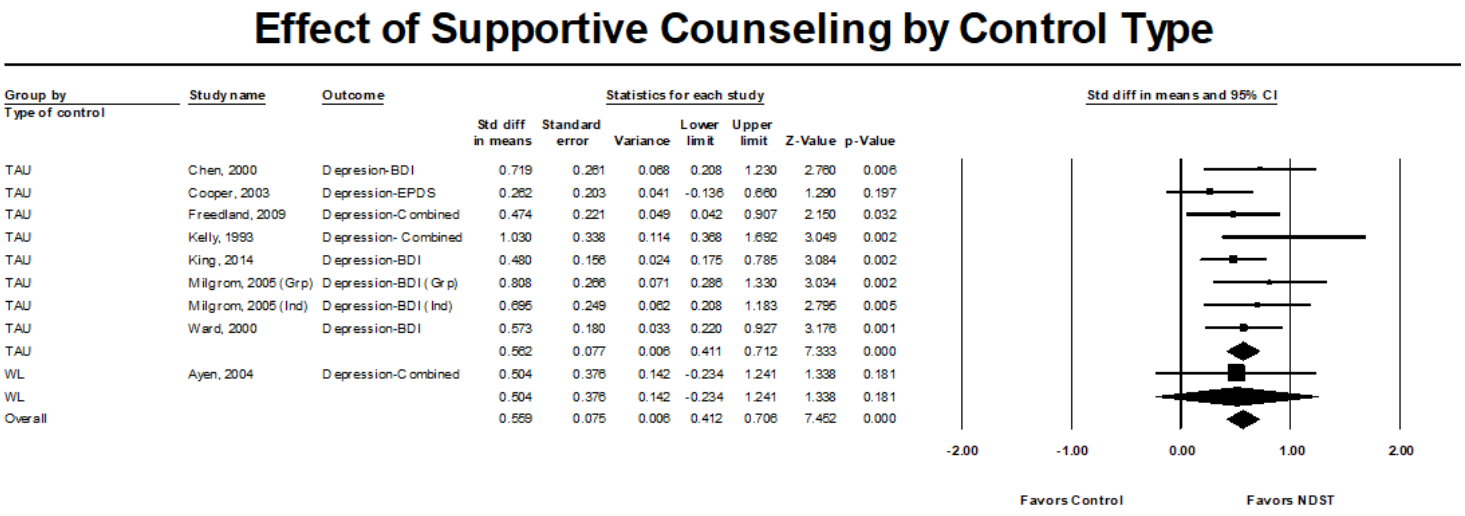


Effect due to Control Type

All of the included studies compared supportive counseling to a non-active control. The two non-active controls used in the RCTs were treatment as usual (TAU)

and a waitlist control (WL). Out of the 8 included studies, only one used a waitlist control design (Ayen & Hautzinger, 2004). All of the remaining studies used treatment as usual as a control group. Overall, the treatment as usual trails found a significant moderate effect, SMD= .562 (SE=.077, 95% CI=.411-.712, *p*=.000; Figure 23). In addition, a significant moderate effect was found for the waitlist control design study, SMD=.504 (SE=.375, 95% CI=-.234-1.241, *p*=.000; Figure 23). Because only one study compared NDST to a waitlist control, the results of the WL meta-analysis should be interpreted with caution. In order to strengthen the results of the WL group, further research must be conducted.

Figure 23: Effect of NDST on Depression due to Control Type

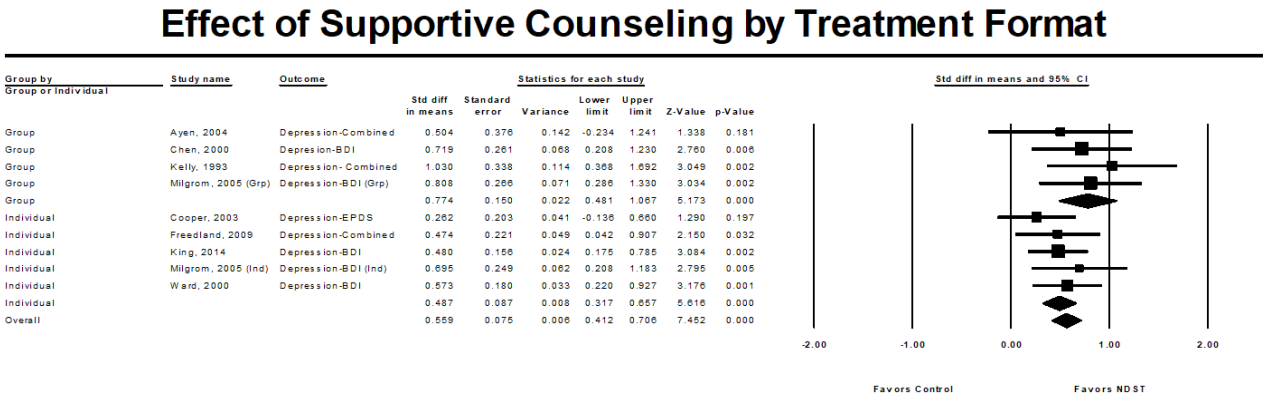


Effect due to Treatment Format

The included studies used two main treatment format options to deliver supportive therapy; these options were individual therapy or group therapy. Milgrom et

al. (2005) included three treatment arms, comparing both individual and group supportive therapy to treatment as usual. They found that both therapies reduced depressive symptomatology but that group therapy is slightly more efficacious. This meta-analysis found similar results. Four of the included studies compared group supportive counseling to a control (Ayen & Hautzinger, 2004; Chen et al., 2000; Kelly et al., 1993; Milgrom et al., 2005) and the remaining five compared individual supportive counseling to a control (Cooper et al., 2003; Freedland et al., 2009; King et al., 2014; Milgrom et al, 2005; Ward et al., 2000). Overall, the results indicate that group NDST results in a significant moderate to large effect, SMD= .774 (SE=.150, 95% CI=.481-1.067, *p*=.000; Figure 24). In addition, a significant moderate effect was found for individual NDST, SMD=.559 (SE=.075, 95% CI=.412-.706, *p*=.000; Figure 24). These results indicate that both forms of NDST are efficacious at reducing depressive symptomatology for individuals suffering from depression. In addition, the results indicate that group counseling is slightly more effective than individual counseling at improving symptomatology. Due to the small number of RCTs included in both meta-analyses, these results must be interpreted with caution.

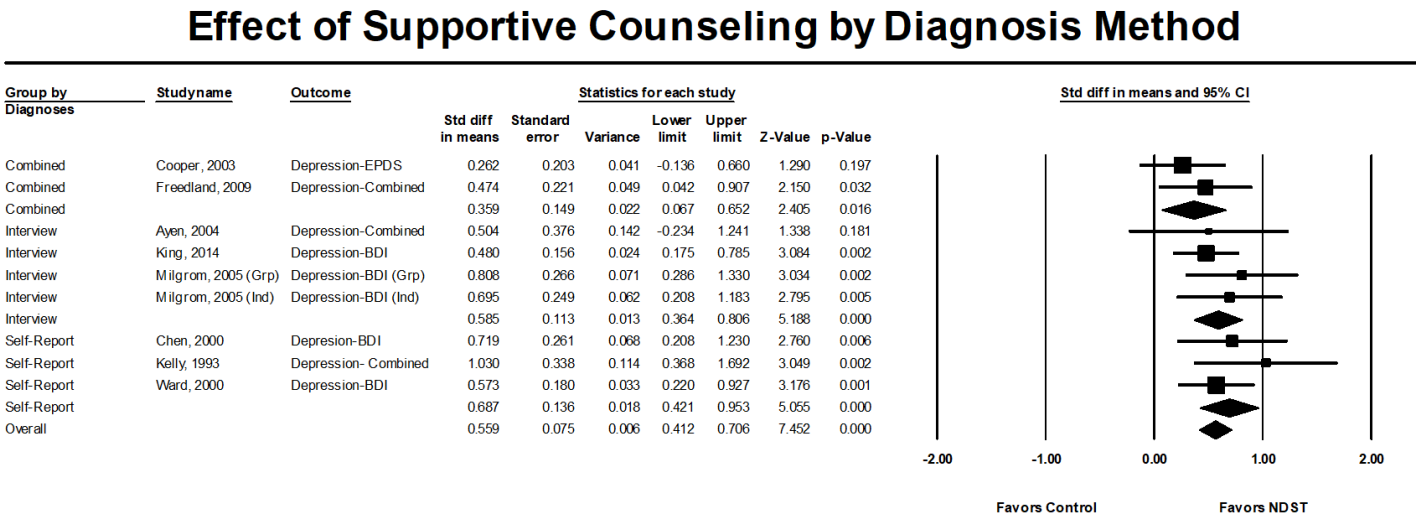
Figure 24: Effect of NDST on Depression due to Treatment Format



Effect due to Diagnosis Method

For inclusion criteria, researchers used a variety methods to measure and diagnose depression. Researchers used either a clinical interview, self-report measures, or both in order to diagnose depression and depression severity. Three of the included studies used a clinical interview in order to diagnose depression and include participants (Ayen & Hautzinger, 2004; King et al., 2014; Milgrom et al, 2005). These studies used a clinical interview to determine if recruited participants met the criteria for a DSM or ICD-10 depressive episode. Three of the studies used self-report scales (e.g. BDI) in order to determine if participants met inclusion criteria (Chen et al., 2000; Kelly et al., 1993; Ward et al., 2000) Only two studies used a combined method, both a self-report measure and clinical interview to diagnose depression (Cooper et al., 2003; Freedland et al., 2009). Overall, the results indicate that studies that used combined methods to diagnose depression result in a significant small effect. (SMD= .359, SE=.149, 95% CI=.067-662, p=.016; Figure 25). The two other means by which researchers diagnosed depression, through interview and self-report measures, resulted in similar outcomes. Studies that use a clinical interview to diagnose depression result in a significantly moderate effect (SMD= .585, SE=.113, 95% CI=.364-.806, p=.000; Figure 25). Finally, studies that used self-report measures to diagnose depression result in a significant moderate effect (SMD= .687, SE=.136, 95% CI=.421-.953, p=.000; Figure 25).

Figure 25: Effect of NDST on Depression due to Diagnosis Method



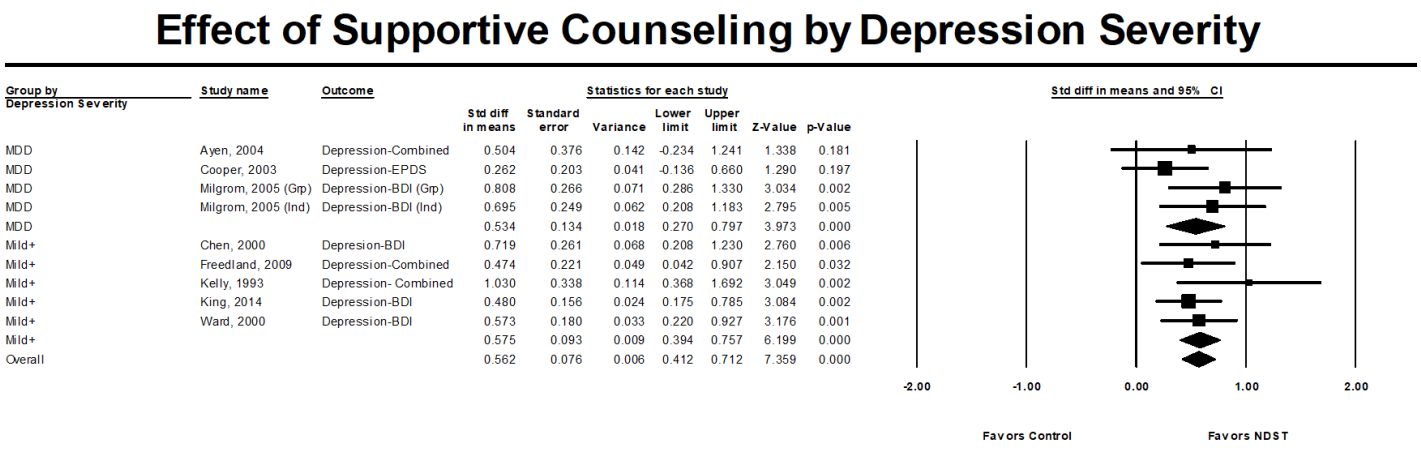
Overall, these results indicate that there is variation in the effectiveness of supportive counseling depending on how participants were diagnosed with depression. When individuals were diagnosed using both a clinical interview and a self-report measure, the effect of NDST was smaller. When individuals were diagnosed using a clinical interview, participants showed greater improvement then when using combined methods, but did not show as great improvement as the self-report group. Of the three methods to diagnose individuals, the self-report group showed the greatest improvement in depressive scores. Due to the small number of RCTs included in the three meta-analysis, the results must be interpreted with caution.

Effect due to Depression Severity

All of the included studies examined the effects of supportive therapy on depression. The severity of depression that researchers studied varied in each RCT. Three

studies examined the effects of NDST on individuals suffering from major depressive disorder (Ayen & Hautzinger, 2004;Cooper et al., 2003; Milgrom et al, 2005). The remaining studies included participants with a wide range of depression levels. In order to determine the level of depression severity for the remaining studies, the minimum degree of depression required by researchers for participation in their study was examined. The scoring criteria for each scale used in order to determine if the minimum inclusion score related to mild, moderate or severe depression was reviewed. The remaining five studies all included participants with at least mild depression (Chen et al., 2000; Freedland et al., 2009; Kelly et al., 1993; King et al., 2014; Ward et al., 2000). The results indicate that NDST has a significant moderate effect on depression in individuals with Major Depressive Disorder (SMD=.534, SE=.134, 95% CI=.270-797, *p*=.000; Figure 26). In addition, NDST has a significant moderate effect on depression in individuals suffering with, at minimum, mild depression (SMD=.575, SE=.093, 95% CI=.394-.757, *p*=.000; Figure 26).

Figure 26: Effect of NDST on Depression due to Depression Severity



Physical Activity

Description of Studies

Results of the Search

The electronic search of 5 databases, grey literature, and hand searching identified 20,745 studies for consideration. Only a fraction of the 20,745 studies examined the effects of physical activity, or exercise, as an intervention for treating depression. Two reviewers (NH, AS) examined the literature results and excluded obviously irrelevant records based on the title using the Rayyan QCRI software (Ouzzani, et al., 2016). After applying the inclusion and exclusion criteria, as specified in the previous chapter, 123 studies were included across all treatment arms. Out of the 123 studies, only 26 met the inclusion criteria for examining exercise as an intervention for depression (Bernard et al., 2015; Blumenthal et al., 2009; Hallgren, Kraepelien, Ojehagen et al., 2015; Helgadottir, Forsell, Hallgren et al., 2017; Hess-Homeier, 1981; Ho et al., 2014; Huang, Liu, Tsai et al, 2015; Legrand, 2014; Mather et al., 2002; McCann & Holmes, 1984; McNeil et al., 1991; Mota-Pereira et al., 2011; Mutrie, 1986; Nystrom et al., 2017; Orth 1981; Schuch, Vasconcelos-Moreno, Borowsky, & Fleck, 2011; Sims, 2009; Sims, Hill, Davidsons, Gunn & Huang, 2006; Singh et al., 2005; Singh, Clements & Singh, 2001; Singh, Clements, & Fiatarone, 1997; Soucy, Provencher, Fortier & McFadden, 2017; Rethorst, Landers, Nagoshi, & Ross, 2010; Robledo- Colonia et al., 2012; Roy, Govindan, & Muralidharan, 2018; Williams & Tappen, 2005). Of the included studies, two examined the effects of various intensities of exercise (Helgadottir et al., 2017; Singh et al., 2005). As a result, three individual treatment arms were included from Helgadottir's (2005)

study and two treatment arms were included from Singh's (2005) study. As a result, 26 studies, and 29 treatment arms, including a total of 2,439 participants were included in this meta-analysis. The actual number of participants analyzed may varied according to the study design and type of intervention.

Characteristics of Included Studies

The final sample consisted of 21 2-arm parallel, four 3-arm parallel, and one 5-arm parallel RCTS. Overall, the studies were conducted all over the world but, as a whole, they were conducted in North America (Blumenthal et al., 2009; Hess-Homeier, 1981; McCann & Holmes, 1984; McNeil et al., 1991; Mutrie, 1986; Orth 1981; Rethorst, et al., 2010; Singh, Clements & Singh, 2001; Soucy, et al., 2017; Singh, Clements, & Fiatarone, 1997; Williams & Tappen, 2005), Europe (Bernard et al., 2015; Hallgren et al, 2015; Helgadottir et al., 2017; Legrand et al.,2014; Mather et al., 2002; Mota-Pereira et al., 2011; Nystom et al., 2017), South America (Robledo-Colonia et al., 2012; Schuch et al, 2011), Asia (Ho et al., 2014; Huang et al., 2015; Roy et al., 2018), and Australia (Sims et al, 2006; Sims et al., 2009; Singh et al., 2005). The majority of the studies occurred in the United States, while two of the North American studies occurred in Canada. The European studies occurred in France (n=2), Sweden (n=2), Germany (n=1), England (n=1), and Portugal (n=1).

Types of depression examined varied greatly across the studies. The majority of the included studies examined the effect of exercise on depression or increased depressive symptomatology. A few students examined specific populations of individuals; these included the elderly (Mather et al., 2002; McNeil et al., 1991; Singh et

al., 2001; Singh et al., 2005; Sims et al., 2006; Singh et al., 1997), college students (McCann et al., 1984; Orth, 1981), and an Asian population (Ho et al., 2014; Roy et al, 2018). Out of the 26 studies, only three examined the effects of exercise on individuals with major depressive disorder (Blumenthal et al., 2009; Schuch et al, 2011; Mota-Pereira et al, 2011).). Lastly, two studies examined depression due to another medical condition, the examined conditions were alcoholism (Williams et al., 2008), and post-stroke depression (Sims et al., 2009).

All included studies reported clear diagnostic, inclusion, and exclusion criteria for their participants. Each study varied when considering the minimum severity of depression participants must be suffering from in order to be included in the study. As stated previously, four examined the effects of exercise on individuals with major depressive disorder. To be included in these studies, participants must have met the DSM diagnostic criteria for MDD and score above a 12 on the BDI or on the Bech Rafaelsen Melancholy scale (BRMS). Of the 26 included studies, nine only included individuals after they were diagnosed with a ICD-10 or DSM diagnosis of depression. The majority of studies used scales to include or exclude individuals. The majority of studies (n=9) used the BDI in order to include participants. The ranges of minimum score needed to be included in a study ranged from 9 (Ho et al., 2014) to above 16 (Mutrie, 1986). Most of the studies that used the BDI as an inclusion measurement included participants who scored above 12. The other scale used most frequently in studies as inclusion criteria was the PHQ-9. Minimum scores need in order to be included ranged from 5 to above 10 (Helgadottir et al., 2017). In addition to a wide variety of inclusion criteria, these studies all used many different measurement inventories to measure depression. The majority of

the studies used either the Beck Depression Inventory (BDI) (n=12) or the Hamilton Rating Scale for Depression (HAMD) (n=7) or a combination of the two. Of the studies that did not use the HAMD or BDI, three of them used the CES-D, three used the GDS, two used the MAPRS, two of them used the PHD-9 and one used the BRMS and MMPI.

The protocol used to administer physical activity was differed across studies. The majority of studies examined the effects of aerobic physical activity on depression symptomatology. The type of aerobic activity varied. Many of the studies included some type of walking or running program. Hess-Homeier (1981) strictly looked at the effect of 25-30 minutes of walking or jogging on depression over 8 weeks. Most studies researched the effect of moderate intensity aerobic exercise. One study, conducted by Helgadottir and colleagues, examined the effects of a moderate intensity and a vigorous intensity aerobic exercise intervention (Helgadottir et al., 2017). Overall, the majority of aerobic exercise interventions were described as being walking or jogging with the exception of three studies. Schuch described their intervention as being a participant's choice but including a stationary bike and elliptical (Schich et al., 2011), Rethorst included cycling sessions (Rethorst et al, 2010), and McCann stated their intervention was aerobic exercise and gave running and dancing as examples (McCann et al., 1984). Overall, the duration of session typically lasted between 30 and 45 minutes, including warm up and warm down. The two notable exceptions to this were the studies performed by Helgadottir and Robledo-Colonia. The aerobic exercise interventions lasted 55 and 50 minutes, respectively, in these studies (Helgadottir et al., 2017; Robledo-Colonia et al., 2015).

The remaining studies used either strength training or a mixed modality form of physical activity. All three studies performed by Singh, for example, involved the same form of progressive resistance training (Singh et al., 1997, 2001, 2005). This intervention involved weight machines that worked major muscle groups; these movements included the shoulder press, chest press, upright row, and leg press. When performing the movements, the trainers had participants lift at 80% 1 rep max and perform 3 sets of 8 repetitions. In addition, strength testing was repeated as individuals got stronger in order to maintain similar effort. Overall only two studies examined the effects of a combined aerobic and strengthening exercise program on depression outcomes. Huang implemented both aerobic and muscle strengthen sessions as accordance with both the American Heart Association and the American College of Sports Medicine guidelines (Huang et al., 2015). Lastly, Mather and colleagues also allowed their participants to take part in aerobic and strengthening classes (Mather et al., 2002).

In addition to inconsistencies in physical activity protocol, studies varied dramatically regarding the length and frequency of the intervention, and how the intervention was implemented. . The length of treatment varied from 10 days (Roy et al., 2018) to six months (Bernard et al., 2015) with the majority of treatment lengths being between 8 and 12 weeks (n=16). The number of sessions completed within each week during the intervention also greatly varied. Some studies had participants exercise anywhere from twice a week (Mather et al., 2002; McCann et al., 1984) and five times a week (Orth, 1981).

Most of the studies had trained staff implementing the physical activity protocols. These individuals supervised participants to ensure they were exercising appropriately. For the aerobic exercise interventions, many studies had goal target heart rates for individuals to achieve while they were exercising. For example, trainers in the study performed by Legrand encouraged participants to sustain a heart rate between 65-80% maximum while working out (Legrand et al., 2014). Other studies stated that their target heart rate for participants was 40%-55% (Ho et al., 2014) to 85% (Blumental et al., 2009)) of maximum heart rate. As previously stated, most studies involved a trainer but there were a few studies that had participants train unsupervised. Blumenthal (2009) had an experimental group that performed at home, unsupervised, aerobic exercise in addition to the supervised exercise group. Another study had participants undergo both supervised and unsupervised exercise sessions each week (McNeil et al., 1991). There was only one study that had individuals receive their intervention through alternative means. In a study performed by Roy (2018), participants received a video assisted aerobic exercise program. Participants performed aerobic exercise in accordance with a structured video for twenty minutes each day throughout the duration of the study.

Of the 26 studies included, all of them compared behavioral activation to a non-active control. A majority of the studies (n=17) compared physical activity to a waitlist control. A total of 10 studies compared physical activity to a treatment as usual control, and the remaining three studies compared the experimental group to a placebo group. Although the majority of studies were two-arm designs, there were some multiarm designs as well. There was a total of 21 studies that compared physical activity to a control All of the other studies compared physical activity to a control and another active

group. Two of the multiarm studies compared physical activity to behavioral activation (Nystrom et al., 2017; Soucy, et al., 2017). The remaining three multiarm trials all compared physical activity to cognitive behavioral therapy as well as a control group (Hallgren et al., 2015; Hess-Homeier, 1981; Huang et al., 2015).

Risk of Bias Assessment

Figures 27 and 28 provides a summary of the risk of bias of the included studies.

Figure 27: Risk of Bias Graph

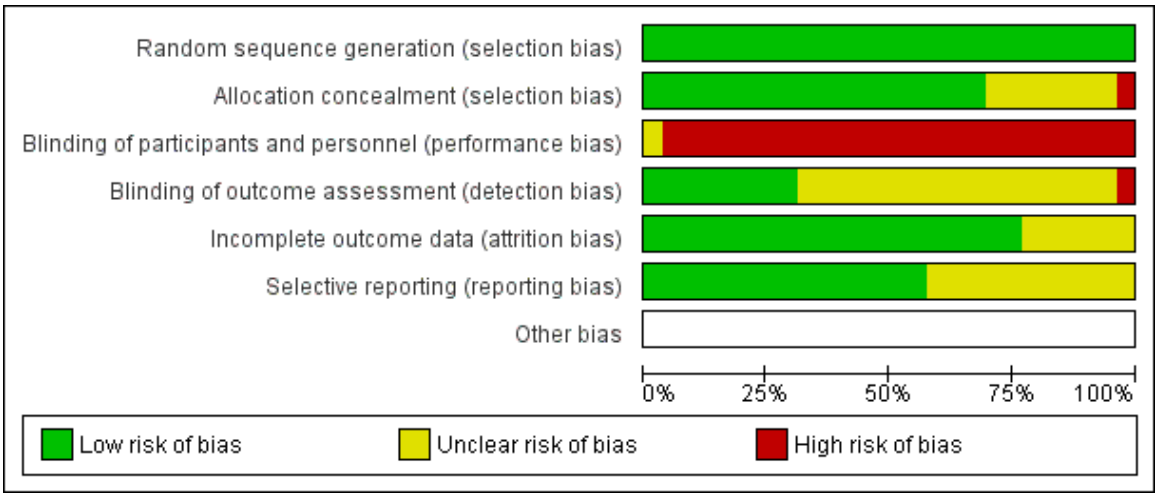


Figure 28: Risk of Bias Summary

Randomization

In order to determine if the studies were randomized, the method by which randomization was achieved was assessed. All included studies reported that the groups were randomized. All of the studies were deemed to have low risk of bias due to the randomization procedure. Studies used a variety of different mrthods to achieve randomization. Ho et al. (2014) stated that "Subjects were randomly allocated using blocked randomization into one of two groups: aerobic exercise group and control group"

(p. 2). Another study stated “Participants were randomly assigned to one of two experimental groups using a computer generated randomization list” (Legrand, 2014, p 359). Hallgren and colleagues did not use a computer generated list in order to preform randomizations. These researchers randomized the participants through an independent clinical research organization (Hallgren et al., 2015). Other studies used individuals independent from the study (Sims et al., 2006) or a computer generation random number generation (Singh et al., 2005). A majority of the included studies stated that randomization occurred but did not provide means by which researchers performed it.

Allocation Concealment

Only a few of the studies reported on allocation concealment. Soucy et al. stated that, “Randomly assigned conditions were sealed in envelopes labelled with participant codes and opened following completion of the baseline questionnaire.” (Soucy et al., 2017, p.497). Another study that reported on allocation concealment was performed by Sims. Researchers stated that allocation was performed by an independent person who ascertained the allocation from a previously generated randomized block list (Sims et al., 2006). Some other studies provided a statement that clearly said allocation was not revealed until the assignment of intervention.

Blinding Interventions

Blinding of the participants was not possible due to the nature of the interventions. As evidenced in Figures 27 and 28, the risk of potential performance bias was high for almost all included studies due to the nature of the behavioral interventions assessed. It was impossible to blind participants to the status of their intervention and

difficult to blind personnel and staff (e.g. counselors or psychologists). Of the 30 included studies, only one received an unclear level of performance bias. Soucy and colleagues attempted to minimize performance bias by following a double blind procedure. Both allocation of conditions and randomization of participants were blinded to the researchers (Soucy et al., 2017). Although it was impossible to completely avoid performance bias while researching these types of interventions, Soucy et al. maximized their blinding procedures to the maximum extent. Another study in which researchers attempted to minimize performance bias was performed by Mota-Pereira. Investigators described the study as a "randomized, investigator blinded, two-arm, parallel assignment" (Mota-Pereira et al., 2011, p 1006). This study was still determined to have a high risk of performance bias due to the fact researchers failed to describe the blinding and allocation process. Many of the studies did not state the nature of blinding for the outcome assessors. One study performed by Sims stated "Those handling the outcome data were blinded to the person's group assignment" (Sims et al., 2006, p. 3). Since blinding of participants is not possible with these types of interventions, blinding of outcome assessors would help decrease detection bias.

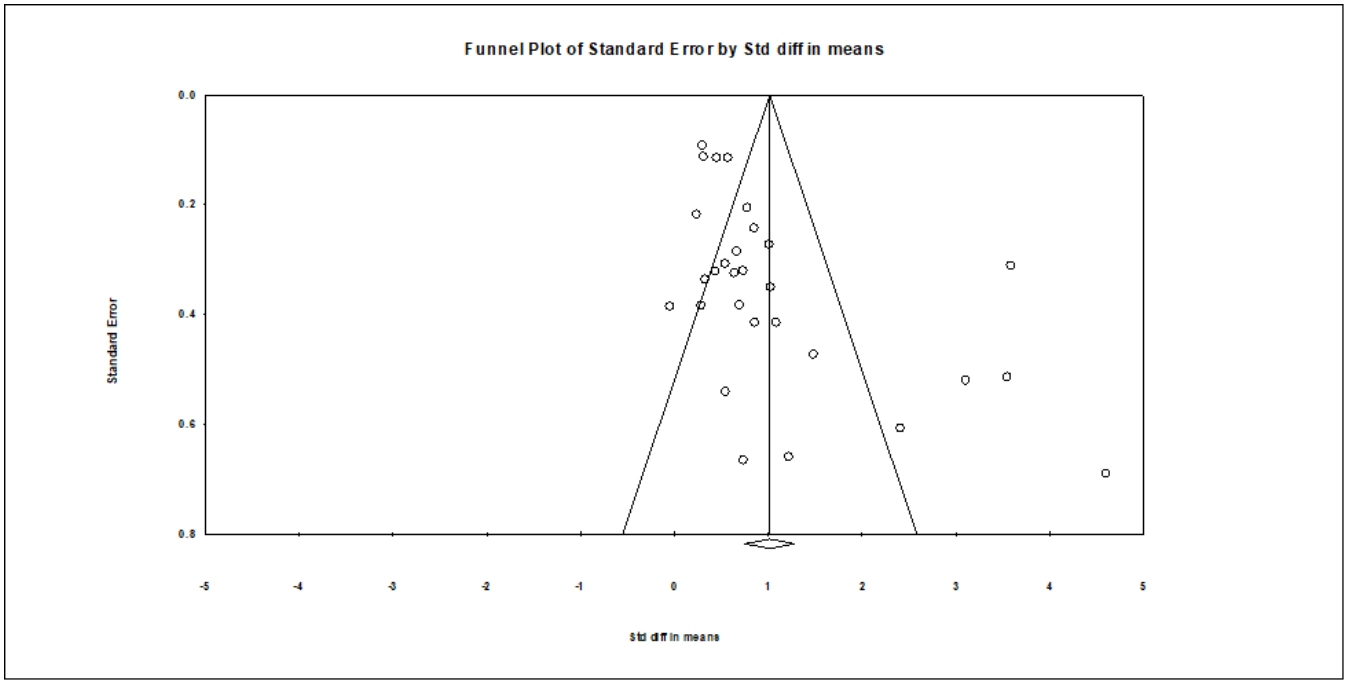
Reporting Bias

In order to assess reporting bias, the likelihood that information was chosen based on multiple outcome measures or multiple analyses of data was examined. As a whole, there was evidence in multiple studies that selective outcome reporting or outcome reporting based off of multiple analysis of data may have occurred.

Assessment of Reporting Bias

Publication bias was examined by visually inspecting a funnel plot according to the guidelines presented by Egger (Egger et al., 1997).

Figure 29. Funnel Plot of Standard Error by SMD



Following inspection of the funnel plot, it is clear that there is evidence of publication bias. The publication bias was judged as being moderate to high due to the asymmetry observed and the variation of where studies are plotted as compared to average (see Figure 29). The results of the funnel plot support the results of the risk of bias assessment. Due to a variety of methodological issues, including reporting bias, selection bias, and performance bias, the risk of publication bias is moderate to high.

Effect of Physical Activity

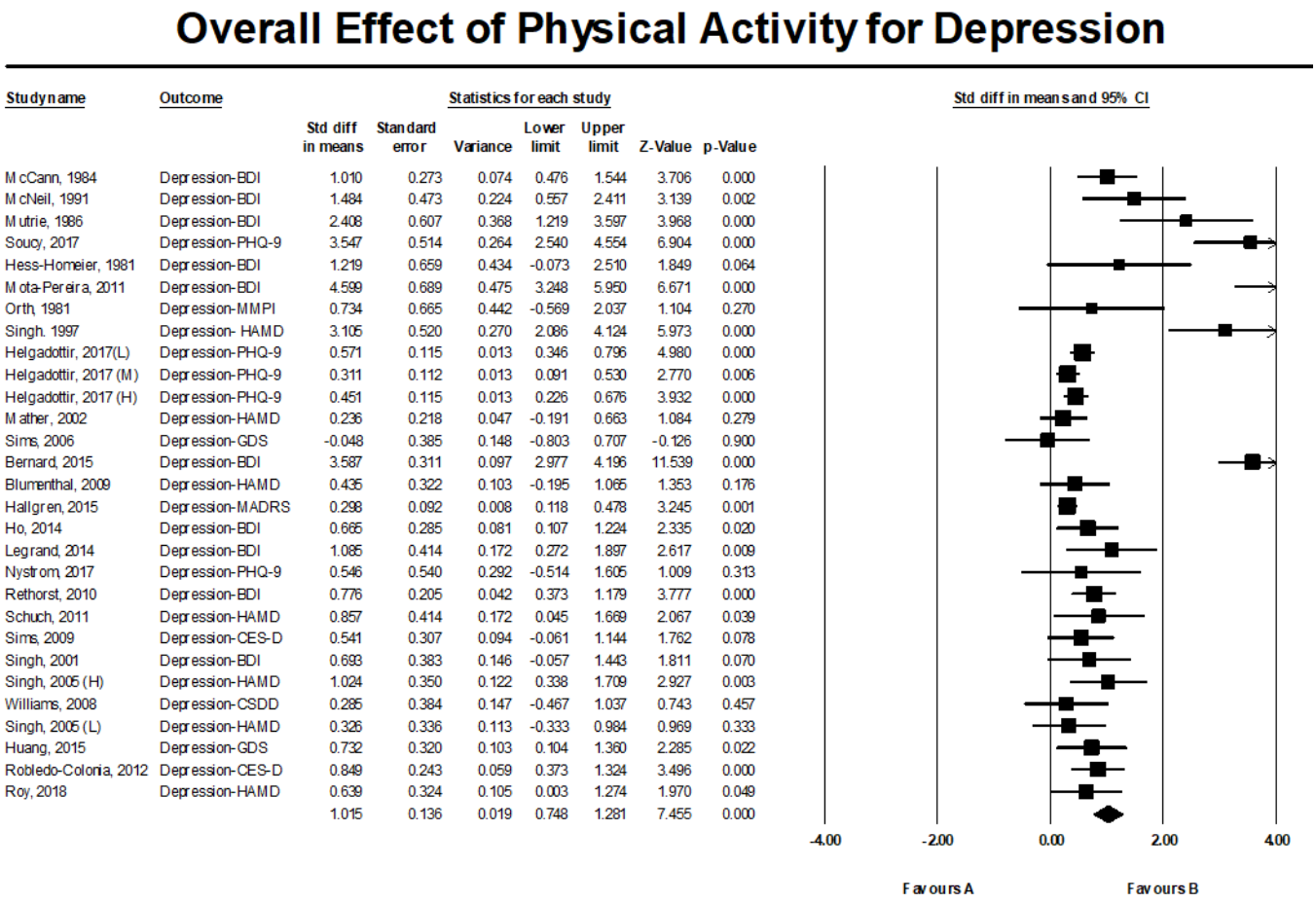
In the following section, the effects of physical activity on depression symptomatology are presented. In addition to the overall effect of PA on the primary

outcome, the results of a series of meta-analyses moderating for specific a-prior defined variables are presented as well.

Overall Effect

In this analysis, data from 26 studies and 29 treatment arms, were pooled together using the standardized mean difference (SMD). A large significant effect was found, SMD= 1.015 (SE=.136, 95% CL=.748-.1.281, p=.000, I^2=52.141; Figure 30). These results indicate that physical activity significantly decreases depressive symptomatology in individuals suffering from depression. The effect size of each study ranged from SMD=-.048 (p=.900) (Sims et al., 2016) to SMD=4.599 (p=.000) (Mota-Pereira et al., 2011). Due to expected heterogeneity, the random effects model was used to conduct the meta-analysis. The I^2 statistic indicates that there was moderate heterogeneity and the results were inconsistent across the studies analyzed. Subsequently, these findings must be interpreted cautiously due to potential publication bias and heterogeneity.

Figure 30: Overall Effect of PA on Depression

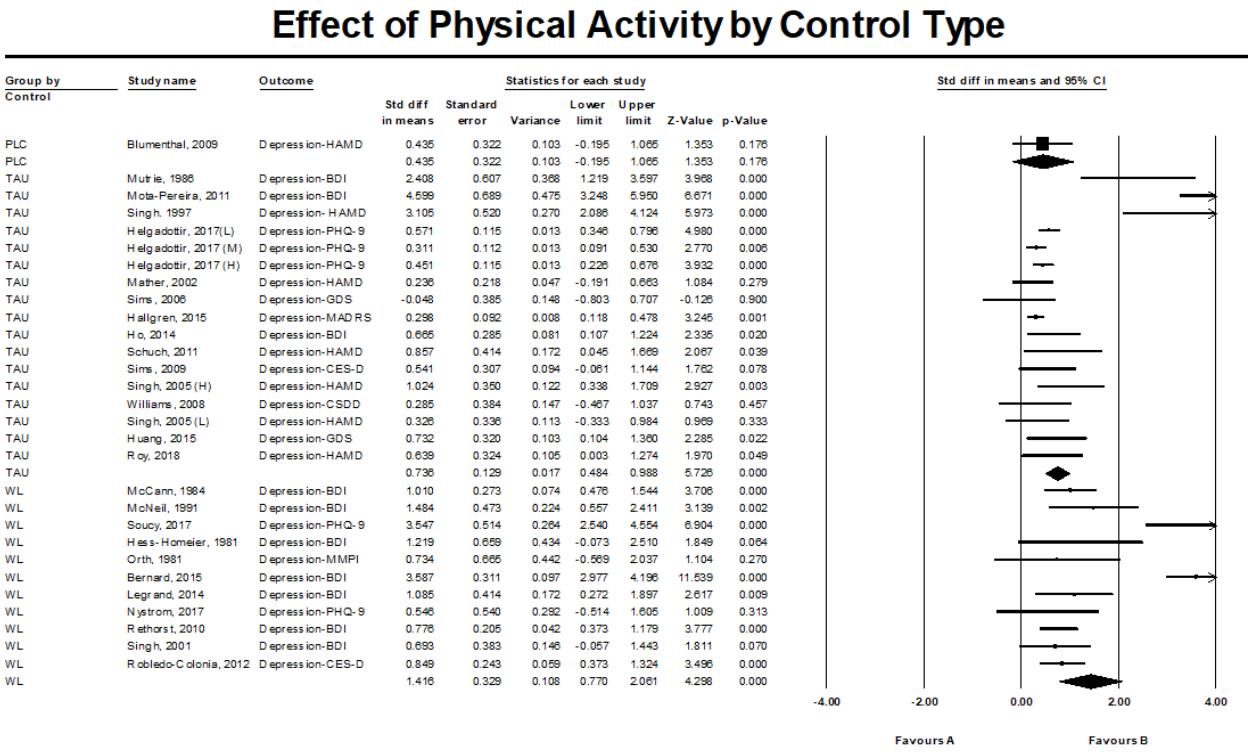


Effect due to Control Type

All of the included studies compared physical activity to a non-active control. The three non-active controls used in the RCTs were treatment as usual (TAU), placebo control (PLC), and a waitlist control (WL). Out of the 26 included studies, only one used a placebo control design (Blumenthal et al., 2009). All of the remaining studies used either waitlist controls (n=11) or treatment as usual (n=14) as a control group. Overall, the treatment as usual trails found a significant moderate to large effect, SMD= .736

(SE=.129, 95% CI=..484-.988, p=.000, I^2=6.188; Figure 31). The treatment as usual subgroup analysis resulted in a low level of heterogeneity, indicating minor inconsistences in included studies. In addition, a significant small to moderate effect was found for the placebo control design study, SMD=.435 (SE=.322, 95% CI=-.195-1.065, p=.176, I^2=0.000; Figure 31). Since only one study compared PA to a placebo, the results of the PLC meta-analysis should be interpreted with caution. In order to strengthen the results of the PLC group, further research must be conducted. Overall, the largest significant effect was found when PA was compared to a waitlist control: a very large significant effect was found (SMD=1.416, SE=.329, 95% CI=.770-2.061, p=.000, I^2=1.988; Figure 31).

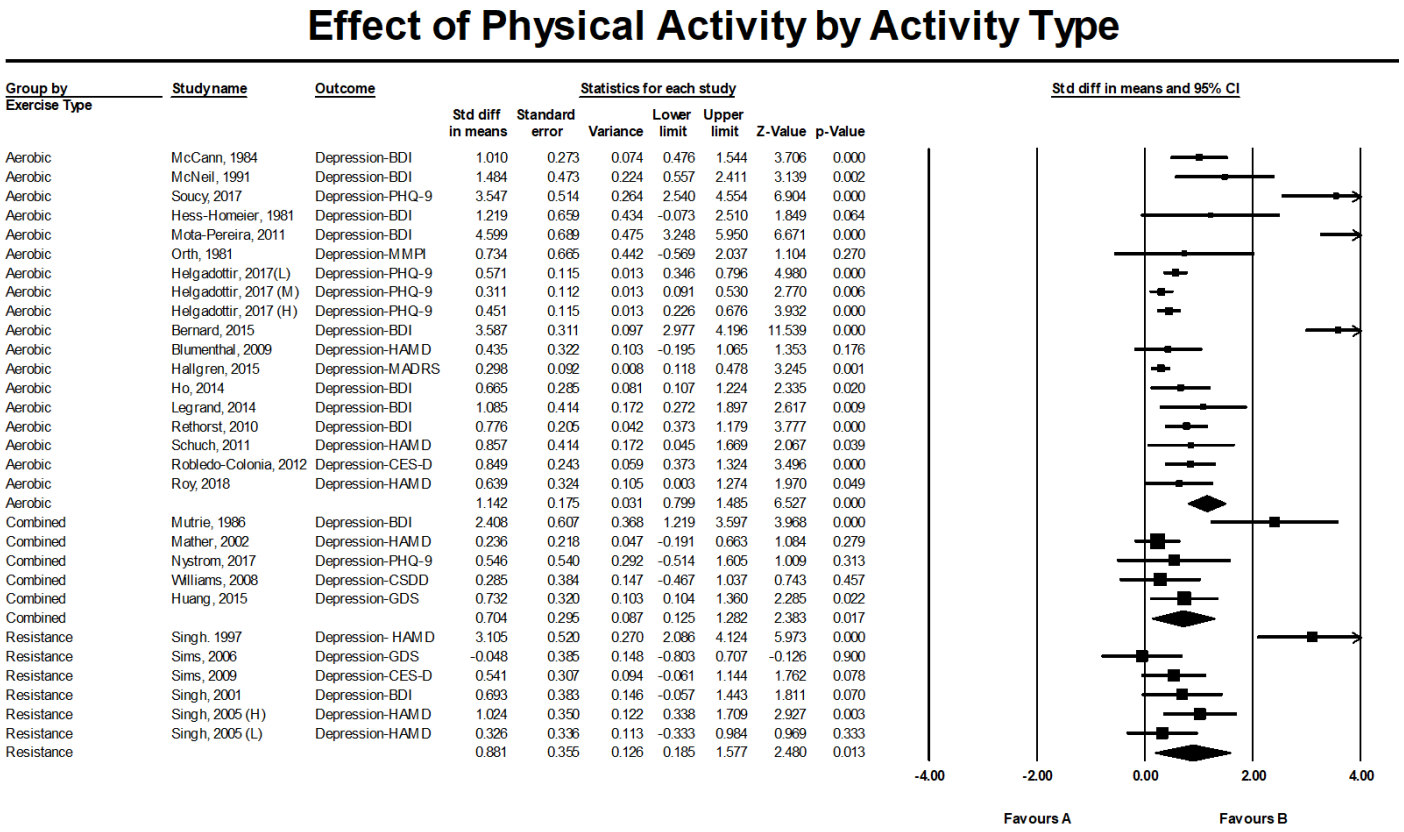
Figure 31: Effect of PA on Depression due to Control Type



Effect due to Physical Activity Type

The 26 included studies analyzed a variety of physical activity types on depression. Physical activity was defined as three different types; aerobic physical activity, resistance (anaerobic), or a combined exercise protocol of aerobic and anaerobic training. The majority of studies (n=16) examined the effects of aerobic exercise training on depression. The rest of the studies either examined resistance training (n=5) or combined training (n=5). Overall, aerobic physical activity was found to have the largest and most significant effect on depression outcomes (SMD=1.142, SE=.175, 95% CI=.799-1.485, p=.000, I^2=58.474; Figure 32). In addition to aerobic physical activity, anaerobic (resistance) training produced a large significant reduction in depressive symptoms (SMD=.881, SE=.355, 95% CI=.185-1.577, p=.013, I^2=32.357; Figure 32). The only exercise type that did not produce a large effect was the combined aerobic and anaerobic exercise treatment. The combined treatment produced a significant moderate to large effect on depressive symptomatology (SMD=.704, SE=.295, 95% CI=.123-1.282, p=.017, I^2=29.439; Figure 32). As a whole, these results indicate that all forms of physical activity are beneficial for decreasing depressive symptomatology, but that some forms of activity (e.g. aerobic) may be superior to other forms (e.g. resistance and combined).

Figure 32: Effect of PA on Depression due to Type of PA



Effect due to Exercise Frequency

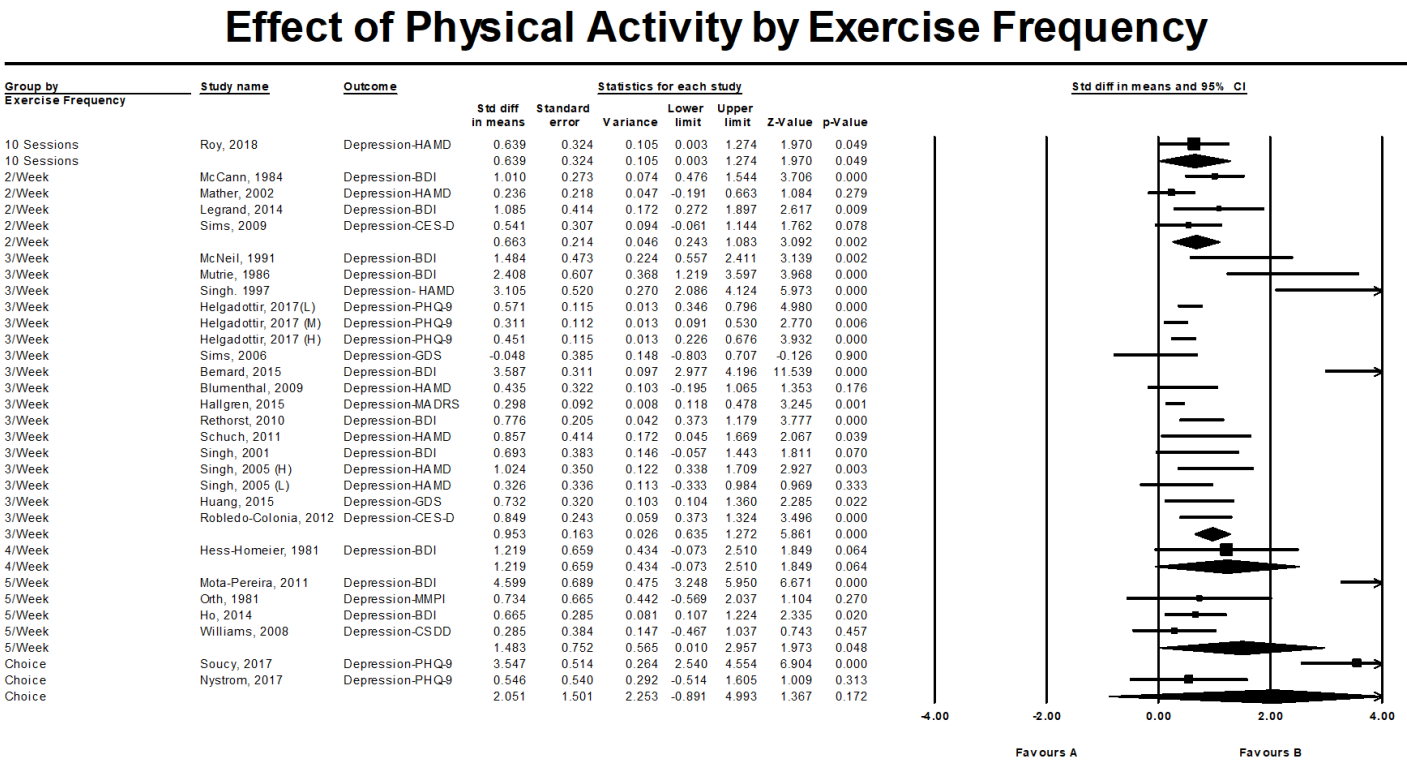
The protocol for implementing a physical activity intervention were highly variable across studies. Researchers had participants exercise between twice a week and five times a week. In addition, a couple of studies allowed participants to choose how many days a week they work out (Soucy et al., 2017; Nystrom et al., 2017) and one study had participants work out every day for 10 days (Roy et al., 2018). The majority of studies had participants exercise three days a week (n=14). The rest of the studies had participants exercise twice a week (n=4), four times a week (n=1), or five times a week (n=4). Overall, the effect of a physical activity intervention on depression symptoms was

influenced by exercise frequency. Exercising twice a week resulted in a significant moderate decrease in depressive symptomatology (SMD=.663, SE=.214, 95% CI=.243-1.083, p=.002, I^2=0.000; Figure 33). As exercise frequency increased to three days a week, a large significant decrease in depression scores was observed (SMD=.953, SE=.163, 95% CI=.635-1.272, p=.000, I^2=52.672; Figure 33). Finally, as exercise frequency increased to four and five days a week, even greater improvement in depressive symptomatology was observed. Only one study researched the effect of exercising four days of week on depression, and it found a very large but insignificant effect (SMD=1.219, SE=.659, CI= -.073-2.510, p=.064, I^2=0.000; Figure 33). Lastly, when pooled, the four studies that examined the effect of working out five days a week on depressive symptoms found a very large significant decrease in symptomatology (SMD=1.483, SE=.752, CI= .010-2.957, p=.048, I^2=41.962; Figure 33). Overall, the results indicate that exercise produces a larger therapeutic effect for depression when practiced more frequently. These results should be interpreted with caution because there were only a few studies that examined the effects of working out four or five times a week.

Effect due to Exercise Intensity

In order to examine the effect of exercise due to exercise intensity, exercise interventions were judged based on the author's description of the intervention. If authors defined the intervention as low, moderate, or vigorous intensity then that rating was used. If authors did not, then the type of physical activity or target heart rate was used to define exercise intensity. The American College of Sports Medicine guidelines were used to

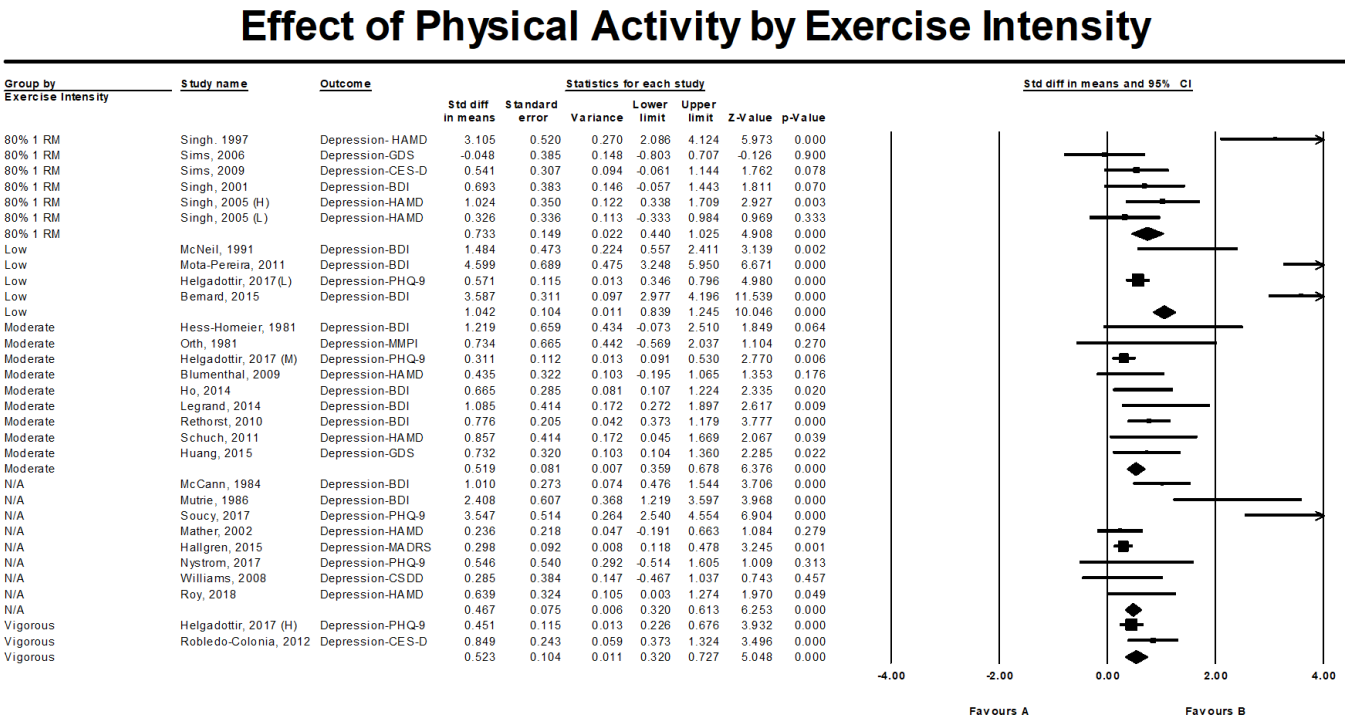
Figure 33: Effect of PA on Depression due to Exercise Frequency



describe aerobic intensity. An exercise intervention was defined as moderate if an individual's goal HR was between 40-60% maximum, and an intervention was vigorous if the target HR was between 60-85% max. If researchers did not give a target heart rate and the intervention was described as walking (not brisk walking), then the intervention was defined as low intensity. All anaerobic exercises studies were defined by how much weight individuals lifted. All of the anaerobic studies (n=6) used a progressive resistance training intervention. Many of the studies did not provide enough information to define the intensity of the exercise intervention (n=8). The pooled analysis of low intensity physical activity treatments found a significantly large decrease in depressive symptomatology (SMD=1.042, SE=.104, CI= .839-1.245, p=.000, I^2=0.000; Figure 34). When participants performed moderate intensity exercise a modest significant decrease

was observed in depressive scores (SMD=.519, SE=.081, CI= .359-.678, p=.000, I^2=0.000; Figure 34). Subsequently, vigorous physical activity interventions produced similar effects as the moderate intensity interventions (SMD=.523, SE=.104, CI= .320-.727, p=.000, I^2=50.339; Figure 34).

Figure 34: Effect of PA on Depression due to Exercise Intensity

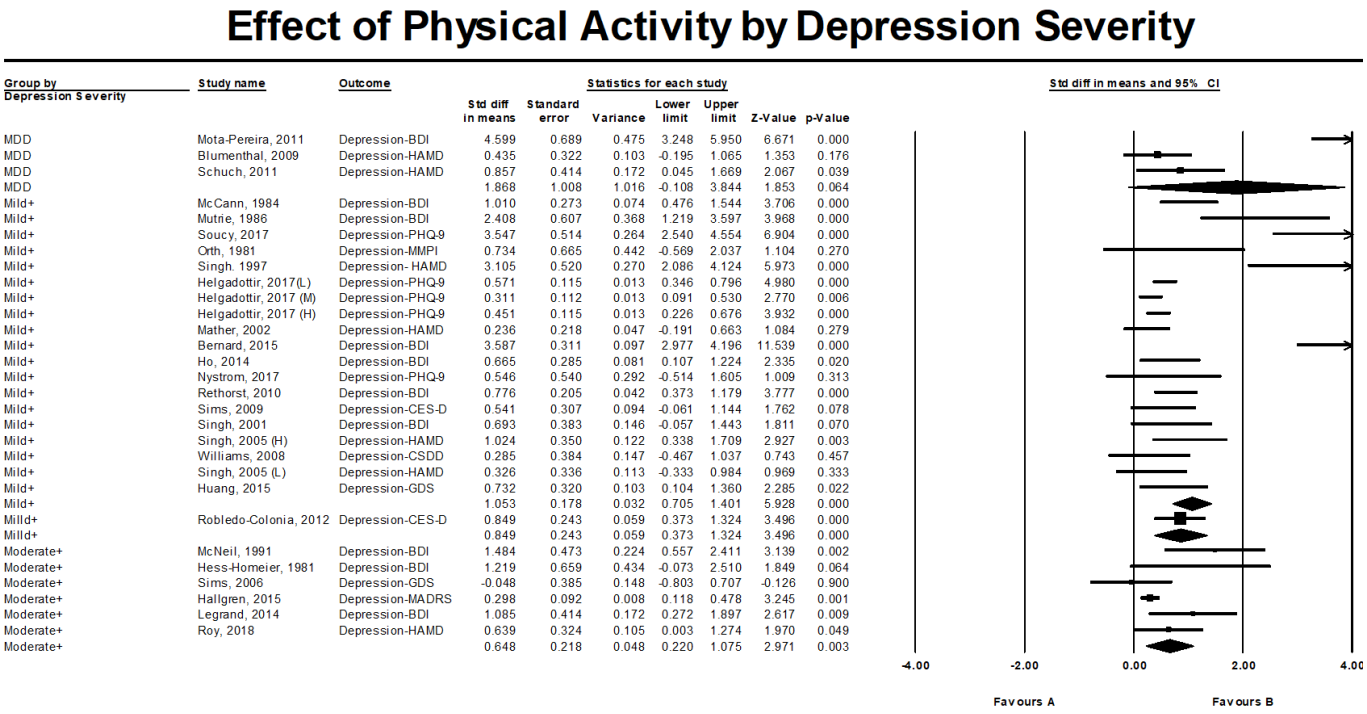


Effect due to Depression Severity

All of the included studies examined the effects of physical activity on depression. The severity of depression that researchers studied varied in each RCT. Three studies examined the effects of PA on individuals suffering from major depressive disorder (Mota-Pereira, 2011; Blumenthal et al., 2009; Schuch et al., 2011). The remaining studies included participants with a wide range of depression levels. In order to

determine the level of depression severity for the remaining studies, the minimum scores on depression scales that researchers allowed for inclusion in their study was examined. The scoring criteria for each scale used to determine if the minimum inclusion score related to mild, moderate or severe depression was measured. Most of the remaining studies all included participants with at least mild depression (n=17). The remaining six studies examined the effect of PA on individuals suffering from at least moderate depression (McNeil et al., 1991; Hess-Homeier, 1981; Sims et al., 2006; Hallgren et al., 2015; Legrand et al., 2014; Roy et al., 2018). The results indicate that physical activity large, but insignificant, effect for improves depression in individuals with Major Depressive Disorder (SMD=1.868, SE=1.008, 95% CI=-.108-3.884, p=.064, I^2=39.786; Figure 35). In addition, PA significantly, and to a large effect, improves depression in individuals suffering with, at minimum, mild depression (SMD=1.053, SE=.178, 95% CI=.705-1.401, p=.000, I^2=47.600; Figure 35). Lastly, when examining participants with at least moderate depression a moderate, significant, diminishing effect on depressive symptomatology is observed (SMD=.648, SE=..218, 95% CI=.220-1.075, p=.003, I^2=7.616; Figure 35).

Figure 35: Effect of PA on Depression due to Depression Severity



CHAPTER 5

RESULTS

Network Meta-Analysis

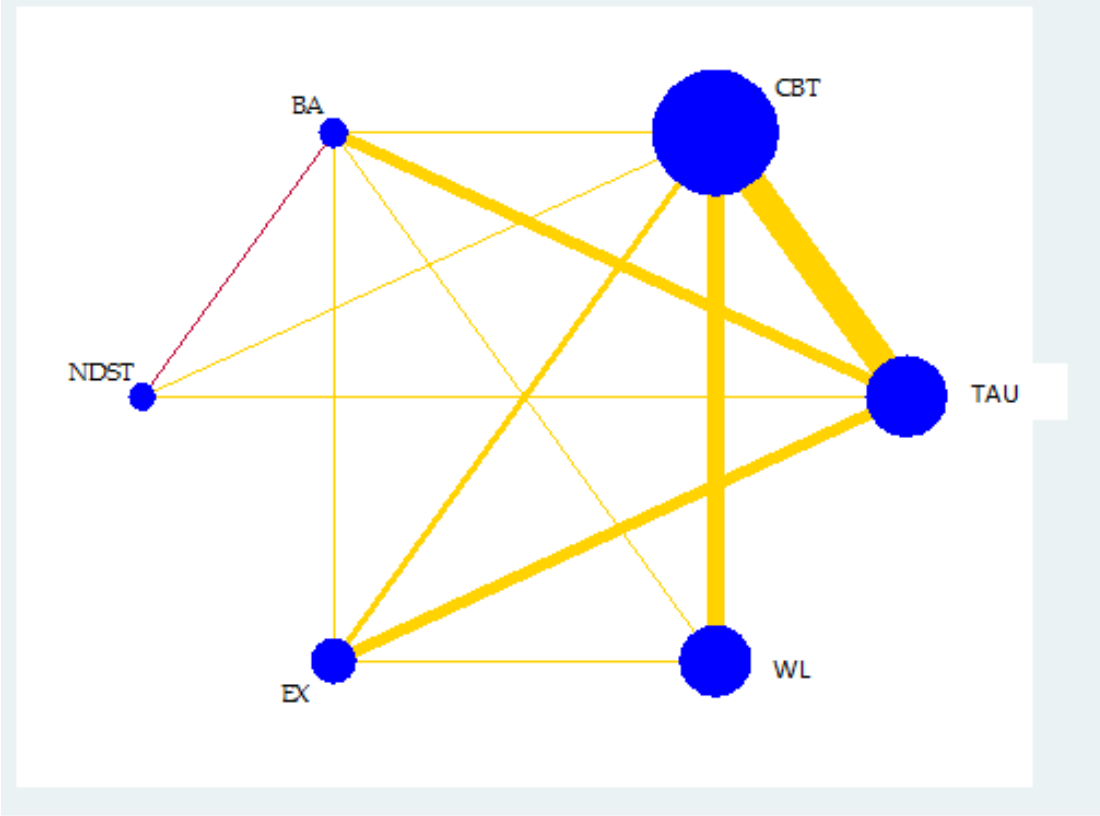
The literature search identified 123 eligible reports by reviewing full text studies. Only 105 studies were included in this meta-analysis because of insufficient statistics or incorrect control group in other studies. One-hundred and five trials involving 10,371 patients provided adequate data for depression outcomes. Detailed results and code are given in Appendices E and F.

Network Plot

In Figure 36, the network plot for efficacy depression treatment network is presented. Both the waitlist and treatment as usual controls were included in this meta-analysis. The nodes were weighted according to the number of studies, including each respective intervention. The figure indicates that both cognitive behavioral therapy and the two controls are the most frequent comparators across studies. The lines between each node, and the weight of each line, represented the number of RCTs directly comparing those two treatment options. As indicated by the plot, the majority of the included studies (n = 33) were comparing CBT to the treatment as usual control or CBT to the waitlist control (n = 32). The remainder of the number of included RCT's varied according to treatment arm. Overall, there were three treatment comparisons that did not have any direct evidence; these comparisons were TAU vs WL, NDST vs EX, and NDST vs WL.

Another important aspect in meta-analysis was the quality of the studies. In order to present the risk of bias in each study, each direct comparison was rated according to the determined risk of bias. In order analyze risk of bias, studies were evaluated on their blinding procedures, allocation concealment, and reporting of data. After evaluating the risk of bias, each direct comparison study was given a rating of 1, 2, or 3, which corresponds to a low, moderate, and high risk of bias respectively. It is evident in the network plot, that the majority of direct evidence had a moderate risk of bias. Only one direct between comparison had an overall high risk of bias. This may be the only treatment arm with a high risk of bias since it was the only treatment arm having one study for direct evidence.

Figure 36: Network Plot for NMA



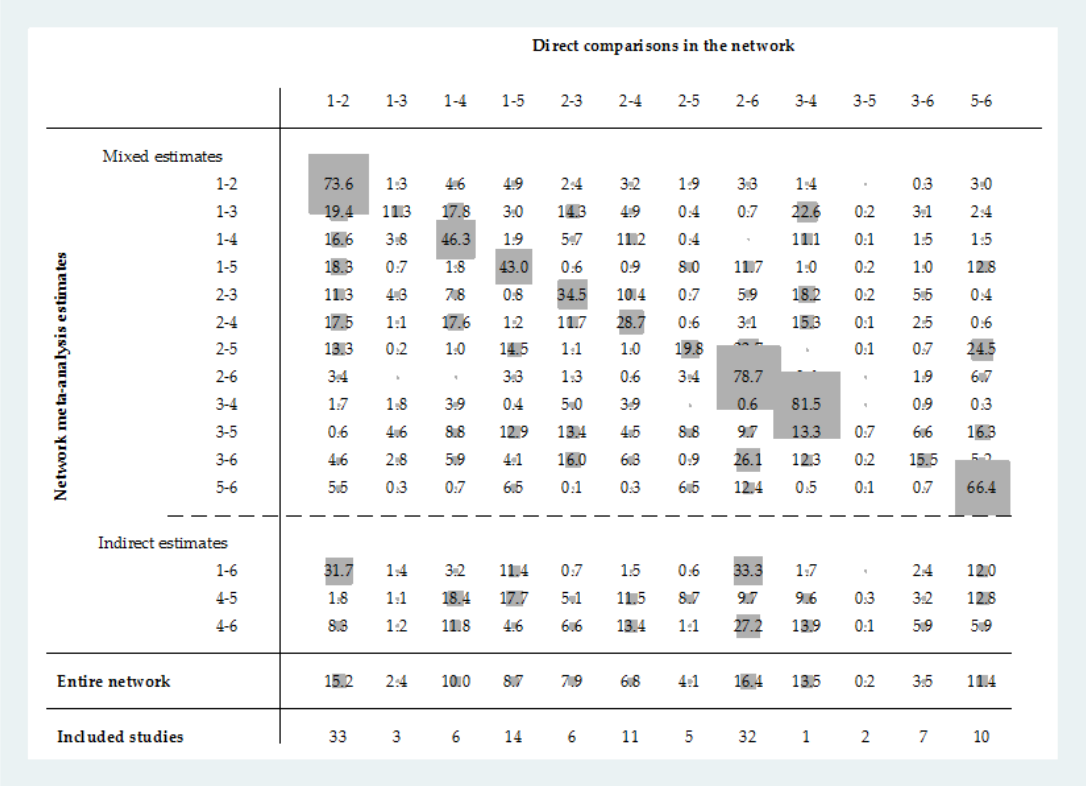
Contribution Plot

The results of the contribution plot indicated the amount of direct, indirect, and mixed evidence that contributed to the overall estimates (See Figure 37). Clearly, direct evidence aided in majority of weight in four comparisons; TAU vs CBT, WL vs CBT, BA vrs NDST, and WL vs EX. Direct evidence made up 73.6%, 78.7%, 81.5, and 66.4% respectively, for these 4 treatment arms. Of the 15 possible comparisons, only three did not have any direct evidence aiding in the overall weight. TAU vs WL, NDST vs EX, and NDST vs WL had no included RCTs examining their comparative effects. It was evident that the NMA estimate for the NDST vs. EX comparison was indirectly informed by all 12 direct comparisons. The estimated weight of these comparisons range from .3% to 18.4%. The most informative direct evidence for NDST vs. EX was TAU vs NDST with an overall contribution of 18.4%. In addition, the NMA estimate for WL vs NDST was indirectly informed by all 12 direct comparisons. Out of the 12 comparisons, the most informative direct evidence came from the WL vs CBT comparison with an overall contribution of 27.2%. The only comparison that was not indirectly informed by all 12 direct comparisons was TAU vs WL. This comparison did not receive any contribution from the BA vs EX comparison.

When examining the weight of informative direct evidence in the entire network, it is clear that the WL vs CBT comparison provided the largest contribution. This comparison provided an overall contribution of 16.4% to the entire network. Furthermore, four other studies also provided over 10% of the direct evidence to the network. These arms included TAU vs CBT (15.2%), BA vs NDST (13.5%), WL vs EX

(11.4%), and TAU vs NDST (10.0%). There were a total of four treatment comparisons which provided less than 5% of the direct evidence to the entire network; these were TAU vs. BA (2.4%), CBT vs EX (4.1%), WL vs BA (3.5%), and BA vs. EX (.2%). Lastly, it is important to note the number of studies that were included in each direct comparison. Noticeably, over half of the studies compared the two control groups to CBT (n=65). Without the TAU-CBT or WL-CBT comparisons, the amount of studies directly comparing two treatment ranged from one (BA vs NDST) to 14 (TAU vs. EX). It is important to note that the stata commands derive the direct estimates through a comparison-specific random effects model. However when there were less than 2 studies, a fixed effects model is employed. Therefore, it is observed that only one comparison had less the 2 studies, BA vs NDST.

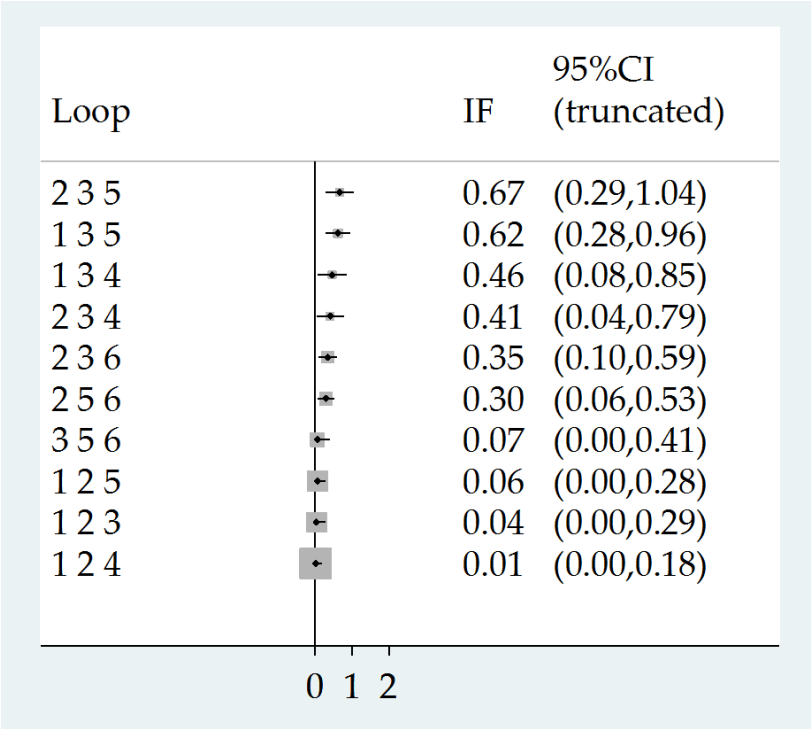
Figure 37: Contribution Plot for NMA



Inconsistency Plot

There were 10 evidence loops found in this network (See Figure 38). The inconsistency factor statistic is the absolute difference between the direct and indirect estimates for one of the comparisons in the loop. The inconsistency factor was calculated based off of a common heterogeneity estimate and loop-specific heterogeneity estimate. When using a common estimate to analyze inconsistency, 6 out of the 10 loops were found to have statistically significant IF values. On the contrary, when loop-specific heterogeneity estimates were used to examine inconsistency, none of the loops experienced statistically significant inconsistency values. Since mixed results were found, depending on the type of heterogeneity estimate used, results of this network must be interpreted with caution.

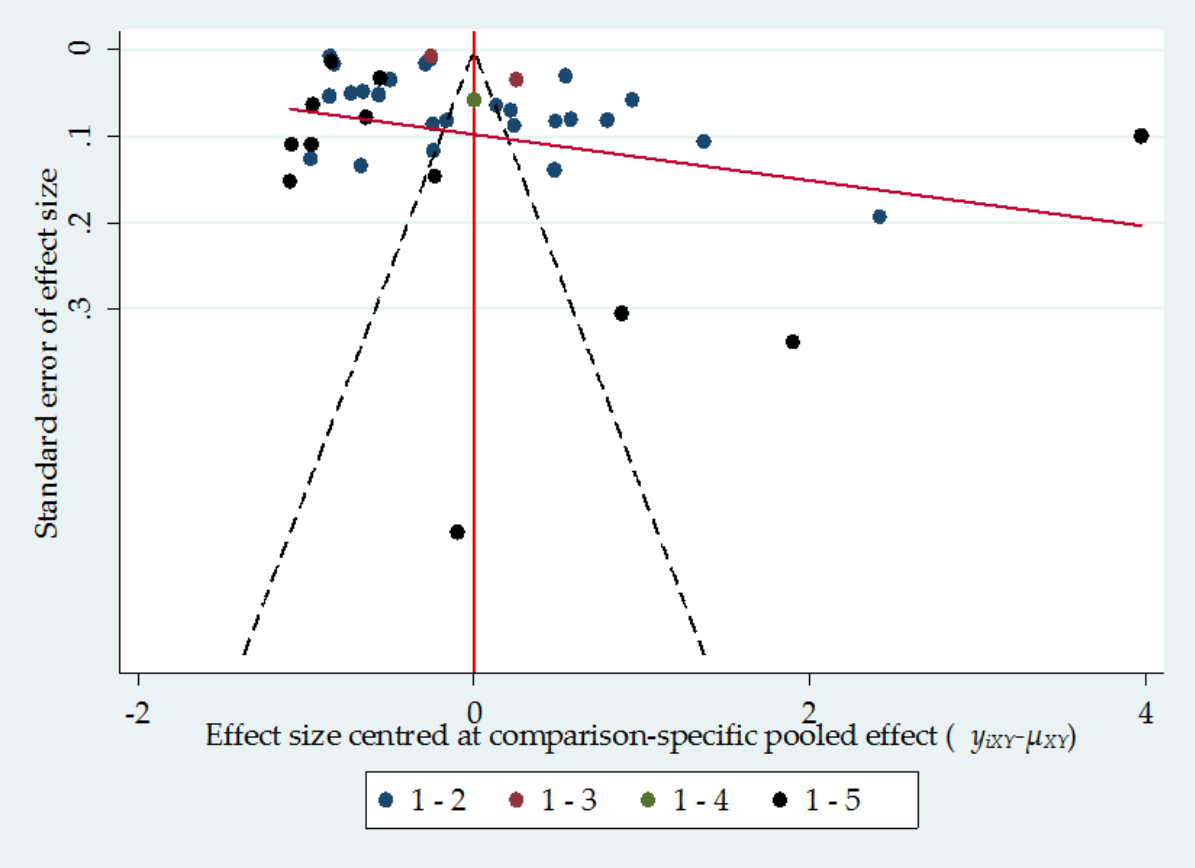
Figure 38: Inconsistency Plot for NMA



Funnel Plot

The comparison-adjusted funnel plot resulted in some asymmetry indicating the possibility of publication bias (See Figure 39). The indication of possible publication bias may help to explain both the heterogeneity and possible inconsistency within the network. The comparison adjusted plot also provided a slight indication of small-study effects, which causes larger effects to be observed in the smaller studies. This plot indicates that small studies tend to show that the active treatments are slightly more effective than their respective comparison-specific weighted average effect.

Figure 39: Funnel Plot for NMA

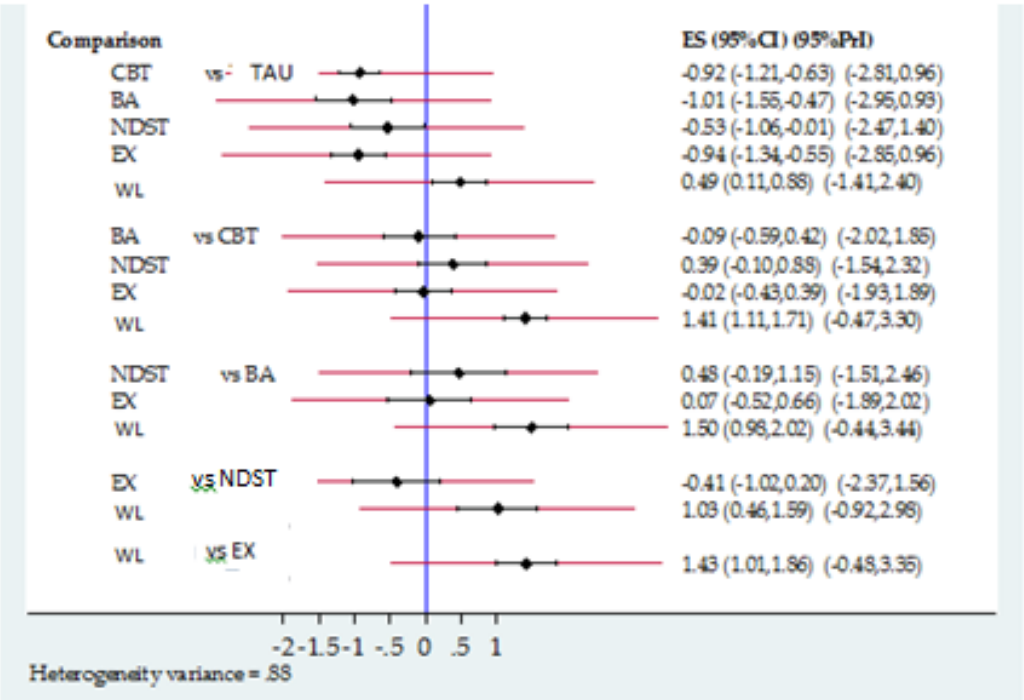


Predictive Interval Plot

Figure 40 presents the estimated effect sizes along with their confidence intervals and corresponding PrI for all comparisons. It is important to note that the estimated between-study variance was .88. Due to this level of heterogeneity, the predictive interval 95% intervals are fairly wide. All of the active treatments produce moderate to large, more beneficial effects then the control. Unfortunately, the PrI was wide enough for all four comparisons that the intervals suggests that in a future study the active treatment could be less effective than a treatment as usual control. The summary of effects comparing two active treatments reveal small between treatment effect sizes between CBT, EX, BA. BA was slightly more efficacious then CBT (SMD=.09). In addition, CBT was marginally less efficacious then EX (SMD=-.02, 95% CI= -.43-.39). Lastly, BA is slightly more efficacious the EX (SMD=.07, 95% CI=-.52-.66). Although very slight differences exist between these three treatment options, the PrI indicate that the outcome of future studies could swing any way. The PrI revealed that when future studies examine the between group effects of any, or all, of these three treatment modalities the outcome could result any of them more efficacious. The estimated effect sizes revealed that NDST produced a moderately less significant effect then the other three treatment modalities. When compared to NDST, CBT produced a small to moderately more therapeutic effect (SMD=.39, 95% CI= -.10-.88), BA produced a moderate, more therapeutic effect (SMD=.48, 95% CI= -.19-1.15), and EX produced a moderately more therapeutic effect (SMD=.41). Again, due to the high level of variance, the PrI indicated that there was a chance that future studies could show that NDST is more effective than EX, BA, or CBT. This possibility is less likely for future studies comparing EX, BA, and CBT, but it is still

a distinct possibility. As expected, the treatment as usual control was found to provide a moderate therapeutic effect when compared to a waitlist control.

Figure 40: Predictive Interval Plot for NMA



Ranking Plots

The ranking plot, presented in Figure 41, indicates the relative probability that each treatment would receive a certain ranking. Clearly, behavioral activation therapy had the highest probability to be ranked first, at 49.5%. Cognitive behavioral therapy was most likely to be ranked second, at 41.5%. Lastly, non-directive supportive therapy had an 81.6% probability to be ranked the least efficacious active treatment. As expected, the treatment as usual control had a 97.3% chance to be the fifth most efficacious treatment, while the waitlist control had a 99.3% chance to be ranked last. Based on the SUCRA

values, the mean rank of each treatment was calculated and presented in Appendix F. Behavioral activation therapy has a mean rank of 1.9 out of the 5 therapies. A tie occurred for the second highest mean rank. Both EX and CBT had a mean rank of 2.2. This occurred because of CBTs high likelihood of being ranked second, and exercises even probability to be ranked 1st, 2nd, or 3rd. The results of the mean rank are supported by the fact there was only a .02 effect size, favoring exercise, between CBT and EX. Lastly, NDSTs' relative mean treatment ranking was 3.8. The mean rankings reveal that BA, CBT, and EX all have relatively close rankings, with the difference between first and third only .3.

Figure 41: Ranking Plot for NMA

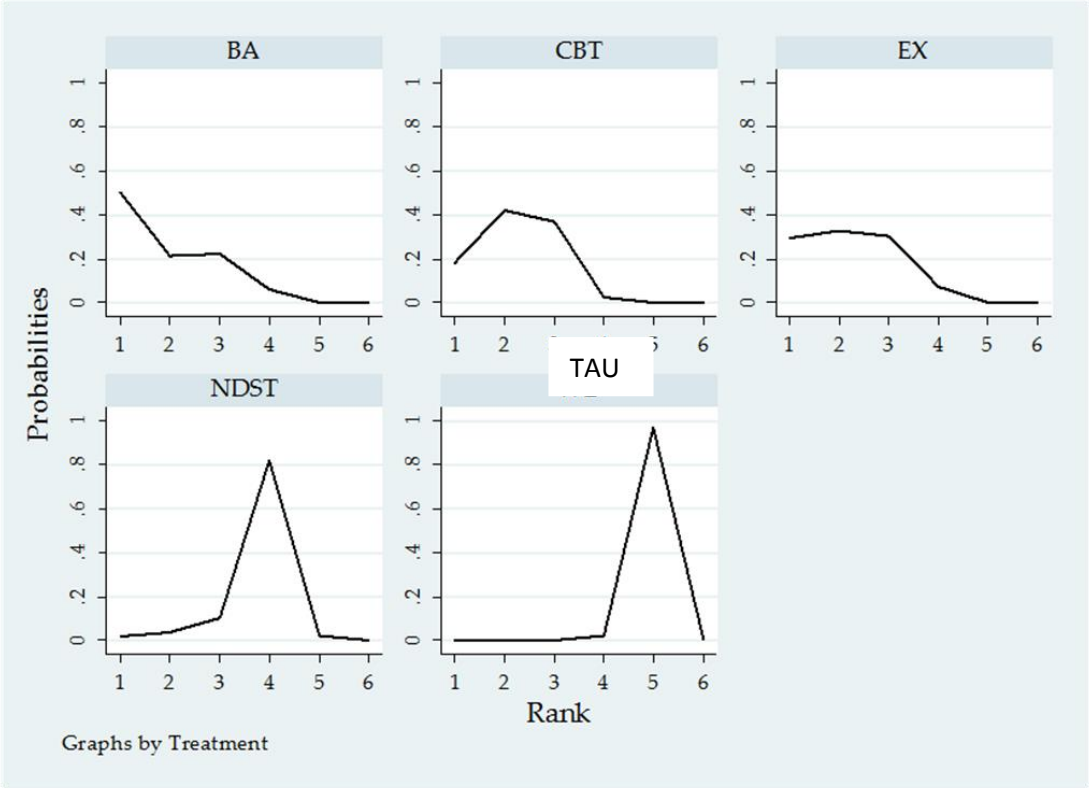
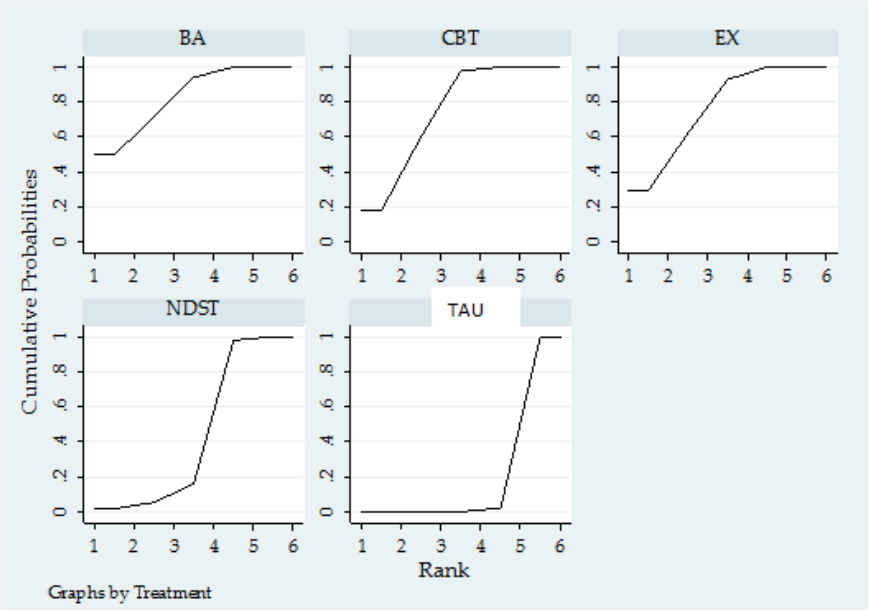


Figure 42 presents a cumulative ranking plot for each of the treatment modalities. Again, it is evident that BA had the highest probability of being ranked first. Interestingly, BA had a 93.8% chance of being ranked either first, second, or third. Similarly, CBT had a 97.2% chance that it would rank within the top three treatments. It had the highest probability of being ranked second, but CBT had an 18.7% chance of being ranked first. Finally, as with the other two treatments, exercise has a 92.5% chance of being ranked in the top three efficacious treatment modalities. Exercise did not have the highest probability for any of the rankings, having approximately a 30% probability to be ranked each first, second, or third. Exercise has a 29.7% chance of being ranked first. As shown in Figure 42, NDST clearly is the fourth most efficacious treatment. Non-directive supportive therapy only had only a 16.3% chance ranking in the top three. Lastly, as expected, the two controls had a very minute probability that they would be ranked above fifth or sixth.

Figure 42: Cumulative Ranking Plot for NMA



Waitlist Network Meta-analysis

In an to attempt to decrease heterogeneity, a network stratified by the two controls was performed. The literature search identified 123 eligible reports by reviewing full text studies. Only 64 studies were included in this meta-analysis due to the following reasons, insufficient statistics or incorrect control groups in rejected studies. Sixty four trials involving 5,813 patients provided adequate data for depression outcomes. Detailed results and code are given in Appendices E and F.

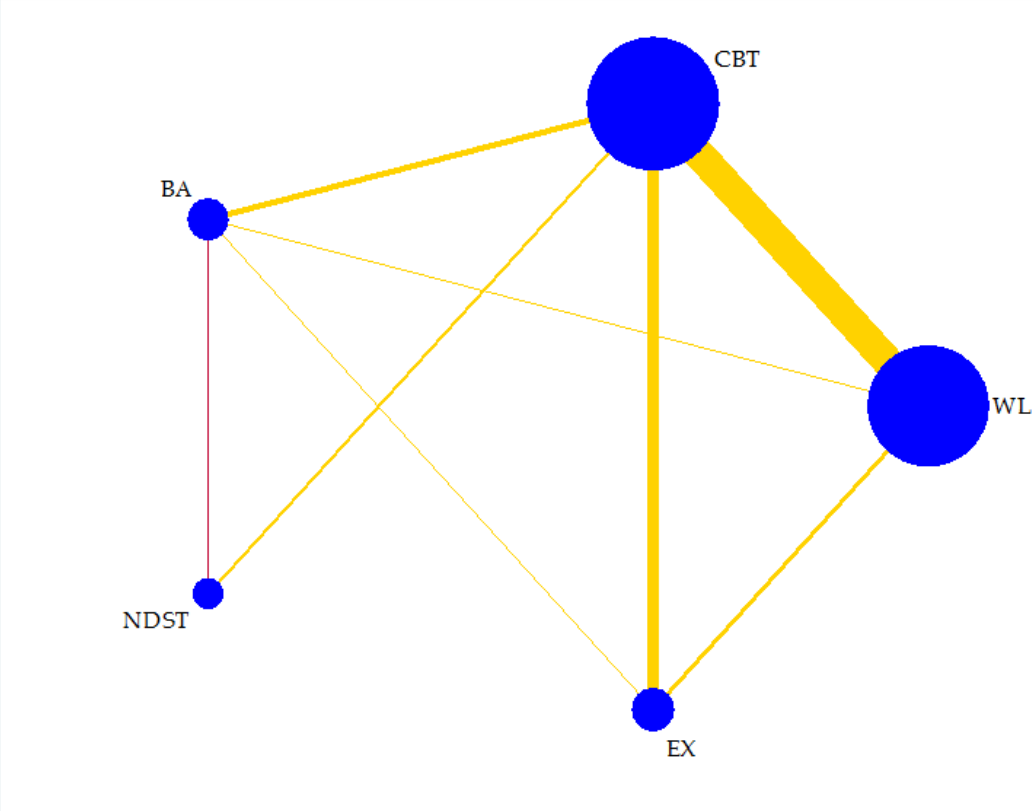
Network Plot

In Figure 43, the network plot for efficacy depression treatment network is presented. The nodes were weighted according to the number of studies, including each respective intervention. The figure indicated that cognitive behavioral therapy was the most frequent comparator across studies, with the waitlist control coming in a close second. The lines between each node, and the weight of each line, represented the number of RCTs directly comparing those two treatment options. As indicated by the plot, the majority of the included studies (n=32) were compared CBT to the waitlist control. The remainder of the number of included RCT's varied according to treatment arm. Overall, there was only two treatment comparisons that did not have any direct evidence; these included supportive therapy versus a waitlist control and supportive therapy versus physical activity.

Another important aspect in meta-analysis is the quality of the studies. In order to present the risk of bias in each study, each direct comparison was rated according to the determined risk of bias. To analyze risk of bias, studies were evaluated for their blinding

procedures, allocation concealment, and reporting of data. After evaluating the risk of bias, each direct comparison study was given a rating of 1, 2, or 3, which corresponds to a low, moderate, and high risk of bias respectively. It was evident in the network plot that the majority of direct evidence had a moderate risk of bias. Only one direct between comparison had an overall high risk of bias, probably because it was the only treatment arm that had one study for direct evidence.

Figure 43: Network Plot for Waitlist NMA

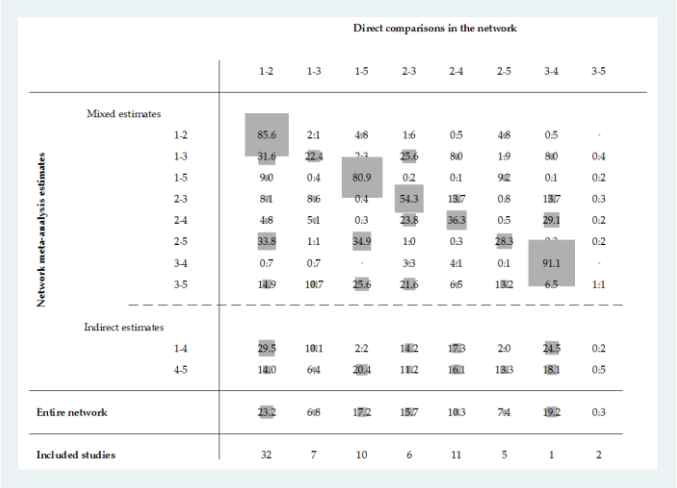


Contribution Plot

The results of the contribution plot indicate the amount of direct, indirect, and mixed evidence that contributed to the overall estimates (See Figure 44). Clearly, direct evidence aided in majority of weight in four comparisons; WL vs CBT, WL vs EX, CBT vs BA, and BA vs NDST. Direct evidence made up 85.6%, 80.9%, 54.3%, and 91.1% respectively, for these 4 treatment arms. Of the 10 possible comparisons, only 2 did not have any direct evidence aiding in the overall weight. Both WL vs NDST and NDST vs EX had no included RCTs examining their comparative effects. It was evident that the NMA estimate for the WL vs NDST comparison was indirectly informed by all eight direct comparisons. The estimated weight of these comparisons ranged from .2% to 29.5%. The most informative direct evidence for WL vs NDST is WL vs CBT with an overall contribution of 29.5%. Four other treatment arms contributed over 10% of the weight for the indirect WL-NDST comparison. These arms included WL vrs BA (10.1%), CBT vs BA (14.2%), CBT vs NDST (17.3%), and BA vs NDST (24.5%). Similarly, the NMA estimate for the NDST vs EX comparison is indirectly informed by all eight direct comparisons. The estimated weight of these comparisons ranged from .5% to 20.4%. The most informative direct evidence for EX vs NDST is WL vs EX with an overall contribution of 20.4%. Five other treatment arms contributed over 10% of the weight for the indirect EX-NDST comparison. These arms included WL vs CBT (14.0%), CBT vs BA (11.2%), CBT vs NDST (16.1%), CBT vs EX (13.3%), and BA vs NDST (18.1%).

When examining the weight of informative direct evidence in the entire network, it was clear that the WL vs CBT comparison provided the largest contribution. This comparison provided an overall contribution of 23.2% to the entire network. Further, four other studies also provide over 10% of the direct evidence to the network. These arms included BA vs NDST (19.2%), WL vs EX (17.2%), CBT vs BA (15.7%), and CBT vs NDST (10.3%). The only study which provided under 5% of the direct evidence to the entire network was BA vrs EX, which only provided .3%. Lastly, it is important to note the number of studies that were included in each direct comparison. Noticeably, there were over 20 more studies directly comparing the waitlist group to CBT (n=32) then the next highest. Without the WL-CBT comparisons, the number of studies directly comparing two treatments ranged from one (BA vs NDST) to 11 (CBT vs NDST). It is important to note that the stata commands derived the direct estimates through a comparison-specific random effects model. However when there are less than 2 studies, a fixed effects model was employed. Therefore, it was observed that only one comparison had less the 2 studies, BA vs NDST.

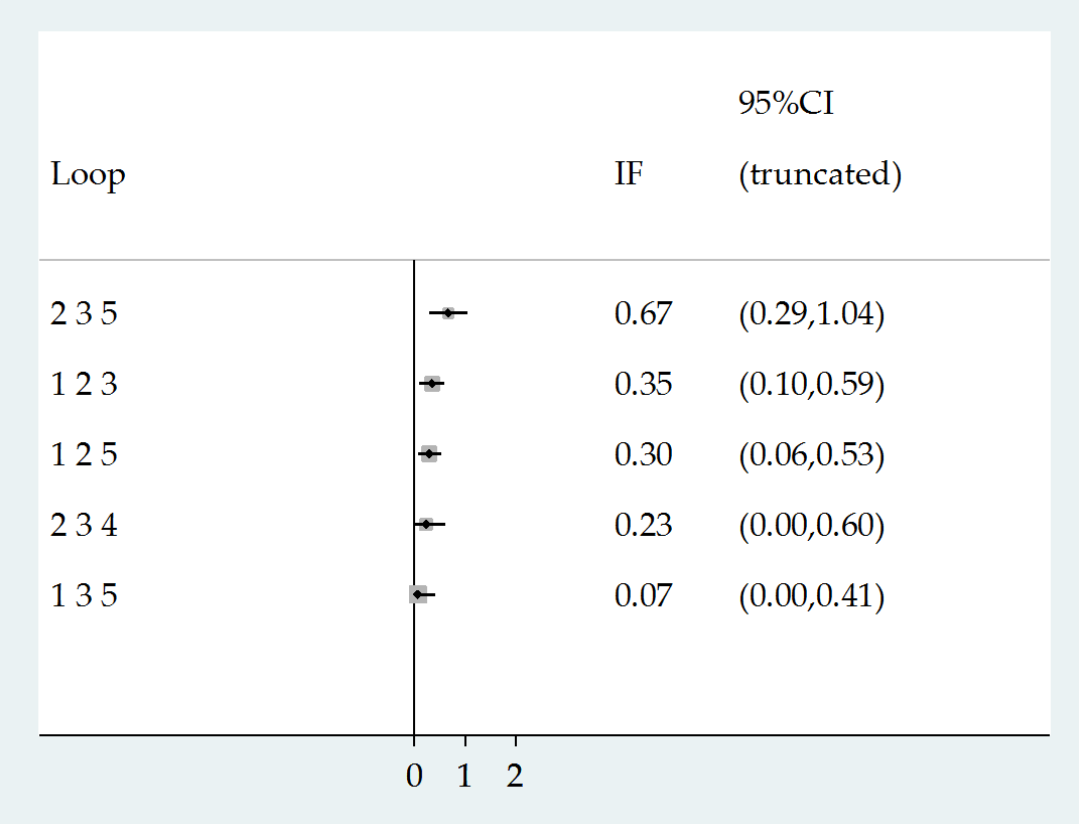
Figure 44: Contribution Plot for Waitlist NMA



Inconsistency Plot

There were five evidence loops found in the WL NMA (See Figure 45). The inconsistency factor statistic is the absolute difference between the direct and indirect estimates for one of the comparisons in the loop. Three out of the five loops showed statistically significant inconsistency. The only two loops that did not result in statistically significant inconsistency were 2-3-4 and 1-3-5. The presence of statistically significant inconsistency raised concerns regarding the validity of the results. Thus, the results of this network must be interpreted with caution.

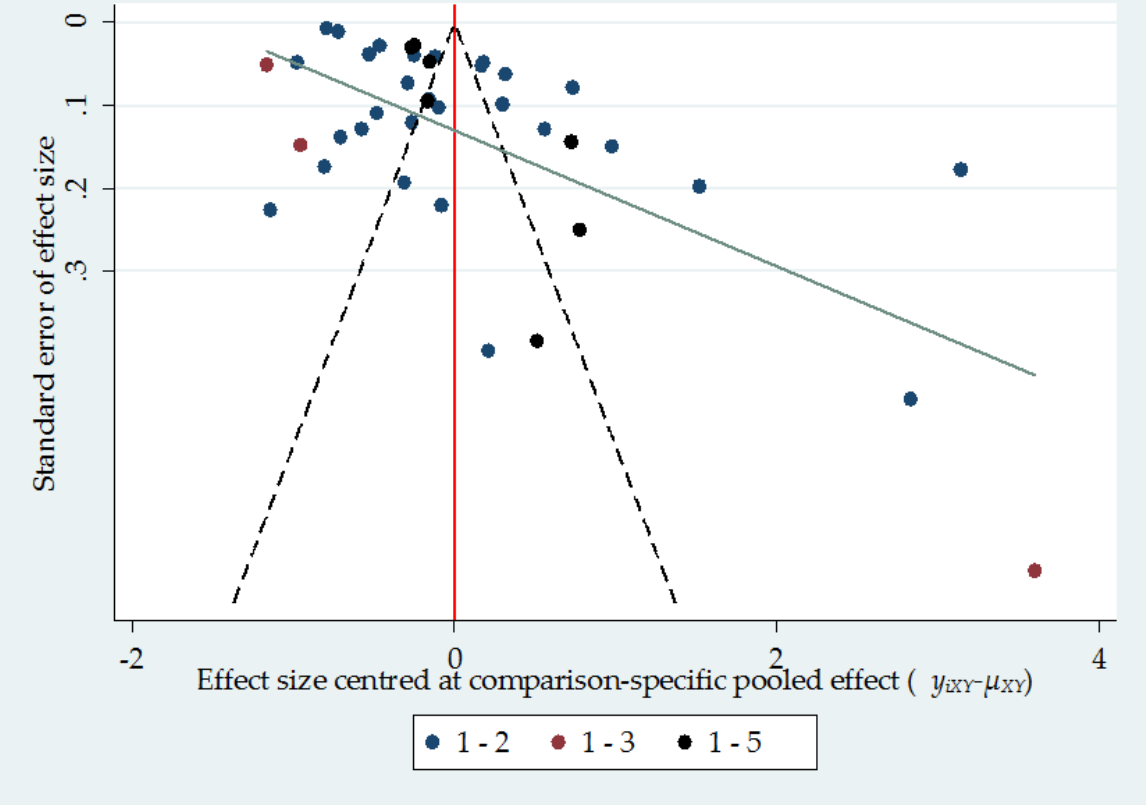
Figure 45: Inconsistency Plot for WL NMA



Funnel Plot

The comparison-adjusted funnel plot resulted in some asymmetry indicating the possibility of publication bias (See Figure 46). The indication of possible publication bias may help to explain both the heterogeneity and inconsistency within the network. The comparison adjusted plot also provided an indication of small-study effects, which causes larger effects to be observed in the smaller studies. This plot indicated that small studies tend to show that the active treatments are more effective than their respective comparison-specific weighted average effect.

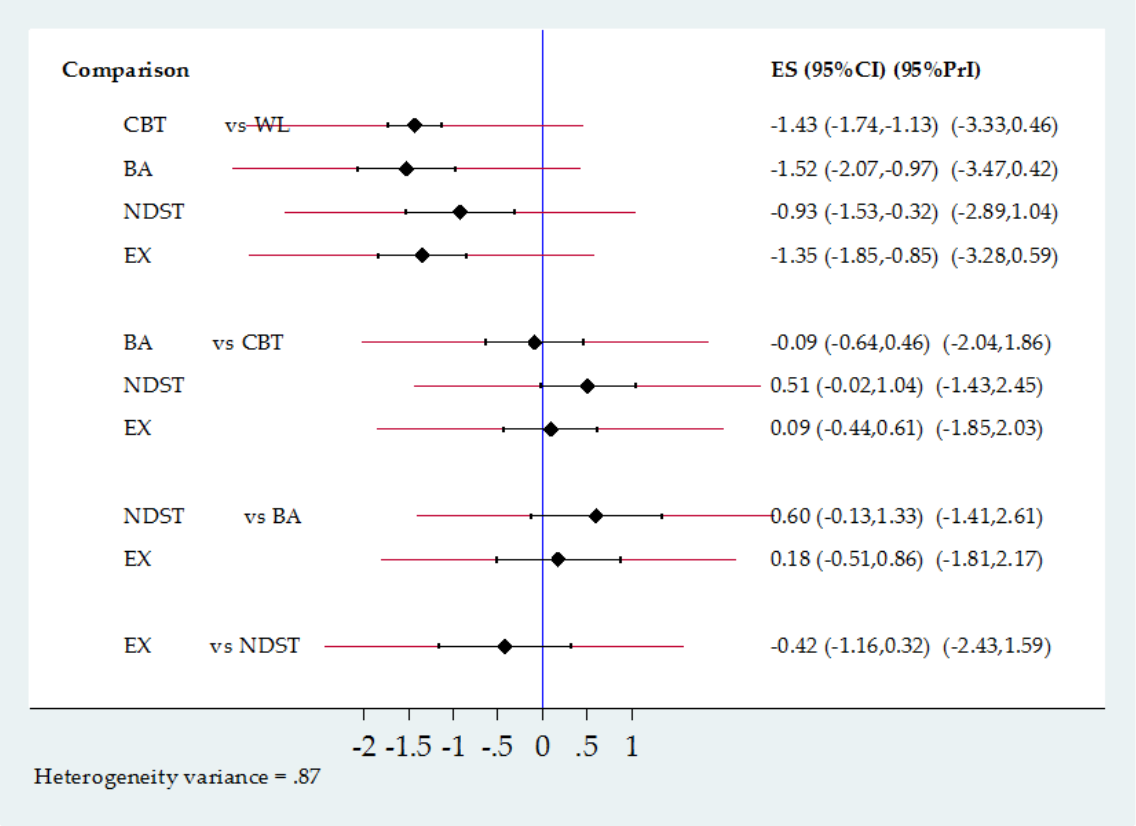
Figure 46: Funnel Plot for WL NMA



Predictive Interval Plot

Figure 47 presents the estimated effect sizes along with their confidence intervals and corresponding PrI for all comparisons. It is important to note that the estimated between-study variance was .87. Due to this level of heterogeneity, the predictive interval 95% intervals were fairly wide. All of the active treatments produced large, more beneficial effects then a placebo. Unfortunately, the PrI is wide enough for all four comparisons that the intervals suggests that in a future study the active treatment could be less effective than a waitlist control. The summary of effects comparing two active treatments revealed small between treatment effect sizes between CBT, EX, and BA. BA was slightly more efficacious then CBT (SMD=.09, 95% CI= -.64-.46). In addition, BA was slightly more efficacious then EX (SMD=.18, 95% CI= -.51-.86). Lastly, CBT was marginally more efficacious the EX (SMD=.09, 95% CI= -.44-.61). Although these slight differences existed between these three treatment options, the PrI indicated that the outcome of future studies could swing any way. The PrI reveal that when future studies examine the between group effects of any, or all, of these three treatment modalities the outcome could determine any of them more efficacious. The estimated effect sizes revealed that NDST produced a moderately less significant effect then the other three treatment modalities. When compared to NDST, CBT produced a moderately more therapeutic effect (SMD=.51, 95% CI= -.02-1.04), BA produced a moderate to large more therapeutic effect (SMD=.60, 95% CI= -.13-1.33), and EX produced a small to moderate more therapeutic effect (SMD=.42). Again, due to the high level of variance, the PrI indicated that there was a chance that future studies could show that NDST is more effective than EX, BA, or CBT. This possibility is less likely for future studies comparing EX, BA, and CBT, but it is still a distinct possibility.

Figure 47: Predictive Interval Plot for WL NMA



Ranking Plots

The ranking plot, presented in Figure 48, indicates the relative probability that each treatment would receive a certain ranking. Clearly, behavioral activation therapy had the highest probability to be ranked first, at 53.1%. Cognitive behavioral therapy is most likely to be ranked second, at 47.1%. Exercise had the highest likelihood of being ranked third, at 41.1%. Lastly, supportive counseling has a 82.8% probability to be ranked the least efficacious active treatment. As expected, the control (waitlist) had a 99.9% chance to be the fifth most efficacious treatment. Based on the SUCRA values, the mean rank of each treatment was calculated and presented in Appendix F. Behavioral

activation therapy had a mean rank of 1.7 out of the 5 therapies. The second highest average was CBT at 2.0. Exercise's mean rank was close, averaging a mean treatment ranking of 2.5. Lastly, NDSTs' relative mean treatment ranking was 3.8. The mean rankings revealed that BA, CBT, and EX all have relatively close rankings, with the difference between first and third only .9.

Figure 48: Ranking Plot for WL NMA

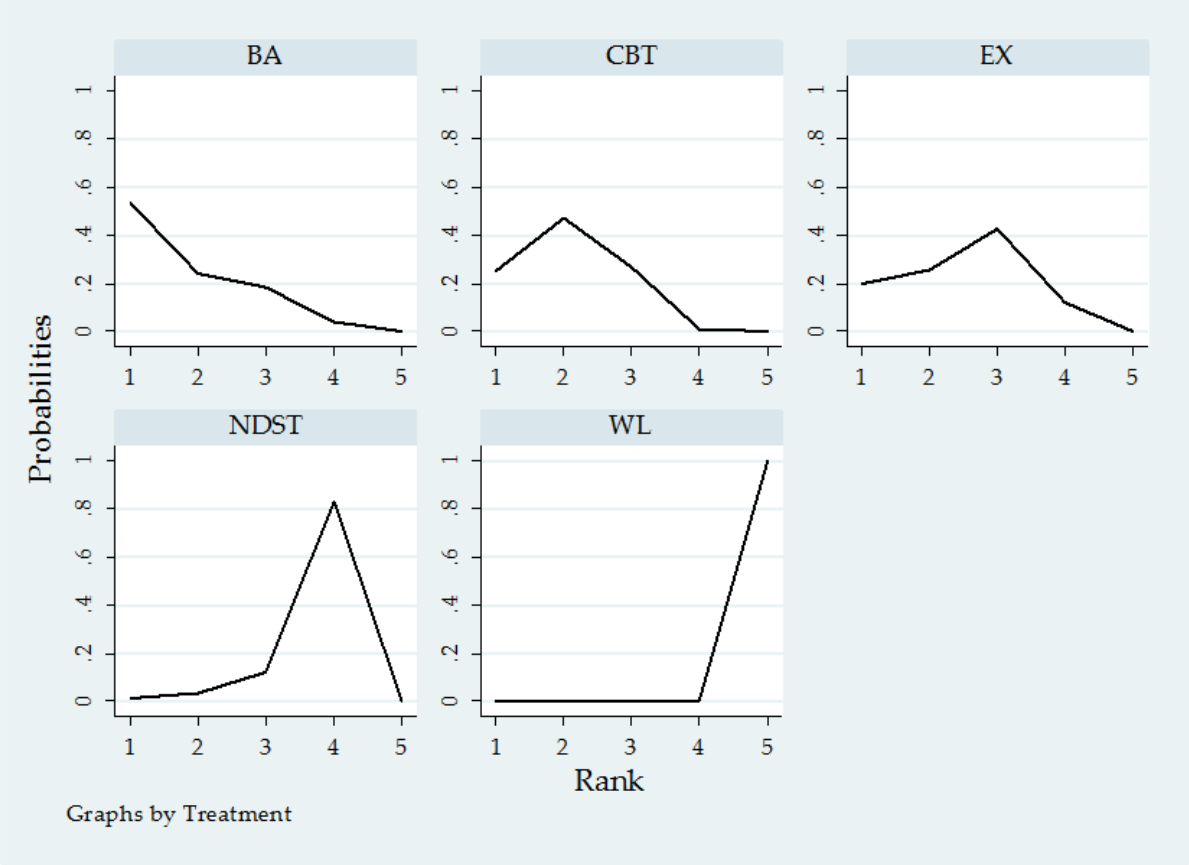
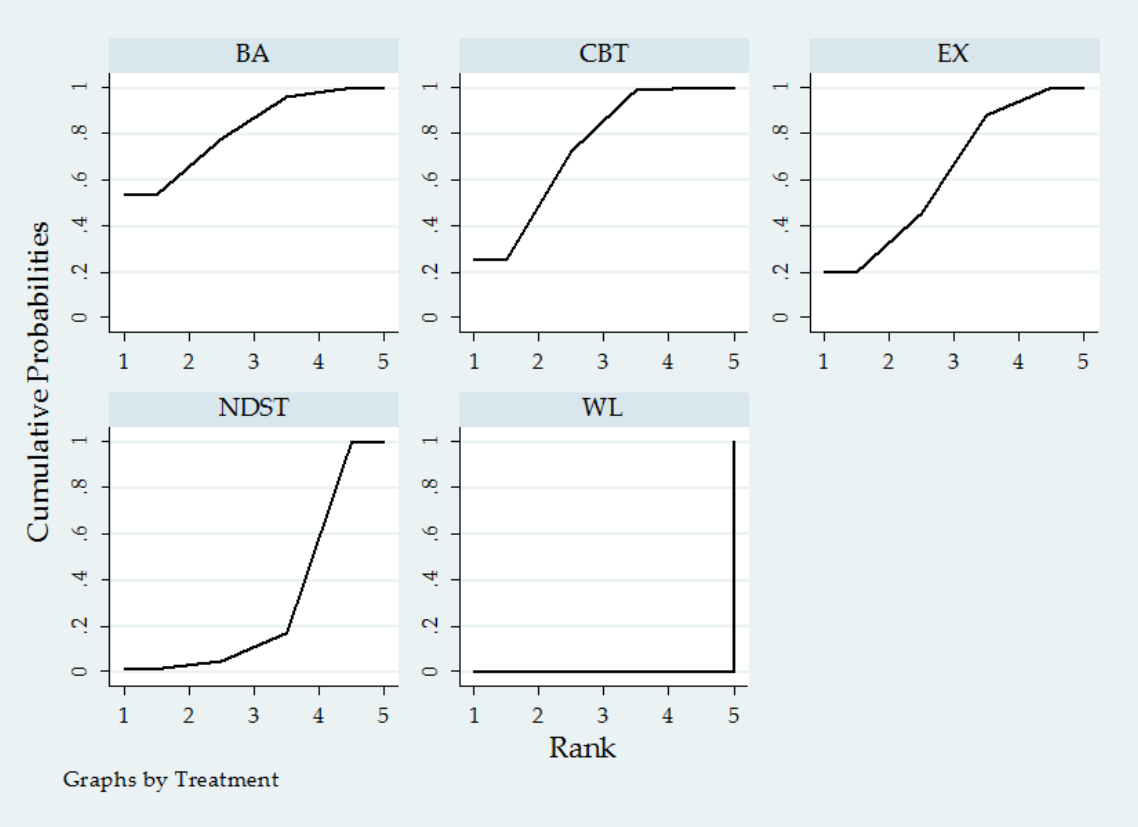


Figure 49, presents a cumulative ranking plot for each of the treatment modalities. Again, it is evident that BA had the highest probability of being ranked first. Interestingly, BA has a 96.5% chance of being ranking either first, second, or third.

Similarly, CBT has a 99.0% chance that it would rank within the top three treatments. It had the highest probability of being ranked second, but CBT did have a 25.3% chance of being ranked first. Finally, as with the other two treatments, exercise has a 87.4% chance of being ranked in the top three most efficacious treatment modalities. Although it had the highest probability of being ranked second, exercise did have a 20.4% chance of being the most efficacious treatment out of the four. As shown in Figure 49, NDST clearly is the fourth most efficacious treatment. Non-directive supportive therapy only has a 17.1% chance of ranking in the top three.

Figure 49: Cumulative Ranking Plot for WL NMA



Treatment as Usual Network Meta-analysis

The literature search identified 123 eligible reports by reviewing full text studies. Only 65 studies were included in this meta-analysis due to the following reasons, insufficient statistics or incorrect control group in the rejected studies. Sixty-five trials involving 7,124 patients provided adequate data for depression outcomes. Detailed results and code are given in Appendices E and F.

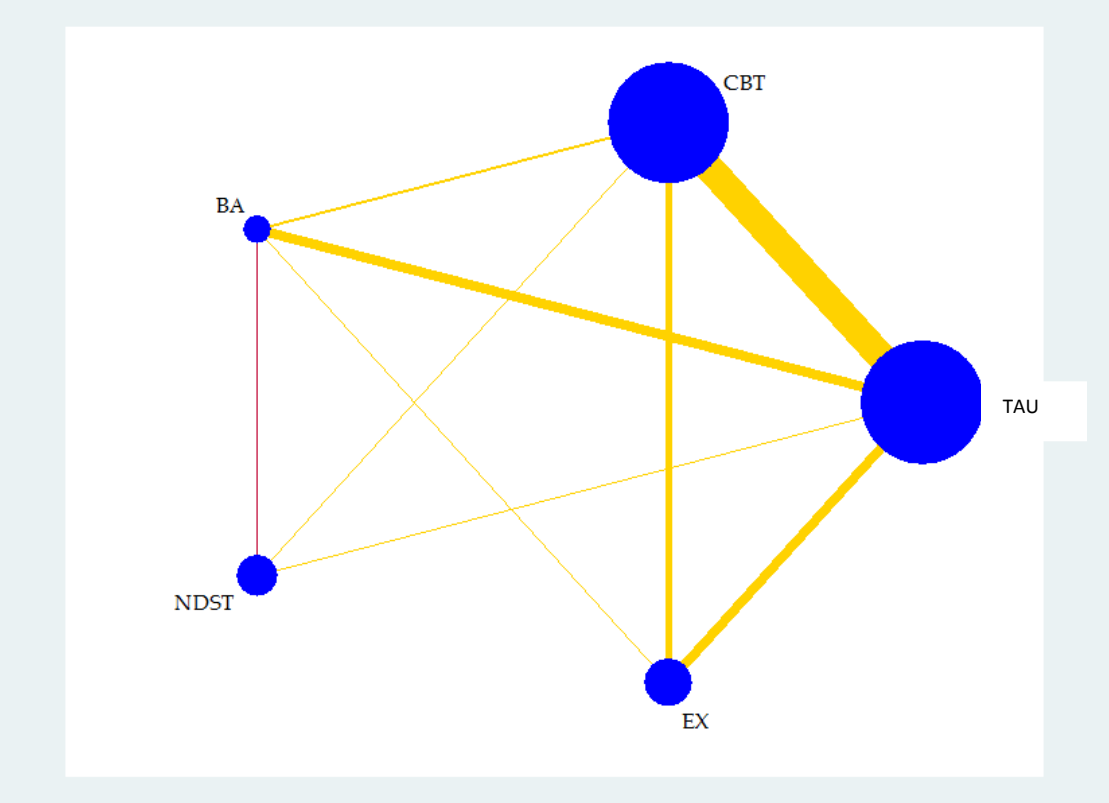
Network Plot

In Figure 50, the network plot for efficacy depression treatment, with a usual care control network is presented. The nodes were weighted according to the number of studies, including each respective intervention. The figure indicated that both cognitive behavioral therapy and the treatment as usual control were the most frequent comparators across studies. The lines between each node, and the weight of each line, represent the number of RCTs directly comparing those two treatment options. As indicated by the plot, the majority of the included studies (n=33) were comparing CBT to the treatment as usual control. The remainder of the number of included RCT's varied according to treatment arm. Overall, there was only one treatment comparison that did not have any direct evidence. This treatment comparison was NDST vs.EX.

Another important aspect in meta-analysis is the quality of the studies. In order to present the risk of bias in each study, each direct comparison was rated according to the determined risk of bias. In order analyze risk of bias, studies were evaluated on their blinding procedures, allocation concealment, and reporting of data. After evaluating the risk of bias, each direct comparison study was given a rating of 1, 2, or 3, which

corresponded to a low, moderate, and high risk of bias respectively. It was evident in the network plot that the majority of direct evidence had a moderate risk of bias. Only one direct between comparison had an overall high risk of bias. One explanation for this may be that the only treatment arm with high risk of bias was the only treatment arm that had one study for direct evidence.

Figure 50: Network Plot for TAU NMA



Contribution Plot

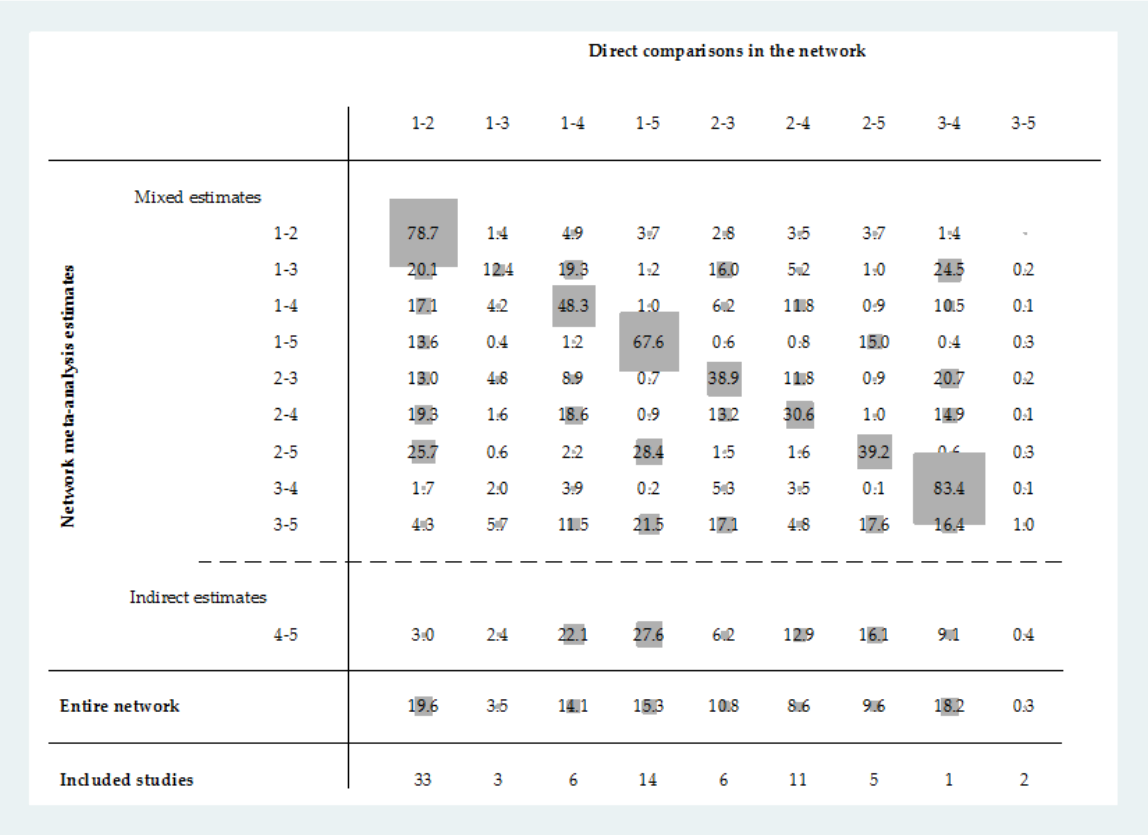
The results of the contribution plot indicate the amount of direct, indirect, and mixed evidence that contributes to the overall estimates (See Figure 51). Clearly, direct evidence aided in majority of weight in three comparisons; TAU vs CBT, TAU vs EX,

and BA vs NDST. Direct evidence made up 78.7%, 67.6%, and 53.4% respectively, for these four treatment arms. Of the 10 possible comparisons, only one did not have any direct evidence aiding in the overall weight. NDST vs EX had no included RCTs examining their comparative effects. It was evident that the NMA estimate for the NDST vs. EX comparison was indirectly informed by all nine direct comparisons. The estimated weight of these comparisons ranged from .4% to 27.6%. The most informative direct evidence for NDST vs. EX is TAU vs EX with an overall contribution of 27.6%. Only three other treatment arms contributed over 10% of the weight for the indirect WL-NDST comparison. These arms included TAU vs NDST (22.1%), CBT vs NDST (12.9%), and BA vs NDST (18.2%).

When examining the weight of informative direct evidence in the entire network, it was clear that the TAU vrs CBT comparison provided the largest contribution. This comparison provided an overall contribution of 19.6% to the entire network. Further, four other studies also provided over 10% of the direct evidence to the network. These arms included BA vs NDST (18.2%), TAU vs EX (15.3%), TAU vs. NDST (14.1%), and CBT vs BA (10.5%). There were a total of two studies which provided under 5% of the direct evidence to the entire network; these were TAU vs. BA (3.5%) and BA vs. EX (.3%). Lastly, it is important to note the number of studies that were included in each direct comparison. Notably, there were over 15 more studies directly comparing the treatment as usual group to CBT (n=33) than the next highest (TAU vs. EX (n=14)). Without the TAU-CBT comparisons, the number of studies directly comparing two treatments ranged from one (BA vrs NDST) to 14 (TAU vs. EX). It is important to note that the stata commands derive the direct estimates through a comparison-specific random effects

model. However when there are less than 2 studies, a fixed effects model is employed. Therefore, it is observed that only one comparison had less the two studies, BA vs NDST.

Figure 51: Contribution Plot for TAU NMA

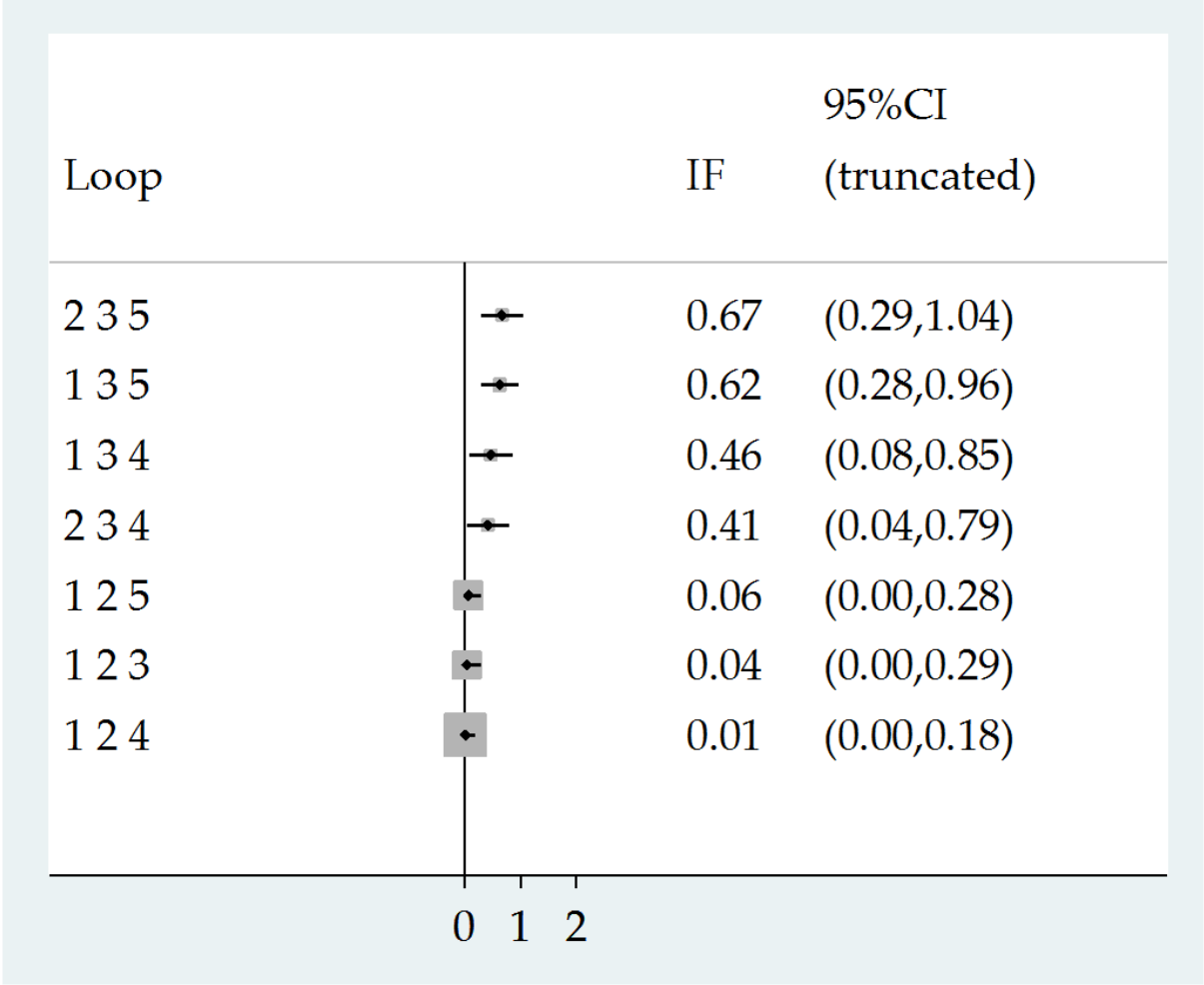


Inconsistency Plot

There were seven evidence loops found in the TAU NMA (See Figure 52). The inconsistency factor statistic was the absolute difference between the direct and indirect estimates for one of the comparisons in the loop. The inconsistency factor was calculated based on a common heterogeneity estimate and loop-specific heterogeneity estimate.

When using a common estimate to analyze inconsistency, four out of the seven loops were found to have statistically significant IF values. On the contrary, when loop-specific heterogeneity estimates were used to examine inconsistency, none of the loops experienced statistically significant inconsistency values. Since mixed results were found, depending on the type of heterogeneity estimate used, results of this network must be interpreted with caution.

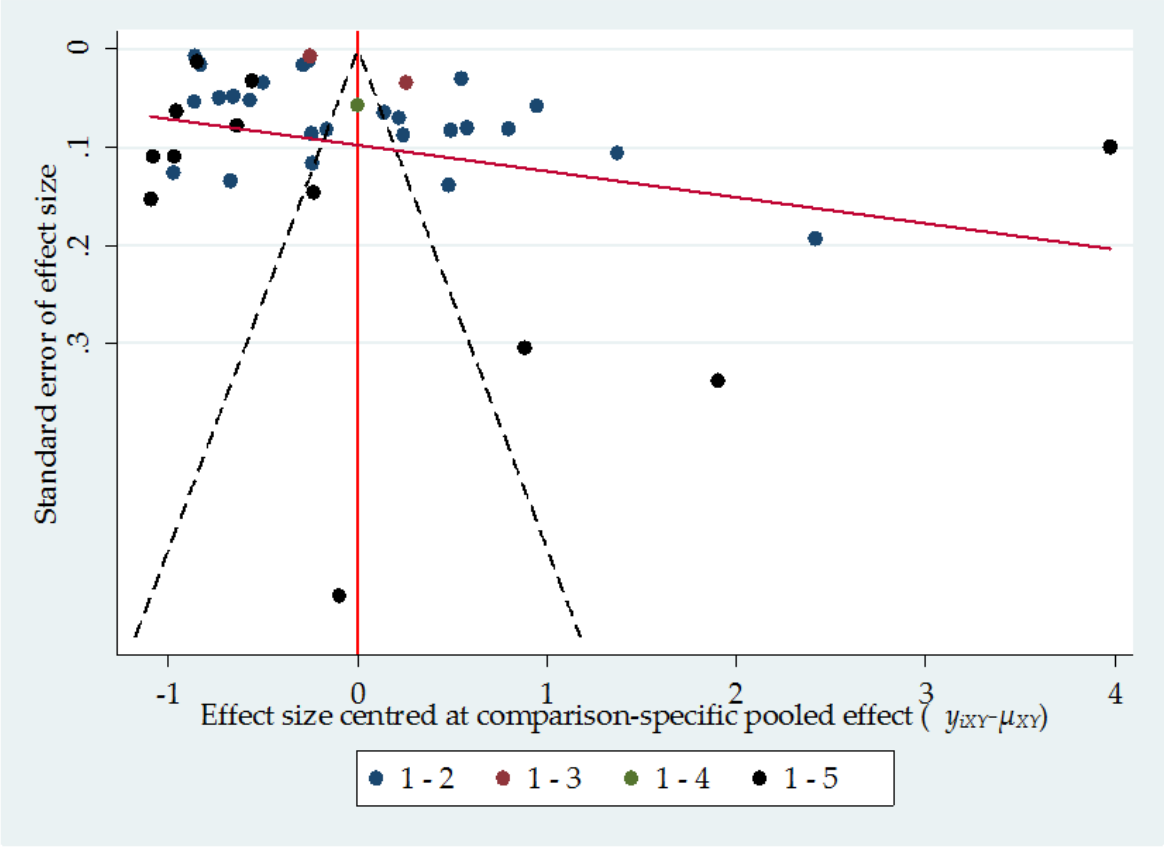
Figure 52: Inconsistency Plot for TAU NMA



Funnel Plot

The comparison adjusted funnel plot resulted in some asymmetry, indicating the possibility of publication bias (See Figure 53). The indication of possible publication bias may help to explain both the heterogeneity and possible inconsistency within the network. The comparison adjusted plot also provided a slight indication of small-study effects, which causes larger effects to be observed in the smaller studies. This plot indicates that small studies tend to show the active treatments are slightly more effective than their respective comparison-specific weighted average effect.

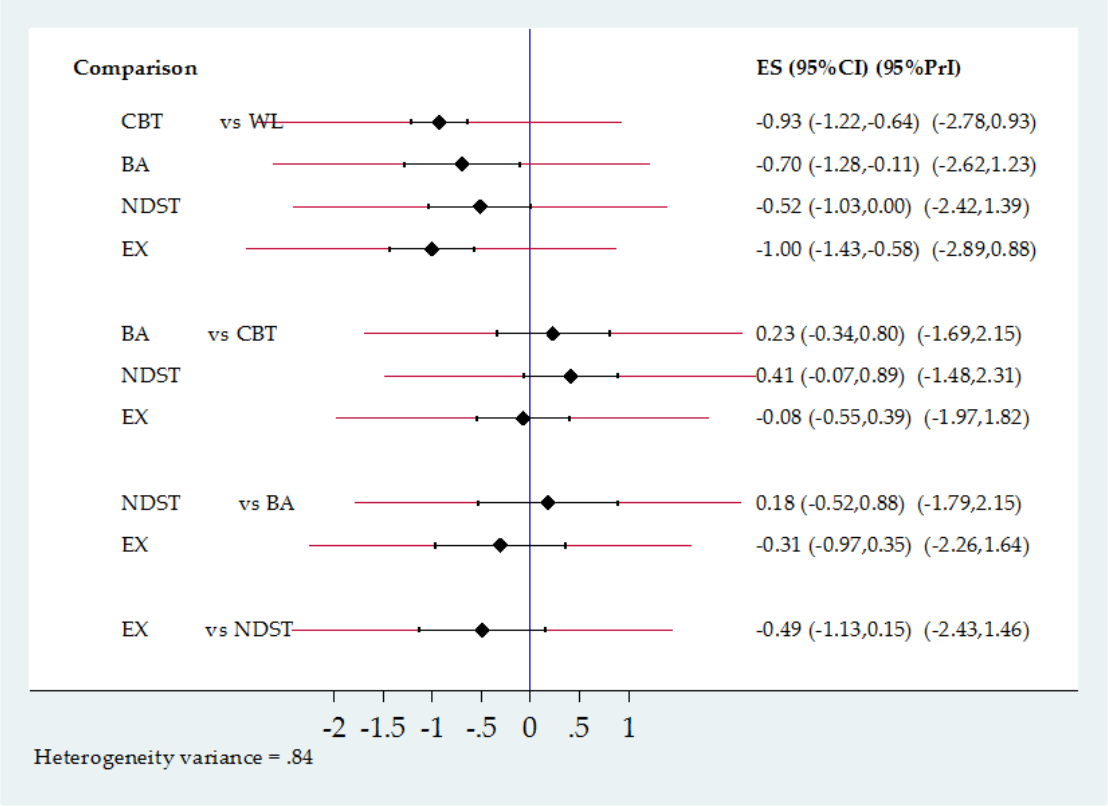
Figure 53: Funnel Plot for TAU NMA



Predictive Interval Plot

Figure 54 presents the estimated effect sizes along with their confidence intervals and corresponding PrI for all comparisons. It is important to note that the estimated between-study variance was .84. Due to this level of heterogeneity, the predictive interval 95% intervals were fairly wide. All of the active treatments produce moderate to large, more beneficial effects then the control. Unfortunately, the PrI is wide enough for all 4 comparisons that the intervals suggests that in a future study the active treatment could be less effective than a treatment as usual control. The summary of effects comparing two active treatments reveal small between treatment effect sizes between CBT, EX, BA. CBT is slightly more efficacious then BA (SMD=.23, 95% CI= -.34-.80). In addition, CBT is marginally less efficacious then EX (SMD=-.08, 95% CI= -.55-.39). Lastly, EX is slightly more efficacious the BA (SMD=.31). Although these slight differences exist between these three treatment options, the PrI indicates that the outcome of future studies could be indeterminate. The PrI revealed that when future studies examine the between group effects of any, or all, of these three treatment modalities the outcome could find any of them more efficacious. The estimated effect sizes revealed that NDST produced a moderately less significant effect then the other three treatment modalities. When compared to NDST, CBT produced a small to moderately more therapeutic effect (SMD=.41, 95% CI= -.07-.89), BA produced a small, more therapeutic effect (SMD=.18, 95% CI= -.52-.88), and EX producd a moderately more therapeutic effect (SMD=.49). Again, due to the high level of variance, the PrI indicated that there was a chance that future studies could show that NDST is more effective than EX, BA, or CBT. This possibility is less likely than future studies comparing EX, BA, and CBT, but it is still a distinct possibility.

Figure 54: Predictive Interval Plot for TAU NMA



Ranking Plots

The ranking plot, presented in Figure 55, indicates the relative probability that each treatment would receive a certain ranking. Clearly, exercise has the highest probability to be ranked first, at 55.9%. Cognitive behavioral therapy is most likely to be ranked second at 51.0%. Behavioral activation therapy has the highest likelihood of being ranked third at 43.0%. Lastly, supportive counseling has an 64.0% probability to be ranked the least efficacious active treatment. As expected, the control (treatment as usual) had a 96.7% chance to be the fifth most efficacious treatment. Based on the SUCRA values, the mean rank of each treatment is calculated and presented in Appendix F.

Exercise has a mean rank of 1.6 out of the 5 therapies. The second highest average was CBT at 1.9. Behavioral activation therapy's mean rank was close as well, averaging a mean treatment ranking of 29. Lastly, NDSTs' relative mean treatment ranking was 3.6. The mean rankings reveal that BA, CBT, and EX all have relatively close rankings, with the difference between first and third only 1.3.

Figure 55: Ranking Plot for TAU NMA

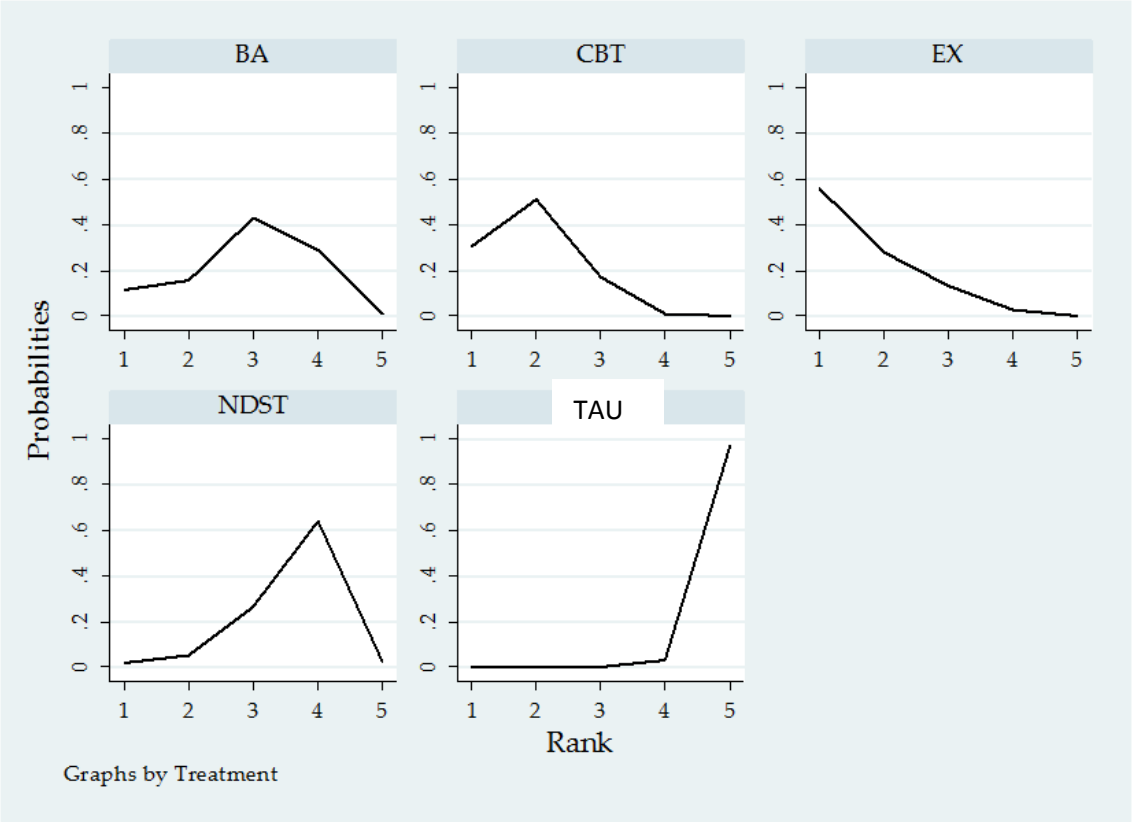
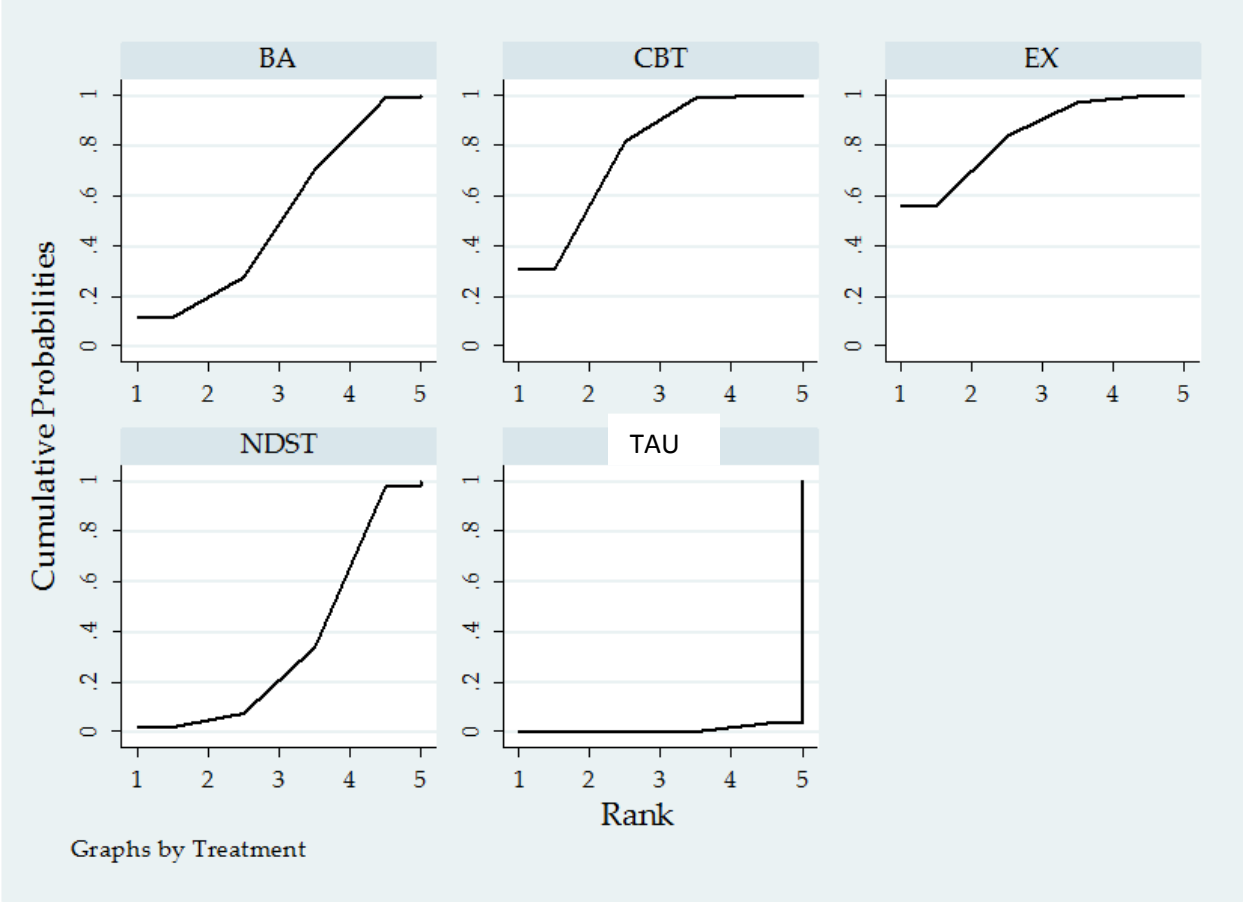


Figure 56, presents a cumulative ranking plot for each of the treatment modalities. Again, it is evident that EX had the highest probability of being ranked first. Interestingly, EX has a 97.1% chance of being ranking either first, second, or third.

Similarly, CBT has a 98.9% chance that it would rank within the top three most treatments. It had the highest probability of being ranked second, but CBT a 30.7% chance of being ranked first. Finally, as with the other two treatments, behavioral activation therapy has a 70.3% chance of being ranked in the top three efficacious treatment modalities. Although it had the highest probability of being ranked third, BA did have a 11.5% chance of being the most efficacious treatment out of the four. As shown in Figure 56, NDST clearly is the fourth most efficacious treatment. Non-directive supportive therapy only has a 33.6% chance of ranking in the top three.

Figure 56: Cumulative Ranking Plot for TAU NMA



CHAPTER 6

DISCUSSION

Summary of Results

Overall, this systematic review and meta-analysis lends additional support to the evidence indicating the efficaciousness of non-directive supportive therapy, behavioral activation therapy, cognitive behavioral therapy and physical activity in alleviating depression symptomatology in those suffering from depression. All four non-pharmacologic treatment modalities were effective at decreasing depressive symptomatology to different degrees.

Cognitive Behavioral Therapy

Cognitive Behavioral Therapy is clearly one of the most heavily studied forms of psychotherapy for depression. Overall, there were 80 studies included in this meta-analysis. It is clear that the meta-analytic results support the conclusion that CBT is an efficacious therapeutic option for treating depressive disorders. The pooled meta-analysis revealed that CBT conferred an overall large and significant improvement in depressive symptomology for those suffering from depression. A recent meta-analysis from 2013, performed by Cuijpers et al., found similar results. In an analysis of 75 studies, they found that CBT greatly improved depression symptomatology. Based on a large number of comparisons, this study provides sufficient evidence that CBT is a efficacious treatment for individuals with depression.

Multiple subgroup analysis were performed examining the effect of intervention length, control type, treatment format, and treatment delivery format on depression outcomes. When moderated by control type, cognitive behavioral therapy was found efficacious when compared to both a waitlist and treatment as usual. CBT was found to confer a very large diminishing effect on depressive symptomatology when compared to a waitlist control. Similarly, when compared to treatment as usual, a large reduction in depression was observed. The overall effect size was slightly larger for the weight list subgroup then the usual care group. This indicates that CBT is overall slightly better at improving depressive symptomatology when compared to a waitlist group rather than individuals undergoing usual care. Another analysis compared the effects of treatment formats (individual or group) on overall depression outcomes. The possible treatment formats were either individual or group therapy. Overall, the subgroup analysis showed that both group and individual CBT therapies are capable of reducing depression scores to a large degree. When comparing the two formats, the overall effect of group therapy was slightly larger than the effects of individual therapy. This suggests that additional therapeutic measures may be involved with group therapy that are not present with individual therapy. One possibility is the additional opportunity to speak and socialize with other individuals before and after therapy sessions.

The subgroup analysis for intervention duration revealed statistically similar results regardless of intervention duration. For the majority of treatment durations, there was an insufficient number of RCTs to draw strong conclusions. However, there were three treatment durations that had sufficient evidence to draw conclusions, namely 8, 10, and 12 weeks. All three intervention durations concluded that CBT results in a large,

significant, improvement in depressive symptomatology. It is evident that further research needs to be done examining the effects of shorter treatment durations (less than 8 weeks) and longer treatment durations (greater than 12 weeks).

Lastly, a subgroup analysis examining the effect of CBT treatment delivery method on depression was performed. This analysis showed that CBT delivered in person, through the telephone, or through bibliotherapy, results in a decrease in depressive symptomatology to a largedegree. The only treatment delivery method in which a large effect was not observed was internet-administered CBT. Internet administered CBT moderately diminished depression scores. These results indicate that therapist contact may play a role in the effectiveness of CBT therapy. Consequently, a large effect is still observed for bibliotherapy. This may be due to the small number of studies that research the efficacy of bibliotherapy for depression. In order to further understand the role of therapist contact in therapy effectiveness, further research should be conducted examining the effectiveness of both bibliotherapy and internet delivered CBT.

Behavioral Activation Therapy

The second form of psychotherapy examined in this systematic review and meta-analysis was behavioral activation therapy. The results of the pair-wise meta-analysis indicate that BA is an effective psychotherapeutic option for treating increased depressive disorders and symptomatology. A pooled analysis of 11 studies found that BA results in a significantly large, diminishing, effect on depressive scores and symptomatology. These results are similar to two previous meta-analyses. In 2006, Cuijpers and colleagues found

that behavioral activation had a large significant effect when compared to a control condition (Cuijpers, Van Straten, & Warmerdamn, 2006). In addition, a more recent updated meta-analysis found that behavioral activation provided an significantly superior therapeutic effect when compared to controls (Ekers, Webster, Van Straten, et al., 2014). Both of these meta-analyses corroborate my findings that behavioral activation significantly decreases depression symptomology in those suffering from depression.

In addition to a meta-analysis examining the overall effect of behavioral activation for depression, several sub-group analyses were conducted to examine possible moderating variables; these variables included type of control, treatment format, diagnosis method, depression severity, and number of treatment sessions. When moderated by control type, behavioral activation was found to be efficacious when compared to both a waitlist and treatment as usual. Behavioral activation was found to confer a very large diminishing effect on depressive symptomatology when compared to a waitlist control. When compared to treatment as usual, a large reduction in depression was observed. Although both subgroups were found to provide a large positive effect on depression, the waitlist control group was found to have a much larger overall effect size. Therefore, the results indicate that behavioral activation reduces depressive symptomatology to a greater extent when compared to waitlist subjects versus usual care participants.

A sub group analysis examining the effect of behavioral activation stratified by treatment format yielded similar results as the effect of CBT on depression. Both group and individual behavioral activation therapy yielded a significant and large effect on

depression symptomatology. Although they both resulted in a large effect, group behavioral activation therapy was found to yield a superior effect then individual therapy. Again, these results match the CBT subgroup analysis and suggest there may be additional therapeutic mechanisms occurring in group behavioral activation therapy that aid in decreasing depressive symptomatology. In order to strengthen the results, more RCTs need to be conducted examining the effects of group therapy on depression.

A subgroup analysis examining the effect of depression severity on the effectiveness of behavioral activation therapy was conducted. This analysis found that behavioral activation provides a large reduction in depression for those suffering from both at least mild and moderate depression. Behavioral activation conferred a much larger effect for those suffering from mild depression, rather than those suffering from moderate depression. Unfortunately, there were no included RCTs that examined the effects of behavioral activation on those suffering from MDD.

The last two subgroup analyses were conducted on diagnosis method and number of sessions. When self-report measures were used to include participants, a large significant effect was observed on depressive symptoms. In contrast, when a combined diagnosis method was used, involving both self-report measures and clinical interviews, a moderate effect was observed. These results indicate that when a stronger method of diagnosis of depression is used, behavioral activation therapy yields inferior results. This result raises questions regarding the capacity for self-report measures to accurately diagnose depression.

Lastly, in order to examine the effects of number of treatment sessions, the analysis was combined into three categories: low, medium and high. The interventions using a low and high number of sessions both yielded a moderate to large significant diminishing effect on depressive symptomatology. The only category that exhibited a large effect was a moderate number of sessions. Due to the number of RCTs included in each category, results of this subgroup analysis should be interpreted with caution. In order to strengthen the results and develop stronger evidence based guidelines for behavioral activation therapy, further research should be conducted to examine how many treatment sessions confer the highest benefit.

Non-Directive Supportive Therapy

The third form of psychotherapy examined in this systematic review and meta-analysis was Non-Directive Supportive Counselling. The results of the pair-wise meta-analysis indicate that NDST is an effective psychotherapeutic option for treating increased depressive disorders and symptomatology. A pooled analysis of eight studies found that NDST results in a significantly moderate effect on depressive scores and symptomology. Out of the four pairwise meta-analysis run, NDST was the only treatment node that did not exhibit a large effect. These results are similar to the most recent meta-analysis. In 2012, Cuijpers and colleagues found that non-directive supportive therapy had a large significant effect when compared to a control condition (Cuijpers, Driessen, Hollon et al., 2012). This meta-analysis found that NDST provided significant therapeutic benefits for those suffering from depression but only to a modest effect. This meta-analysis corroborates my findings that non-directive supportive therapy significantly

decreases depression symptomatology in those suffering from depression by a modest effect. The results of this meta-analysis and all subgroup analyses need to be interpreted with caution due to the low number of included studies.

In addition to a meta-analysis examining the overall effect of non-directive supportive therapy for depression, several sub-group analyses were conducted to examine possible moderating variables; these variables included type of control, treatment format, diagnosis method, and depression severity. When moderated by control type, NDST was found to be efficacious when compared to both waitlist and treatment as usual. NDST was found to confer a moderate diminishing effect on depressive symptomatology when compared to a waitlist control. When compared to treatment as usual, a slightly larger modest reducing effect was observed. Although both subgroups were found to provide a moderate effect, the usual care group was found to have a slightly larger overall effect size. Therefore, the results indicate that non-directive supportive therapy reduces depressive symptomatology to a greater extent when compared to usual care subjects versus waitlist participants. This is the exact opposite result that was observed in the other three treatment nodes. One possible explanation for this result is the lack of RCTs comparing NDST to a waitlist control. This subgroup analysis only had one study that was included in that group. In order to draw conclusions, it is important for further research to be conducted.

The subgroup analysis comparing treatment format had an equal number of studies in both the individual and group non-directive supportive therapy groups. This analysis concluded that individual NDST conferred a small to moderate effect on

depressive symptomatology while group NDST conferred a moderate to large effect. This finding is in line with the outcomes of the three other meta-analyses. These results indicate that group counseling is superior over individual counseling in decreasing depressive symptomatology. As previously discussed, these results suggest that there are additional therapeutic benefits provided by group counseling. The variable that produces this increased therapeutic benefit is not known, but intervention protocol indicates that increase socialization may play an important role.

A subgroup analysis examining the effect of depression severity on the effectiveness of non-directive supportive therapy. In analyzing the depression severity of included participants, three RCTs examined individuals with MDD while the rest looked at participants with, at minimum, mild depression. This subgroup analysis concluded that NDST was equally as beneficial at improving depressive symptomatology for those suffering from MDD as for those with mild depression. Non-directive supportive therapy provided a significant, moderate, reduction in depressive symptomatology regardless of depression severity.

The final subgroup analysis examined the effects of diagnosis method on the outcome. The eight RCTs included three different forms of diagnosis methods, which were clinical interview, self-report, and combined. The results were similar to those found in the behavioral activation subgroup analysis. When using a combined method of diagnosis, NDST only conferred a small, but significant therapeutic effect for depressive symptomology. When a clinical interview was used, NDST provided a slightly larger, moderate effect. Finally, when only a self-report measure was used NDST provided a

moderate to large effect at reducing depression scores. These results indicate that the method of diagnosis matters when predicting the overall therapeutic benefit that NDST can confer. As the overall strength of the diagnosis increases, the overall therapeutic benefit of NDST decreases. This conclusion is based on the premise that a self-report measure is the least accurate form of diagnosis out of the three, and a combined diagnosis method is the most accurate.

Research Question #1

Physical Activity

The first research question that this paper sought to address was the efficacy of physical activity as a treatment for depression. It is clear that the meta-analytic results support the conclusion that physical activity is a therapeutic option for treating increased depressive symptomology. The pooled analysis of 26 studies found that physical activity confers significantly large improvements in depressive symptomatology when compared to a control. Previous meta-analyses examining the effects of physical activity on depression had reached similar conclusions. Kvam et al. (2016) found that exercise decreases depressive symptomatology with a moderate to large effect. In addition, the other most recent meta-analysis performed by Schuch et al. (2016) found that exercise confers a large alleviating effect on depressive symptomology. Both of these meta-analytic results collaborate my findings and aid in providing sufficient evidence that exercise is effective in treating depression.

When compared to the overall effect, statistically similar improvements were seen stratified across several sub-group analyses. When moderated by control type, exercise was found efficacious when compared to both waitlist and treatment as usual. Exercise was found to confer a very large diminishing effect on depressive symptomatology when compared to a waitlist control. When compared to treatment as usual, a moderate to large reducing effect was observed. Therefore, this evidence suggests that physical activity as a therapeutic approach is slightly more efficacious when being compared to individuals who are receiving no treatment rather than individuals receiving their usual care. In addition to control type, a sub-group analysis moderated by physical activity type revealed significantly large effects. The pooled analysis of both aerobic and anaerobic (resistance) physical activity resulted in large effects in decreasing depressive symptomatology. Although both resulted in large effects, aerobic activity conferred greater improvements then anaerobic training (SMD= 1.142 vrs .881). These results indicate that aerobic training may serve as a better therapeutic option when treating depression.

The remaining three subgroup analyses examined the effects of exercise frequency, exercise intensity, and depression severity on depression scores. When exercise frequency was examined as the moderator, a correlation between number of sessions per week and overall effect was observed. When participants exercise two times per week, a moderate reducing effect on depressive scores was observed. As exercise frequency increased, from two days a weeks to five days a week, the overall extent of the effect was greatly increased. RCTs that had participants exercise five days a week found that exercise provided a very large therapeutic effect on depressive symptomatology. The

analysis of exercise intensity revealed that those who undergo low to moderate intensity exercise receive the largest overall benefit. Although both moderate and vigorous physical activity reduce depressive symptomatology, they only do so to a moderate effect.

Overall, these results provide evidence that physical activity should be considered an evidence based therapeutic option for those suffering from depression. The mechanism by which physical activity improves depressive symptomatology are not yet well understood, just as the etiology of depression is not well understood. Interestingly, there is evidence that physical activity acts on many of the behavioral, biological, and cognitive aspects that have been implicated in the pathogenesis of depression. Exercise, for instance, has been shown to effect many of the biological mechanisms associated with depression. In a study done in 1997, scientists used animal models to research the connection between aerobic activity and the reduction of depression. These researchers subjected mice to chronic exercise by running them on a wheel, and then studied the changes norepinephrine (NE), dopamine, and gamma aminobutyric acid (GABA) levels in the brain (Anderson, 2013). The results showed that chronic running caused an increase in NE levels in the hindbrain at rest and protected against future NE depletion. The levels of NE are increased in the brain regions that are linked to cognitive function, including the amygdala and hippocampus, therefore providing a possible connection between NE and exercise enhanced cognitive function. Research provides evidence that physical activity causes biological changes that effects monoamines, the HPA axis, BDNF, and neurogenesis; all have been implicated as possible mechanistic explanations for depression.

In addition to the biological mechanisms that explain improvement of depressive symptomatology, there are ample psychological and behavioral explanations through which exercise my benefit the depressed. There are many possible behavioral and psychological mechanisms for the therapeutic aspects of exercise: these include mastery, capacity for change, generalization, distraction, and positive habit. The concept of mastery is that physical activity allows individuals to feel like they control something and, therefore, it can create an overwhelming feeling that they are able to control other circumstances within their life. In addition, through physical activity providing a sense of mastery individuals will be able to develop a stronger sense of self-efficacy. As previously discussed, when an individual is suffering from depression their feelings of self-efficacy may be greatly diminished. The idea of mastery is an important concept to study in relation with generalization. Generalization is the ability to adapt the feelings you get through doing physical activity and develop the same feelings in other aspects of your life. Therefore, if individuals develop feelings of mastery and increased self-efficacy through running, it is hoped that they will be able to generalize those feeling to other aspects of their life. The ability to relate positive feelings during exercise to other daily aspects of life is a very important aspect of the therapeutic approach of exercise for depression.

The next two possible reasons that exercise confers a beneficial therapeutic effects for those suffering from depression include the capacity for change. Depressive disorders may be marked by an individual feeling stagnant or unable to control what is occurring in their life. Through exercising, individuals are able to break this mindset and see that they are capable of having control and changing their life. Individuals are able to

create and control change as they go from being sedentary and motivated to performing physical activity and improve their overall emotional well-being. Individuals are now aware of their ability for capacity of change and now can take that ability to create therapeutic change in other aspects of their life.

In addition, exercise as a therapeutic experience for depression may lie in its ability to provide distraction and become a positive habit. When individuals exercise, they report positive feelings and sensations that may distract them from outside occurrences. These distractions could be both dissociative or associative in nature. Whether individuals are preoccupied with how their bodies are feeling or features in the environment, these distractions can help individuals forget about feelings of depression or anxiety even if it is just for a short period of time. Physical activity can be a positive habit for those suffering from depression. The addition of a positive addiction in life can create feelings of confidence, self-awareness, increased ability to cope, and self-esteem. All of these psychological and cognitive enhancement functions of physical activity can aid in decreasing negative thoughts.

As discussed in the beginning of this paper, there is evidence that the etiology of depression may be multifactorial, and integrative models have been developed in order to explain the pathology (Craighead et al., 2008). While examining the conceptual framework of an integrated model of depression, it is clear that physical activity effects multiple aspects of the model. The multifaceted nature of physical activity as a treatment modality may subsequently be part of the reason it provides such a large therapeutic benefit for those suffering from depression.

Unlike some other forms of therapy, there are special considerations that mental health providers must take into account when suggesting a physical activity intervention. The patient's age, medical problems, and nay medication he may be taking all need to be considered before a physical activity intervention is prescribed. Because of these special considerations, physicians and therapists may be hesitant to recommend exercise as a therapeutic option, despite all of the evidence based benefits. In order to counteract this, special training for mental health professionals as well as the development of an evidence based physical activity treatment manual would be beneficial.

Network Meta-Analysis

The network meta-analysis clearly showed the effectiveness of physical activity as a treatment for depression. The overall analysis showed that the mean rank for exercise was 2.2, which was the same as cognitive behavioral therapy and only slightly less than behavioral activation therapy (1.9). In addition, the probability that exercise would rank as the most efficacious treatment was almost 30%. Interestingly, the network analysis revealed similar results to the four pairwise meta-analyses conducted separately. These analyses showed that behavioral activation produced the largest effect, followed by exercise, cognitive behavioral therapy, and then non-directive supportive therapy. Although the overall rankings for each treatment provided interesting results, they must be interpreted with caution. The large heterogeneity value observed in the network raises concerns. In order to combat this level of heterogeneity, two separate network meta-analyses were performed stratifying the included studies by control type.

Unfortunately, both of these meta-analyses had sufficiently high levels of heterogeneity as well. The network performed with the waitlist studies resulted in similar results as the overall NMA. The treatment as usual network produced slightly different results. This network found that EX was the most beneficial treatment, followed by CBT and then BA. There were a couple of commonalities observed in all three networks. First, out of the four active treatments, supportive therapy is always ranked fourth. This makes sense because the other three treatment modalities all contain aspects of supportive therapy. Typically, when individuals exercise there are social, supportive interactions between an individual and other exercisers or an individual and their trainer. Secondly, CBT, BA, and EX all produced similar effects, with only slight differences in effect sizes. Lastly, all four of the treatment modalities are more efficacious then the control treatments.

Limitations

While both the meta-analytic results, and network results, showed the effectiveness of physical activity as a therapeutic option for decreasing depression symptomatology, the included studies suffered from many methodological issues and inconsistencies. Some methodological limitations include small sample sizes, selective reporting of data and protocol, publication bias, multiple outcome and multiple time point measures. Although these methodological issues were observed in the exercise trials as well as the psychotherapeutic RCTs.

First, there are several different types of bias that must be addressed. Due to the nature of all four therapeutic interventions, it is impossible to blind participants to

counseling or exercise treatment; therefore, performance bias is a distinct possibility. The lack of blinding for participants is compounded by the fact that many of the studies used the Becks Depression Inventory as the primary outcome measure. Beck's Depression Inventory is a self-report scale for depression. Because it is a self-report scale, and participants are aware of their intervention, participants may be more likely to answer how they believe the researcher wants, therefore suffering response bias. This is a limitation of all treatment arms, not just exercise interventions. In addition to blinding of participants, many studies did not specify the blinding parameters of personnel and outcome assessors. This presents further limitations, especially for the studies that used the Hamilton's Rating Scale for Depression as the outcome measure. There are concerns evolving blinding of outcome assessors and the use of the HAMD because clinical judgement is evolved in administering the scale. Since the structured interview guide for the HAMD was developed in 1988 (Williams, 1988), the inter-rater reliability had been found to be high, with a alpha-coefficient between .80 and .98 (Bagby et al., 2004). None of the studies that used the HAMD as an outcome measure stated that the structured interview guide was used. This raises concerns surrounding the possible effects of assessor blinding and performance bias. For future studies, researchers should employ more rigorous blinding procedures and report all of the ways that blinding was achieved throughout the entity of the study.

Another limitation of the included studies was selective reporting of data. There were several studies in which within group effect sizes could not be computed due to insufficient or missing data. In addition, two studies reported non-parametric statistics, only reporting the median scores of the intervention groups. It can be inferred that

researchers did not provide effect sizes or provided insufficient data due to the lack of statistical effect or significance. In future studies, authors should report all statistics necessary to compute effect sizes, whether significant or not, in order to increase the ability of researchers to perform meta-analaysis. Lastly, all of the funnel plots, other than for NDST, revealed publication bias. Previous studies of psychotherapy (Cuijpers, Smit, Bohlemijer et al., 2010) and exercise (Schuch et al., 2016) for depression have demonstrated that publication bias is evident in TCTs, and, therefore, the effect sizes have been overstated. Only one meta-analysis that examined the effects of exercise on depression adjusted for publication bias, and it showed that exercise has a large and significant antidepressant effect (Schuch et al., 2016). This meta-analysis suggested that the effect of exercise might actually be underestimated due to publication bias (Schuch et al., 2016). Researchers across all areas of psychotherapy and psychosocial research must be cognizant of publication bias and work to limit it in future studies. As evidenced by Schuch (2016), future studies that restrict publication bias may result in exercise producing a higher effect and significant reduction in depressive scores.

Despite numerous efforts to strengthen inclusion criteria, a large portion of the findings yielded heterogeneous outcomes. In addition, a few of the subgroup analyses, particularly involving NDST and BA, only included a few studies, thus weakening the external validity of the results. The level of heterogeneity raises concerns surrounding the basic network meta-analysis assumptions. One assumption that must hold true is transitivity. Due to heterogeneity, the transitivity assumption may be difficult to defend. It must be stated that similar methodological inconsistencies were observed throughout all of the treatment arms. This provides some evidence to strength the assumption,

however questions regarding the strength of the assumption still remain. Due to the heterogeneous outcomes, and the questions regarding basic network meta-analytic assumptions, it is imperative that the results of this study are interpreted with caution.

One possible limitation that must be noted is the use of s frequentist framework to conduct the network meta-analyses. In a recent oral discussion, researchers presented evidence that differences in effect sizes did occur depending on whether a Bayesian or Frequentist approach was used (Sadeghirad, Brignardello-Petersen, Johnston, Guyatt, & Beyene, 2017). Sadeghirad et al. (2017) re-analyzed data from 14 NMAs and found differences in the magnitude of effect estimates, but rarely found differences in the direction or treatment rankings.

As previously stated, there were multiple studies that did not report essential information. In addition, there were a few studies that met my inclusion criteria but did not provide full texts online. Initially, I attempted to contact researchers regarding full texts or missing data. Of all the researchers, only one responded with the full text. Due to time constraints, multiple attempts to obtain the missing studies and data could not be performed and those studies could not be included in this thesis.

Strengths

This was the first network meta-analytic study comparing the efficacy of exercise to other treatment modalities for depression. In addition, it is one of the first network meta-analyses that produced comprehensive results and subgroup analyses on four

pairwise meta-analyses. There are many strength to this study; a few in particular that should be explicitly discussed.

The first, and primary, strength in this paper was the extensive literature search performed by medical librarian Stephanie Roth. Li et al. (2014) produced a comprehensive analysis of the search methods used in 249 network meta-analyses. They found that the median number of databases used was three, with a interquartile range of 3-5. In addition, the most common supplemental search methods included examining reference lists of included studies (48%), reference lists of other systematic reviews (40%), and clinical trial registries (32%) (Li et al., 2014). This meta-analysis and network meta-analysis included 5 database searches, 2 grey literature searches, and a comprehensive hand search. Due to the comprehensive search conducted by Stephanie Roth, the likelihood of retrieving all relevant studies was increased greatly. In addition, Li and colleagues found that only 6% of NMAs noted the involvement of a librarian in the literature search process (2014). Effective literature searchers requires a iterative methodology based on expert knowledge of databases, knowledge of research methodology, and familiarity with the subject (McGowan, 2001). The involvement of a librarian helps with the selection of databases and grey literature sources and aids in the development of a comprehensive search strategy to retrieve eligible studies. Consequently, literature searches carried out by librarians were more likely to be reproducible and search more databases and search terms (Golder, Loke & McIntosh, 2008). It is imperative that future systematic reviews and meta-analyses employ the use of information specialist in conducting research. The use of such individuals will aid in strengthening outcomes and quality of research.

The second strength of this review is the wide ranging expertise of the authors. Authors were selected based off their expertise and their ability to produce quality results. A wide range of authors was utilized, including doctoral students and students with advanced degrees in public health, sport psychology, analytics, and statistics. Multiple individuals had extensive knowledge base in psychotherapy due to counseling or clinical psychology degrees.

Clinical Implications and Recommendations for Future Studies

In patients suffering from increased depressive symptomology, exercise appeared to improve overall depression. These improvements were observed throughout exercise frequencies, exercise intensities, type of exercise, and exercise durations. In addition, exercise produces comparable antidepressant results to other forms of psychotherapies. All three of the psychotherapies examined are considered evidence based, thus suggested exercise should be considered an evidence based treatment for depression. The results of the network meta-analysis provides clinicians with cautiously optimistic evidence of an effective, and relatively safe alternative intervention to treating depression. Although clinicians must take a patient's medical history and other diagnoses into consideration when suggesting physical activity as a therapeutic measure, it is clear that it provides substantial benefits to patients suffering from depression. Physical activity as a therapeutic option for depression has the ability to produce health benefits in other areas of a patients well-being. Other possible health concerns that may receive benefits due to the administration of an exercise intervention for depression include heart disease, stroke, high blood pressure, diabetes, obesity, and osteoporosis.

Clearly, extensive research has been conducted examining the effects of exercise on depression. Future studies in this field should focus on strengthening the methodological protocol for conducting interventional studies analyzing psychotherapy or exercise on depression. The overall goal of strengthening the methodology is to decrease the risk of overall bias and publication bias, therefore strengthening the generalizability of the results. In addition, authors should adhere to CONSORT guidelines when reporting their studies to allow better evaluation of methodological quality and should also provide complete statistical data. Future studies should evaluate the effects of training intensity, duration, frequency and type of exercise through currently existing, or yet-to-be formed, expert protocols. There was substantial variation in the aerobic exercise studies. All of the anaerobic exercise studies used the progressive resistance training methodology for conducting the interventional study. The similarity in protocol across strengthen these results making them more generalizable. Unfortunately, there were only a handful of studies examining the effect of anaerobic training on depression, therefore increasing the possibility of a Type I error. In order to decrease the probability of this occurring, more studies must be performed. On the contrary, many studies have been performed examining the effects of aerobic physical activity, but the variation in protocol between them is very high. Future studies examining the effects of aerobic training on depression should attempt to standardize protocol, whether that means examining heart rate for intensity, or training frequency and duration. The majority of included studies examined the effects of running or walking on depressive scores. In order to examine if the therapeutic benefit is due to the aerobic training or some mechanism just associated with running (or walking), studies examining the effects of

other aerobic activities should be conducted. One such study is examining the effects of an indoor aerobic activity (i.e. swimming) on depression. The simple variable of whether the activity is inside or outside may have a substantial impact on the therapeutic benefit.

As previously noted, the results of this study had heterogeneous findings. One of the factors that contributed to this is the lack of a conclusive theoretical framework or mechanism of action regarding exercise effects on depression. Thus, research must continue to be conducted examining the mechanisms of action of depression and the possible mechanisms by which exercise may be diminishing symptomology. Currently, a multidimensional, biopsychosocial model provides the best integrative explanation surrounding the etiology of depression. Interestingly enough, exercise provides a therapeutic approach that may treat multiple aspects of the biopsychosocial model. Therefore, physical activity may provide the most complete form of therapy. Further research may be able to examine this claim through the examination of exercise as a therapeutic measure for treatment resistant depression. Of the included studies one examined the effects of exercise on patients with treatment resistant depression (Mota-Pereire et al., 2011). Researchers found that a 12/week walking intervention can improve depression symptomology and can lead to depression remission (Mota-Pereire et al., 2011). The therapeutic aspects of exercise in individuals with treatment resistant depression yield evidence that exercise may provide a more comprehensive form of treatment when compared to other therapies.

Conclusions

There is considerable evidence that exercise provides therapeutic benefits to individuals suffering from depression, but it has yet to be listed as an evidence based treatment for depressive disorder. In order to provide evidence that exercise should be evidence based, this review sought to compare it to other, evidence based, psychological treatments. Physical Activity, like any other therapy, has its limitations and challenges; however, evidence does show some promising utility for it as a therapy and this should encourage the future development of protocol for exercise as a therapy for depression. This paper provided evidence that exercise is a therapy of comparable benefits to other psychological therapies, but its ranking amongst them must be evaluated with caution. Exercise provides individuals with a wide-array of beneficial social and psychological aspects that may aid in its therapeutic benefits; these include feelings of mastery, self-efficacy, a form of distraction, and motivation. One main challenge of implementing physical activity for depression is that individuals suffering from depression are typically highly amotivated. Therefore, clinicians should examine ways to assist individuals in getting motivated to become physically active. These ways could include adjunctive use of psychotherapy, like behavioral activation, short-term use of psychotropic medication, or use of a sport and exercise psychologist. As research continues to show the beneficial and therapeutic effects of exercise for depression, the necessity of developing a therapy manual to assist mental health practitioners becomes paramount. The fact that clinicians do not use exercise as a form treatment for depression may stem from the lack of knowledge about exercise as a therapy and how to use it as an intervention. A treatment manual would provide therapists with clear and practical guidelines on how to use

exercise to treat their depressed clients. As with any manual, the manual could be updated and altered as further research is conducted.

Depression is a worldwide problem affecting millions of people. New interventions are needed to treat this pervasive mental illness. Exercise is a proven intervention which warrants further study and implementation.

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APPENDIX A
PRISMA NMA

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	***i***
ABSTRACT			***iii***
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, *including mention of why a network meta-analysis has been conducted.*	***3***
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	70
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly*	***71***

		describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	75
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	75
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	76
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	76
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	77
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	***79***
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	77
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	78
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	78
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	78

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	**77**
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	***78***
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	*
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	*****
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	*****
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	*
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	*
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	*****
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix.*	*****

		League tables and forest plots may be considered to summarize pairwise comparisons. If additional summary measures were explored (such as treatment rankings), these should also be presented.	
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	*****
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	*
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, *alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth).	*****
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	186
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).*	200
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	208
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	***N/A***

PICOS = population, intervention, comparators, outcomes, study design.
* Text in italics indicateS wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.

† Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

- Multiple NMAs were conducted so no page number can be provided

APPENDIX B

Search Strategies for PubMed (NLM)
Last date searched: 3/7/18

Search 1: Behavioral Activation & Control

("behavior therapy"[MESH] OR "behavior therapy"[tiab] OR "behavioral therapy"[tw] OR "behavior therapies"[tw] OR "behavioral therapies"[tw] OR (("behavior"[MeSH Terms] OR "behavior"[tw] OR "behavioral"[tw])) AND activation[tw] OR activational[tw] OR activations[tw] OR activity[tw] OR activities[tw]) OR (ACT[tw] OR "behavioral activation"[tw] OR "behavior activation" OR "behavioral activation therapy"[tw] OR BA[tw] OR "behavioral techniques"[tw] OR BATD[tw] OR "BATD R"[tw] OR "Brief behavioral activation treatment"[tw] OR "behavioral activity"[tw] OR "behavioral activities"[tw] OR "behaviour therapy"[tw] OR "behaviour therapies"[tw] OR "behavioural therapy"[tw] OR "behavioural therapies"[tw] OR "behavioural activation"[tw] OR "behaviour activation"[tw] OR "behavioural activation therapy"[tw] OR "behaviour techniques"[tw] OR "behavioural activity"[tw] OR "behavioural activities"[tw]) AND (((("control groups"[MeSH Terms] OR (("control"[tw] AND "groups"[tw]) OR (control[tw] AND group[tw]) OR (placebo[tw] AND group[tw]) OR (placebo[tw] AND groups[tw])) OR "control groups"[tiab] OR “control group”[tw] OR “controlled group”[tw] OR “controlled groups”[tw] OR “controls group”[tw] OR “placebo group”[tw] OR placebo[tw] OR “placebo controlled”[tw] OR “standard treatment”[tw] OR “standard treatments”[tw] OR “gold standard”[tw] OR "Placebos"[Mesh] OR placebos[tiab] OR “sham treatment”[tw] OR “sham treatments”[tw])))) AND (((((("Mental Disorders/therapy"[Mesh] OR "mental disorders"[tiab] OR "mental disorder"[tw] OR "Psychiatric Diagnosis"[tw] OR "Behavior Disorders" OR "severe mental disorder"[tw] OR "severe mental disorders"[tw] OR "Depressive Disorder, Major/therapy"[Mesh] OR "Major Depressive Disorders"[tiab] OR "Major Depressive"[tw] OR "Major Depressive Disorder"[tw] OR psychosis[tw] OR Psychosis[tw] OR psychoses[tw] OR "major depression"[tw] OR "severe mental illness"[tw] OR insanity OR "mental disorders"[tw] OR "diagnosed mental disorders"[tw] OR "diagnosed mental disorder"[tw] OR depressed[tw] OR depression[tw] OR depressive[tw] OR "depression were"[tw] OR "depression the"[tw] OR "depression symptoms"[tw] OR "depression severity"[tw] OR "severity of depression"[tw] OR "depression score"[tw] OR "depression scores"[tw] OR "depression rating"[tw] OR "depression ratings"[tw] OR "Depressive Disorder, Treatment-Resistant"/therapy[Mesh] OR "Treatment resistant depressive disorder"[tiab] OR "depression in"[tw] OR "depression inventory"[tw] OR "depression and"[tw] OR "depression rating scale"[tw] OR mdd[tw] OR "major depression"[tw] OR "Depressive Disorder/therapy"[Mesh] OR "Depression/therapy"[Mesh])))))) AND ((((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading]))) AND (((((("therapy"[Subheading] OR "therapy"[tiab] OR "treatment"[tw] OR "therapeutics"[MeSH Terms] OR "therapeutics"[tiab] OR "treatment outcome"[MESH] OR "treatment outcome"[tiab])))))) NOT ((((((("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))))))

1,747 Results Date last searched: 3/7/18

Search 2: Exercise & Behavioral Activation

(("behavior therapy"[MESH] OR "behavior therapy"[tiab] OR "behavioral therapy"[tw] OR "behavior therapies"[tw] OR "behavioral therapies"[tw] OR (("behavior"[MeSH Terms] OR "behavior"[tw] OR "behavioral"[tw])) AND activation[tw] OR activational[tw] OR activations[tw] OR activity[tw] OR

activities[tw]) OR (ACT[tw] OR "behavioral activation"[tw] OR "behavior activation" OR "behavioral activation therapy"[tw] OR BA[tw] OR "behavioral techniques"[tw] OR BATD[tw] OR "BATD R"[tw] OR "Brief behavioral activation treatment"[tw] OR "behavioral activity"[tw] OR "behavioral activities"[tw] OR "behaviour therapy"[tw] OR "behaviour therapies"[tw] OR "behavioural therapy"[tw] OR "behavioural therapies"[tw] OR "behavioural activation"[tw] OR "behaviour activation"[tw] OR "behavioural activation therapy"[tw] OR "behaviour techniques"[tw] OR "behavioural activity"[tw] OR "behavioural activities"[tw]) AND (("exercise"[MeSH Terms] OR "exercise"[tiab] OR "physical activity"[tw] OR walking[tiab] OR running[tiab] OR sports[tiab] OR "sports"[MESH] OR athletics[tw] OR sport[tw] OR athletic[tw] OR gym[tw] OR "Resistance Training"[Mesh] OR "resistance training"[tiab] OR "exercise program"[tw] OR "exercise programs"[tw] OR "strength training"[tw] OR "strength train"[tw] OR "weight lifting"[tw] OR "weight lift"[tw] OR "weight bearing exercise"[tw] OR "strengthening program"[tw] OR "strengthening programs"[tw] OR fitness[tw] OR "physical fitness"[MESH] OR "physical fitness"[tiab] OR "walking"[MESH] OR "running"[MESH] OR "jogging"[MESH] OR jogging[tiab]))) AND (((((("Mental Disorders/therapy"[Mesh] OR "mental disorders"[tiab] OR "mental disorder"[tw] OR "Psychiatric Diagnosis"[tw] OR "Behavior Disorders" OR "severe mental disorder"[tw] OR "severe mental disorders"[tw] OR "Depressive Disorder, Major/therapy"[Mesh] OR "Major Depressive Disorders"[tiab] OR "Major Depressive"[tw] OR "Major Depressive Disorder"[tw] OR psychosis[tw] OR Psychosis[tw] OR psychoses[tw] OR "major depression"[tw] OR "severe mental illness"[tw] OR insanity OR "mental disorders"[tw] OR "diagnosed mental disorders"[tw] OR "diagnosed mental disorder"[tw] OR depressed[tw] OR depression[tw] OR depressive[tw] OR "depression were"[tw] OR "depression the"[tw] OR "depression symptoms"[tw] OR "depression severity"[tw] OR "severity of depression"[tw] OR "depression score"[tw] OR "depression scores"[tw] OR "depression rating"[tw] OR "depression ratings"[tw] OR "Depressive Disorder, Treatment-Resistant"/therapy[Mesh] OR "Treatment resistant depressive disorder"[tiab] OR "depression in"[tw] OR "depression inventory"[tw] OR "depression and"[tw] OR "depression rating scale"[tw] OR mdd[tw] OR "major depression"[tw] OR "Depressive Disorder/therapy"[Mesh] OR "Depression/therapy"[Mesh])))))) AND ((((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])))) AND (((((("therapy"[Subheading] OR "therapy"[tiab] OR "treatment"[tw] OR "therapeutics"[MeSH Terms] OR "therapeutics"[tiab] OR "treatment outcome"[MESH] OR "treatment outcome"[tiab])))))) NOT ((((((("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))))))

725 results Date last searched in PubMed (NLM) 3/7/18

Search 3: Exercise & Control

("exercise"[MeSH Terms] OR "exercise"[tiab] OR “physical activity”[tw] OR walking[tiab] OR running[tiab] OR sports[tiab] OR “sports”[MESH] OR athletics[tw] OR sport[tw] OR athletic[tw] OR gym[tw] OR "Resistance Training"[Mesh] OR “resistance training”[tiab] OR “exercise program”[tw] OR “exercise programs”[tw] OR “strength training”[tw] OR “strength train”[tw] OR “weight lifting”[tw] OR “weight lift”[tw] OR “weight bearing exercise”[tw] OR “strengthening program”[tw] OR “strengthening programs”[tw] OR fitness[tw] OR “physical fitness”[MESH] OR “physical fitness”[tiab] OR “walking”[MESH] OR “running”[MESH] OR “jogging”[MESH] OR jogging[tiab]) AND ((("control groups"[MeSH Terms] OR (("control"[tw] AND "groups"[tw]) OR (control[tw] AND group[tw]) OR (placebo[tw] AND group[tw]) OR (placebo[tw] AND groups[tw])) OR "control groups"[tiab] OR “control group”[tw] OR “controlled group”[tw] OR “controlled groups”[tw] OR “controls group”[tw] OR “placebo group”[tw] OR placebo[tw] OR “placebo controlled”[tw] OR “standard treatment”[tw] OR “standard treatments”[tw] OR “gold

standard”[tw] OR "Placebos"[Mesh] OR placebos[tiab] OR “sham treatment”[tw] OR “sham treatments”[tw]))) AND ((("Mental Disorders/therapy"[Mesh] OR "mental disorders"[tiab] OR "mental disorder"[tw] OR "Psychiatric Diagnosis"[tw] OR "Behavior Disorders" OR "severe mental disorder"[tw] OR "severe mental disorders"[tw] OR "Depressive Disorder, Major/therapy"[Mesh] OR "Major Depressive Disorders"[tiab] OR "Major Depressive"[tw] OR "Major Depressive Disorder"[tw] OR psychosis[tw] OR Psychosis[tw] OR psychoses[tw] OR "major depression"[tw] OR "severe mental illness"[tw] OR insanity OR "mental disorders"[tw] OR "diagnosed mental disorders"[tw] OR "diagnosed mental disorder"[tw] OR depressed[tw] OR depression[tw] OR depressive[tw] OR "depression were"[tw] OR "depression the"[tw] OR "depression symptoms"[tw] OR "depression severity"[tw] OR "severity of depression"[tw] OR "depression score"[tw] OR "depression scores"[tw] OR "depression rating"[tw] OR "depression ratings"[tw] OR "Depressive Disorder, Treatment-Resistant"/therapy[Mesh] OR "Treatment resistant depressive disorder"[tiab] OR "depression in"[tw] OR "depression inventory"[tw] OR "depression and"[tw] OR "depression rating scale"[tw] OR mdd[tw] OR "major depression"[tw] OR "Depressive Disorder/therapy"[Mesh] OR "Depression/therapy"[Mesh]))) AND ((((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading]))) AND ((((("therapy"[Subheading] OR "therapy"[tiab] OR "treatment"[tw] OR "therapeutics"[MeSH Terms] OR "therapeutics"[tiab] OR "treatment outcome"[MESH] OR "treatment outcome"[tiab]))))) NOT ((((("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))))))

702 results Date last searched in PubMed (NLM) 3/7/18

Search 4: Exercise & Cognitive Behavioral Therapy (CBT)

("exercise"[MeSH Terms] OR "exercise"[tiab] OR “physical activity”[tw] OR walking[tiab] OR running[tiab] OR sports[tiab] OR “sports”[MESH] OR athletics[tw] OR sport[tw] OR athletic[tw] OR gym[tw] OR "Resistance Training"[Mesh] OR “resistance training”[tiab] OR “exercise program”[tw] OR “exercise programs”[tw] OR “strength training”[tw] OR “strength train”[tw] OR “weight lifting”[tw] OR “weight lift”[tw] OR “weight bearing exercise”[tw] OR “strengthening program”[tw] OR “strengthening programs”[tw] OR fitness[tw] OR “physical fitness”[MESH] OR “physical fitness”[tiab] OR “walking”[MESH] OR “running”[MESH] OR “jogging”[MESH] OR jogging[tiab]) AND ("cognitive therapy"[MeSH Terms] OR ("cognitive"[tw] AND "therapy"[tw]) OR "cognitive therapy"[tw] OR ("cognitive"[tw] AND "behavioral"[tw] AND "therapy"[tw]) OR "cognitive behavioral therapy"[tw] OR CBT[tw] OR “cognitive behavior therapy”[tw] OR “cognition”[MESH] OR “cognitive behavior therapy”[tw] OR “cognitive therapies”[tw] OR “cognitive therapies”[tw] OR “cognition therapy”[tw] OR “cognitive psychotherapy”[tw] OR “cognitive psychotherapies”[tw] OR “cognition therapy”[tw] OR “cognitive behaviour therapy”[tw] OR “cognitive behavioural therapies”[tw]) AND ((("Mental Disorders/therapy"[Mesh] OR "mental disorders"[tiab] OR "mental disorder"[tw] OR "Psychiatric Diagnosis"[tw] OR "Behavior Disorders" OR "severe mental disorder"[tw] OR "severe mental disorders"[tw] OR "Depressive Disorder, Major/therapy"[Mesh] OR "Major Depressive Disorders"[tiab] OR "Major Depressive"[tw] OR "Major Depressive Disorder"[tw] OR psychosis[tw] OR Psychosis[tw] OR psychoses[tw] OR "major depression"[tw] OR "severe mental illness"[tw] OR insanity OR "mental disorders"[tw] OR "diagnosed mental disorders"[tw] OR "diagnosed mental disorder"[tw] OR depressed[tw] OR depression[tw] OR depressive[tw] OR "depression were"[tw] OR "depression the"[tw] OR "depression symptoms"[tw] OR "depression severity"[tw] OR "severity of depression"[tw] OR "depression score"[tw] OR "depression scores"[tw] OR "depression rating"[tw] OR "depression

ratings"[tw] OR "Depressive Disorder, Treatment-Resistant"/therapy[Mesh] OR "Treatment resistant depressive disorder"[tiab] OR "depression in"[tw] OR "depression inventory"[tw] OR "depression and"[tw] OR "depression rating scale"[tw] OR mdd[tw] OR "major depression"[tw] OR "Depressive Disorder/therapy"[Mesh] OR "Depression/therapy"[Mesh]))) AND ((((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])))

363 results Date last searched in PubMed (NLM) 3/7/18

Search 5: Cognitive Behavioral Therapy (CBT) & Control

("cognitive therapy"[MeSH Terms] OR ("cognitive"[tw] AND "therapy"[tw]) OR "cognitive therapy"[tw] OR ("cognitive"[tw] AND "behavioral"[tw] AND "therapy"[tw]) OR "cognitive behavioral therapy"[tw] OR CBT[tw] OR "cognitive behavior therapy"[tw] OR "cognition"[MESH] OR "cognitive behavior therapy"[tw] OR "cognitive therapies"[tw] OR "cognitive therapies"[tw] OR "cognition therapy"[tw] OR "cognitive psychotherapy"[tw] OR "cognitive psychotherapies"[tw] OR "cognition therapy"[tw] OR "cognitive behaviour therapy"[tw] OR "cognitive behavioural therapies"[tw]) AND ((((("control groups"[MeSH Terms] OR (("control"[tw] AND "groups"[tw]) OR (control[tw] AND group[tw]) OR (placebo[tw] AND group[tw]) OR (placebo[tw] AND groups[tw])) OR "control groups"[tiab] OR "control group"[tw] OR "controlled group"[tw] OR "controlled groups"[tw] OR "controls group"[tw] OR "placebo group"[tw] OR placebo[tw] OR "placebo controlled"[tw] OR "standard treatment"[tw] OR "standard treatments"[tw] OR "gold standard"[tw] OR "Placebos"[Mesh] OR placebos[tiab] OR "sham treatment"[tw] OR "sham treatments"[tw]))))) AND (((((("Mental Disorders/therapy"[Mesh] OR "mental disorders"[tiab] OR "mental disorder"[tw] OR "Psychiatric Diagnosis"[tw] OR "Behavior Disorders" OR "severe mental disorder"[tw] OR "severe mental disorders"[tw] OR "Depressive Disorder, Major/therapy"[Mesh] OR "Major Depressive Disorders"[tiab] OR "Major Depressive"[tw] OR "Major Depressive Disorder"[tw] OR psychosis[tw] OR Psychosis[tw] OR psychoses[tw] OR "major depression"[tw] OR "severe mental illness"[tw] OR insanity OR "mental disorders"[tw] OR "diagnosed mental disorders"[tw] OR "diagnosed mental disorder"[tw] OR depressed[tw] OR depression[tw] OR depressive[tw] OR "depression were"[tw] OR "depression the"[tw] OR "depression symptoms"[tw] OR "depression severity"[tw] OR "severity of depression"[tw] OR "depression score"[tw] OR "depression scores"[tw] OR "depression rating"[tw] OR "depression ratings"[tw] OR "Depressive Disorder, Treatment-Resistant"/therapy[Mesh] OR "Treatment resistant depressive disorder"[tiab] OR "depression in"[tw] OR "depression inventory"[tw] OR "depression and"[tw] OR "depression rating scale"[tw] OR mdd[tw] OR "major depression"[tw] OR "Depressive Disorder/therapy"[Mesh] OR "Depression/therapy"[Mesh])))))) AND ((((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])))) AND ((((((("therapy"[Subheading] OR "therapy"[tiab] OR "treatment"[tw] OR "therapeutics"[MeSH Terms] OR "therapeutics"[tiab] OR "treatment outcome"[MESH] OR "treatment outcome"[tiab])))))) NOT (((((("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))))))

2,152 results Date last searched in PubMed (NLM) 3/7/18

Search 6: Cognitive Behavioral Therapy (CBT) & Behavioral Activation

("behavior therapy"[MESH] OR "behavior therapy"[tiab] OR "behavioral therapy"[tw] OR "behavior therapies"[tw] OR "behavioral therapies"[tw] OR (("behavior"[MeSH Terms] OR "behavior"[tw] OR "behavioral"[tw])) AND activation[tw] OR activational[tw] OR activations[tw] OR activity[tw] OR

activities[tw]) OR (ACT[tw] OR "behavioral activation"[tw] OR "behavior activation" OR "behavioral activation therapy"[tw] OR BA[tw] OR "behavioral techniques"[tw] OR BATD[tw] OR "BATD R"[tw] OR "Brief behavioral activation treatment"[tw] OR "behavioral activity"[tw] OR "behavioral activities"[tw] OR "behaviour therapy"[tw] OR "behaviour therapies"[tw] OR "behavioural therapy"[tw] OR "behavioural therapies"[tw] OR "behavioural activation"[tw] OR "behaviour activation"[tw] OR "behavioural activation therapy"[tw] OR "behaviour techniques"[tw] OR "behavioural activity"[tw] OR "behavioural activities"[tw]) AND (("cognitive therapy"[MeSH Terms] OR ("cognitive"[tw] AND "therapy"[tw]) OR "cognitive therapy"[tw] OR ("cognitive"[tw] AND "behavioral"[tw] AND "therapy"[tw]) OR "cognitive behavioral therapy"[tw] OR CBT[tw] OR “cognitive behavior therapy”[tw] OR “cognition”[MESH] OR “cognitive behavior therapy”[tw] OR “cognitive therapies”[tw] OR “cognitive therapies”[tw] OR “cognition therapy”[tw] OR “cognitive psychotherapy”[tw] OR “cognitive psychotherapies”[tw] OR “cognition therapy”[tw] OR “cognitive behaviour therapy”[tw] OR “cognitive behavioural therapies”[tw])) AND (((((("Mental Disorders/therapy"[Mesh] OR "mental disorders"[tiab] OR "mental disorder"[tw] OR "Psychiatric Diagnosis"[tw] OR "Behavior Disorders" OR "severe mental disorder"[tw] OR "severe mental disorders"[tw] OR "Depressive Disorder, Major/therapy"[Mesh] OR "Major Depressive Disorders"[tiab] OR "Major Depressive"[tw] OR "Major Depressive Disorder"[tw] OR psychosis[tw] OR Psychosis[tw] OR psychoses[tw] OR "major depression"[tw] OR "severe mental illness"[tw] OR insanity OR "mental disorders"[tw] OR "diagnosed mental disorders"[tw] OR "diagnosed mental disorder"[tw] OR depressed[tw] OR depression[tw] OR depressive[tw] OR "depression were"[tw] OR "depression the"[tw] OR "depression symptoms"[tw] OR "depression severity"[tw] OR "severity of depression"[tw] OR "depression score"[tw] OR "depression scores"[tw] OR "depression rating"[tw] OR "depression ratings"[tw] OR "Depressive Disorder, Treatment-Resistant"/therapy[Mesh] OR "Treatment resistant depressive disorder"[tiab] OR "depression in"[tw] OR "depression inventory"[tw] OR "depression and"[tw] OR "depression rating scale"[tw] OR mdd[tw] OR "major depression"[tw] OR "Depressive Disorder/therapy"[Mesh] OR "Depression/therapy"[Mesh])))))) AND ((((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])))) AND (((((("therapy"[Subheading] OR "therapy"[tiab] OR "treatment"[tw] OR "therapeutics"[MeSH Terms] OR "therapeutics"[tiab] OR "treatment outcome"[MESH] OR "treatment outcome"[tiab])))))) NOT ((((((("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))))))

1,624 results Date last searched in PubMed (NLM) 3/7/18

Search 7: Supportive Counseling & (behavioral Activation, Cognitive behavioral therapy, & Exercise)

("behavior therapy"[MESH] OR "behavior therapy"[tiab] OR "behavioral therapy"[tw] OR "behavior therapies"[tw] OR "behavioral therapies"[tw] OR (("behavior"[MeSH Terms] OR "behavior"[tw] OR "behavioral"[tw])) AND activation[tw] OR activational[tw] OR activations[tw] OR activity[tw] OR activities[tw]) OR (ACT[tw] OR "behavioral activation"[tw] OR "behavior activation" OR "behavioral activation therapy"[tw] OR BA[tw] OR "behavioral techniques"[tw] OR BATD[tw] OR "BATD R"[tw] OR "Brief behavioral activation treatment"[tw] OR "behavioral activity"[tw] OR "behavioral activities"[tw] OR "behaviour therapy"[tw] OR "behaviour therapies"[tw] OR "behavioural therapy"[tw] OR "behavioural therapies"[tw] OR "behavioural activation"[tw] OR "behaviour activation"[tw] OR "behavioural activation therapy"[tw] OR "behaviour techniques"[tw] OR "behavioural activity"[tw] OR "behavioural activities"[tw]) OR ((("exercise"[MeSH Terms] OR "exercise"[tiab] OR “physical activity”[tw] OR walking[tiab] OR running[tiab] OR sports[tiab] OR “sports”[MESH] OR athletics[tw] OR sport[tw] OR athletic[tw] OR gym[tw] OR "Resistance Training"[Mesh] OR “resistance training”[tiab] OR “exercise program”[tw] OR “exercise programs”[tw] OR “strength training”[tw] OR “strength train”[tw] OR “weight

lifting”[tw] OR “weight lift”[tw] OR “weight bearing exercise”[tw] OR “strengthening program”[tw] OR “strengthening programs”[tw] OR fitness[tw] OR “physical fitness”[MESH] OR “physical fitness”[tiab] OR “walking”[MESH] OR “running”[MESH] OR “jogging”[MESH] OR jogging[tiab]) OR ("cognitive therapy"[MeSH Terms] OR ("cognitive"[tw] AND "therapy"[tw]) OR "cognitive therapy"[tw] OR ("cognitive"[tw] AND "behavioral"[tw] AND "therapy"[tw]) OR "cognitive behavioral therapy"[tw] OR CBT[tw] OR “cognitive behavior therapy”[tw] OR “cognition”[MESH] OR “cognitive behavior therapy”[tw] OR “cognitive therapies”[tw] OR “cognitive therapies”[tw] OR “cognition therapy”[tw] OR “cognitive psychotherapy”[tw] OR “cognitive psychotherapies”[tw] OR “cognition therapy”[tw] OR “cognitive behaviour therapy”[tw] OR “cognitive behavioural therapies”[tw]) OR(“supportive counseling”[tw] OR “supportive counselling”[tw] OR “supportive therapy”[tw] OR “supportive therapies”[tw] OR “person centered therapy”[tw] OR “person centered counseling”[tw] AND (supportive[tw] AND ("counselling"[tw] OR "counseling"[MeSH Terms] OR "counseling"[tiab])) AND (((((("Mental Disorders/therapy"[Mesh] OR "mental disorders"[tiab] OR "mental disorder"[tw] OR "Psychiatric Diagnosis"[tw] OR "Behavior Disorders" OR "severe mental disorder"[tw] OR "severe mental disorders"[tw] OR "Depressive Disorder, Major/therapy"[Mesh] OR "Major Depressive Disorders"[tiab] OR "Major Depressive"[tw] OR "Major Depressive Disorder"[tw] OR psychosis[tw] OR Psychosis[tw] OR psychoses[tw] OR "major depression"[tw] OR "severe mental illness"[tw] OR insanity OR "mental disorders"[tw] OR "diagnosed mental disorders"[tw] OR "diagnosed mental disorder"[tw] OR depressed[tw] OR depression[tw] OR depressive[tw] OR "depression were"[tw] OR "depression the"[tw] OR "depression symptoms"[tw] OR "depression severity"[tw] OR "severity of depression"[tw] OR "depression score"[tw] OR "depression scores"[tw] OR "depression rating"[tw] OR "depression ratings"[tw] OR "Depressive Disorder, Treatment-Resistant"/therapy[Mesh] OR "Treatment resistant depressive disorder"[tiab] OR "depression in"[tw] OR "depression inventory"[tw] OR "depression and"[tw] OR "depression rating scale"[tw] OR mdd[tw] OR "major depression"[tw] OR "Depressive Disorder/therapy"[Mesh] OR "Depression/therapy"[Mesh])))))) AND ((((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])))) AND (((((("therapy"[Subheading] OR "therapy"[tiab] OR "treatment"[tw] OR "therapeutics"[MeSH Terms] OR "therapeutics"[tiab] OR "treatment outcome"[MESH] OR "treatment outcome"[tiab])))))) NOT ((((((("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))))))

70 results Date last searched in PubMed (NLM) 3/7/18

Search Strategies for Cochrane (Wiley) Database
Last date searched: 3/7/18

ID Search Hits

#1 [mh "behavior therapy"] or [mh behavior] 79888

#2 "behavior therapy":ti,ab,kw or "behavioral therapy":ti,ab,kw or "behavior therapies":ti,ab,kw or "behavioral therapies":ti,ab,kw 11081

#3 ACT:ti,ab,kw or "behavioral activation":ti,ab,kw or "behavior activation" or "behavioral activation therapy":ti,ab,kw or BA:ti,ab,kw or "behavioral techniques":ti,ab,kw or BATD:ti,ab,kw or "BATD R":ti,ab,kw or "Brief behavioral activation treatment":ti,ab,kw or "behavioral activity":ti,ab,kw or "behavioral activities":ti,ab,kw or "behaviour therapy":ti,ab,kw or "behaviour therapies":ti,ab,kw or "behavioural therapy":ti,ab,kw or "behavioural therapies":ti,ab,kw or "behavioural activation":ti,ab,kw or "behaviour activation":ti,ab,kw or

"behavioural activation therapy":ti,ab,kw or "behaviour techniques":ti,ab,kw or "behavioural activity":ti,ab,kw or "behavioural activities":ti,ab,kw 9440

#4 "control groups":ti,ab,kw or "control group":ti,ab,kw or "controlled group":ti,ab,kw or "controlled groups":ti,ab,kw or "controls group":ti,ab,kw or "placebo group":ti,ab,kw or placebo:ti,ab,kw or "placebo controlled":ti,ab,kw or "standard treatment":ti,ab,kw or "standard treatments":ti,ab,kw or "gold standard":ti,ab,kw or placebos:ti,ab or "sham treatment":ti,ab,kw or "sham treatments":ti,ab,kw 306357

#5 [mh "control groups"] or [mh Placebos] 23624

#6 #1 or #2 or #3 90534

#7 #4 or #5 313894

#8 #6 and #7 29072

#9 [mh "Mental Disorders/therapy"] or "mental disorders":ti,ab or "mental disorder":ti,ab,kw or "Psychiatric Diagnosis":ti,ab,kw or "Behavior Disorders" or "severe mental disorder":ti,ab,kw or "severe mental disorders":ti,ab,kw or [mh "Depressive Disorder, Major/therapy"] or "Major Depressive Disorders":ti,ab or "Major Depressive":ti,ab,kw or "Major Depressive Disorder":ti,ab,kw or psychosis:ti,ab,kw or Psychosis:ti,ab,kw or psychoses:ti,ab,kw or "major depression":ti,ab,kw or "severe mental illness":ti,ab,kw or insanity or "mental disorders":ti,ab,kw or "diagnosed mental disorders":ti,ab,kw or "diagnosed mental disorder":ti,ab,kw or depressed:ti,ab,kw or depression:ti,ab,kw or depressive:ti,ab,kw or "depression were":ti,ab,kw or "depression the":ti,ab,kw or "depression symptoms":ti,ab,kw or "depression severity":ti,ab,kw or "severity of depression":ti,ab,kw or "depression score":ti,ab,kw or "depression scores":ti,ab,kw or "depression rating":ti,ab,kw or "depression ratings":ti,ab,kw 63039

#10 #8 and #9 in Trials 6062

#11 [mh therapeutics] or therapeutics:ti,ab,kw or [mh "treatment outcome"] or "treatment outcome":ti,ab,kw 365181

#12 #10 and #11 in Trials 765

Exercise & Behavioral Activation & depression (239 Results 3/7/18)

ID Search Hits

#1 [mh "behavior therapy"] 15048

#2 ACT:ti,ab,kw or "behavioral activation":ti,ab,kw or "behavior activation" or "behavioral activation therapy":ti,ab,kw or BA:ti,ab,kw or "behavioral techniques":ti,ab,kw or BATD:ti,ab,kw or "BATD R":ti,ab,kw or "Brief behavioral activation treatment":ti,ab,kw or "behavioral activity":ti,ab,kw or "behavioral activities":ti,ab,kw or "behaviour therapy":ti,ab,kw or "behaviour therapies":ti,ab,kw or "behavioural therapy":ti,ab,kw or "behavioural therapies":ti,ab,kw or "behavioural activation":ti,ab,kw or "behaviour activation":ti,ab,kw or "behavioural activation therapy":ti,ab,kw or "behaviour techniques":ti,ab,kw or "behavioural activity":ti,ab,kw or "behavioural activities":ti,ab,kw 9440

#3 #1 or #2 22915

#4 [mh "Mental Disorders/therapy"] or "mental disorders":ti,ab or "mental disorder":ti,ab,kw or "Psychiatric Diagnosis":ti,ab,kw or "Behavior Disorders" or "severe mental disorder":ti,ab,kw or "severe mental disorders":ti,ab,kw or [mh "Depressive Disorder, Major/therapy"] or "Major Depressive Disorders":ti,ab or "Major Depressive":ti,ab,kw or "Major Depressive Disorder":ti,ab,kw or psychosis:ti,ab,kw or Psychosis:ti,ab,kw or psychoses:ti,ab,kw or "major depression":ti,ab,kw or "severe mental illness":ti,ab,kw or insanity or "mental disorders":ti,ab,kw or "diagnosed mental disorders":ti,ab,kw or "diagnosed mental disorder":ti,ab,kw or depressed:ti,ab,kw or depression:ti,ab,kw or depressive:ti,ab,kw or "depression were":ti,ab,kw or "depression the":ti,ab,kw or "depression symptoms":ti,ab,kw or "depression severity":ti,ab,kw or "severity of depression":ti,ab,kw or "depression score":ti,ab,kw or "depression scores":ti,ab,kw or "depression rating":ti,ab,kw or "depression ratings":ti,ab,kw 63039

#5 #3 and #4 6067

#6 ([mh exercise] or exercise:ti,ab or "physical activity":ti,ab,kw or walking:ti,ab or running:ti,ab or sports:ti,ab or [mh sports] or athletics:ti,ab,kw or sport:ti,ab,kw or athletic:ti,ab,kw or gym:ti,ab,kw or [mh "Resistance Training"] or "resistance training":ti,ab or "exercise program":ti,ab,kw or "exercise programs":ti,ab,kw or "strength training":ti,ab,kw or "strength train":ti,ab,kw or "weight lifting":ti,ab,kw or "weight lift":ti,ab,kw or "weight bearing exercise":ti,ab,kw or "strengthening program":ti,ab,kw or "strengthening programs":ti,ab,kw or fitness:ti,ab,kw or [mh "physical fitness"] or "physical fitness":ti,ab or [mh walking] or [mh running] or [mh jogging] or jogging:ti,ab) 74737

#7 #5 and #6 389

#8 [mh therapeutics] or therapeutics:ti,ab,kw or [mh "treatment outcome"] or "treatment outcome":ti,ab,kw 365181

#9 #7 and #8 in Trials 239

Exercise & Control Group & depression (1,043 Results 3/7/18)

ID Search Hits

#1 ([mh exercise] or exercise:ti,ab or "physical activity":ti,ab,kw or walking:ti,ab or running:ti,ab or sports:ti,ab or [mh sports] or athletics:ti,ab,kw or sport:ti,ab,kw or athletic:ti,ab,kw or gym:ti,ab,kw or [mh "Resistance Training"] or "resistance training":ti,ab or "exercise program":ti,ab,kw or "exercise programs":ti,ab,kw or "strength training":ti,ab,kw or "strength train":ti,ab,kw or "weight lifting":ti,ab,kw or "weight lift":ti,ab,kw or "weight bearing exercise":ti,ab,kw or "strengthening program":ti,ab,kw or "strengthening programs":ti,ab,kw or fitness:ti,ab,kw or [mh "physical fitness"] or "physical fitness":ti,ab or [mh walking] or [mh running] or [mh jogging] or jogging:ti,ab) 74737

#2 "control groups":ti,ab,kw or "control group":ti,ab,kw or "controlled group":ti,ab,kw or "controlled groups":ti,ab,kw or "controls group":ti,ab,kw or "placebo group":ti,ab,kw or placebo:ti,ab,kw or "placebo controlled":ti,ab,kw or "standard treatment":ti,ab,kw or "standard treatments":ti,ab,kw or "gold standard":ti,ab,kw or placebos:ti,ab or "sham treatment":ti,ab,kw or "sham treatments":ti,ab,kw 306357

#3 [mh "Mental Disorders/therapy"] or "mental disorders":ti,ab or "mental disorder":ti,ab,kw or "Psychiatric Diagnosis":ti,ab,kw or "Behavior Disorders" or "severe mental disorder":ti,ab,kw or "severe mental disorders":ti,ab,kw or [mh "Depressive Disorder, Major/therapy"] or "Major Depressive Disorders":ti,ab or "Major Depressive":ti,ab,kw or "Major Depressive Disorder":ti,ab,kw or psychosis:ti,ab,kw or Psychosis:ti,ab,kw or psychoses:ti,ab,kw or "major depression":ti,ab,kw or "severe mental illness":ti,ab,kw or insanity or "mental disorders":ti,ab,kw or "diagnosed mental disorders":ti,ab,kw or "diagnosed mental disorder":ti,ab,kw or depressed:ti,ab,kw or depression:ti,ab,kw or depressive:ti,ab,kw or "depression were":ti,ab,kw or "depression the":ti,ab,kw or "depression symptoms":ti,ab,kw or "depression severity":ti,ab,kw or "severity of depression":ti,ab,kw or "depression score":ti,ab,kw or "depression scores":ti,ab,kw or "depression rating":ti,ab,kw or "depression ratings":ti,ab,kw 63039

#4 [mh therapeutics] or therapeutics:ti,ab,kw or [mh "treatment outcome"] or "treatment outcome":ti,ab,kw 365181

#5 #1 and #2 and #3 and #4 in Trials 1,043

Exercise & Cognitive Behavioral Therapy (CBT) & depression (284 Results 3/7/18)

ID	Search	Hits
#1	([mh "cognitive therapy"] or (cognitive:ti,ab,kw and therapy:ti,ab,kw) or "cognitive therapy":ti,ab,kw or (cognitive:ti,ab,kw and behavioral:ti,ab,kw and therapy:ti,ab,kw) or "cognitive behavioral therapy":ti,ab,kw or CBT:ti,ab,kw or "cognitive behavior therapy":ti,ab,kw or [mh cognition] or "cognitive behavior therapy":ti,ab,kw or "cognitive therapies":ti,ab,kw or "cognitive therapies":ti,ab,kw or "cognition therapy":ti,ab,kw or "cognitive psychotherapy":ti,ab,kw or "cognitive psychotherapies":ti,ab,kw or "cognition therapy":ti,ab,kw or "cognitive behaviour therapy":ti,ab,kw or "cognitive behavioural therapies":ti,ab,kw)	28928
#2	([mh exercise] or exercise:ti,ab or "physical activity":ti,ab,kw or walking:ti,ab or running:ti,ab or sports:ti,ab or [mh sports] or athletics:ti,ab,kw or sport:ti,ab,kw or athletic:ti,ab,kw or gym:ti,ab,kw or [mh "Resistance Training"] or "resistance training":ti,ab or "exercise program":ti,ab,kw or "exercise programs":ti,ab,kw or "strength training":ti,ab,kw or "strength train":ti,ab,kw or "weight lifting":ti,ab,kw or "weight lift":ti,ab,kw or "weight bearing exercise":ti,ab,kw or "strengthening program":ti,ab,kw or "strengthening programs":ti,ab,kw or fitness:ti,ab,kw or [mh "physical fitness"] or "physical fitness":ti,ab or [mh walking] or [mh running] or [mh jogging] or jogging:ti,ab)	74737
#3	[mh "Mental Disorders/therapy"] or "mental disorders":ti,ab or "mental disorder":ti,ab,kw or "Psychiatric Diagnosis":ti,ab,kw or "Behavior Disorders" or "severe mental disorder":ti,ab,kw or "severe mental disorders":ti,ab,kw or [mh "Depressive Disorder, Major/therapy"] or "Major Depressive Disorders":ti,ab or "Major Depressive":ti,ab,kw or "Major Depressive Disorder":ti,ab,kw or psychosis:ti,ab,kw or Psychosis:ti,ab,kw or psychoses:ti,ab,kw or "major depression":ti,ab,kw or "severe mental illness":ti,ab,kw or insanity or "mental disorders":ti,ab,kw or "diagnosed mental disorders":ti,ab,kw or "diagnosed mental disorder":ti,ab,kw or depressed:ti,ab,kw or depression:ti,ab,kw or depressive:ti,ab,kw or "depression were":ti,ab,kw or "depression the":ti,ab,kw or "depression symptoms":ti,ab,kw or "depression severity":ti,ab,kw or "severity of depression":ti,ab,kw or "depression score":ti,ab,kw or "depression scores":ti,ab,kw or "depression rating":ti,ab,kw or "depression ratings":ti,ab,kw	63039
#4	[mh therapeutics] or therapeutics:ti,ab,kw or [mh "treatment outcome"] or "treatment outcome":ti,ab,kw	365181
#5	#1 and #2 and #3 and #4 in Trials	284

Cognitive Behavioral Therapy (CBT) & Control Group & depression (1,521 Results 3/7/18)

ID Search Hits

#1 ([mh "cognitive therapy"] or (cognitive:ti,ab,kw and therapy:ti,ab,kw) or "cognitive therapy":ti,ab,kw or (cognitive:ti,ab,kw and behavioral:ti,ab,kw and therapy:ti,ab,kw) or "cognitive behavioral therapy":ti,ab,kw or CBT:ti,ab,kw or "cognitive behavior therapy":ti,ab,kw or [mh cognition] or "cognitive behavior therapy":ti,ab,kw or "cognitive therapies":ti,ab,kw or "cognitive therapies":ti,ab,kw or "cognition therapy":ti,ab,kw or "cognitive psychotherapy":ti,ab,kw or "cognitive psychotherapies":ti,ab,kw or "cognition therapy":ti,ab,kw or "cognitive behaviour therapy":ti,ab,kw or "cognitive behavioural therapies":ti,ab,kw) 28928

#2 "control groups":ti,ab,kw or "control group":ti,ab,kw or "controlled group":ti,ab,kw or "controlled groups":ti,ab,kw or "controls group":ti,ab,kw or "placebo group":ti,ab,kw or placebo:ti,ab,kw or "placebo controlled":ti,ab,kw or "standard treatment":ti,ab,kw or "standard treatments":ti,ab,kw or "gold standard":ti,ab,kw or placebos:ti,ab or "sham treatment":ti,ab,kw or "sham treatments":ti,ab,kw 306357

#3 [mh "Mental Disorders/therapy"] or "mental disorders":ti,ab or "mental disorder":ti,ab,kw or "Psychiatric Diagnosis":ti,ab,kw or "Behavior Disorders" or "severe mental disorder":ti,ab,kw or "severe mental disorders":ti,ab,kw or [mh "Depressive Disorder, Major/therapy"] or "Major Depressive Disorders":ti,ab or "Major Depressive":ti,ab,kw or "Major Depressive Disorder":ti,ab,kw or psychosis:ti,ab,kw or Psychosis:ti,ab,kw or psychoses:ti,ab,kw or "major depression":ti,ab,kw or "severe mental illness":ti,ab,kw or insanity or "mental disorders":ti,ab,kw or "diagnosed mental disorders":ti,ab,kw or "diagnosed mental disorder":ti,ab,kw or depressed:ti,ab,kw or depression:ti,ab,kw or depressive:ti,ab,kw or "depression were":ti,ab,kw or "depression the":ti,ab,kw or "depression symptoms":ti,ab,kw or "depression severity":ti,ab,kw or "severity of depression":ti,ab,kw or "depression score":ti,ab,kw or "depression scores":ti,ab,kw or "depression rating":ti,ab,kw or "depression ratings":ti,ab,kw 63039

#4 [mh therapeutics] or therapeutics:ti,ab,kw or [mh "treatment outcome"] or "treatment outcome":ti,ab,kw 365181

#5 #1 and #2 and #3 and #4 in Trials 1521

Cognitive Behavioral Therapy (CBT) & Behavioral Activation & depression (3,462 Results 3/7/18)

ID Search Hits

#1 [mh "behavior therapy"] or [mh behavior] 79888

#2 "behavior therapy":ti,ab,kw or "behavioral therapy":ti,ab,kw or "behavior therapies":ti,ab,kw or "behavioral therapies":ti,ab,kw 11081

#3 ACT:ti,ab,kw or "behavioral activation":ti,ab,kw or "behavior activation" or "behavioral activation therapy":ti,ab,kw or BA:ti,ab,kw or "behavioral techniques":ti,ab,kw or BATD:ti,ab,kw or "BATD R":ti,ab,kw or "Brief behavioral activation treatment":ti,ab,kw or "behavioral activity":ti,ab,kw or "behavioral activities":ti,ab,kw or "behaviour therapy":ti,ab,kw or "behaviour therapies":ti,ab,kw or "behavioural therapy":ti,ab,kw or "behavioural therapies":ti,ab,kw or "behavioural activation":ti,ab,kw or "behaviour activation":ti,ab,kw or "behavioural activation therapy":ti,ab,kw or "behaviour techniques":ti,ab,kw or "behavioural activity":ti,ab,kw or "behavioural activities":ti,ab,kw 9440

#4 ([mh "cognitive therapy"] or (cognitive:ti,ab,kw and therapy:ti,ab,kw) or "cognitive therapy":ti,ab,kw or (cognitive:ti,ab,kw and behavioral:ti,ab,kw and therapy:ti,ab,kw) or "cognitive behavioral therapy":ti,ab,kw or CBT:ti,ab,kw or "cognitive behavior therapy":ti,ab,kw or [mh cognition] or "cognitive behavior therapy":ti,ab,kw or "cognitive therapies":ti,ab,kw or "cognitive therapies":ti,ab,kw or "cognition therapy":ti,ab,kw or "cognitive psychotherapy":ti,ab,kw or "cognitive psychotherapies":ti,ab,kw or "cognition therapy":ti,ab,kw or "cognitive behaviour therapy":ti,ab,kw or "cognitive behavioural therapies":ti,ab,kw) 28928

#5 #1 or #2 or #3 90534

#6 #4 and #5 15354

#7 [mh "Mental Disorders/therapy"] or "mental disorders":ti,ab or "mental disorder":ti,ab,kw or "Psychiatric Diagnosis":ti,ab,kw or "Behavior Disorders" or "severe mental disorder":ti,ab,kw or "severe mental disorders":ti,ab,kw or [mh "Depressive Disorder, Major/therapy"] or "Major Depressive Disorders":ti,ab or "Major Depressive":ti,ab,kw or "Major Depressive Disorder":ti,ab,kw or psychosis:ti,ab,kw or Psychosis:ti,ab,kw or psychoses:ti,ab,kw or "major depression":ti,ab,kw or "severe mental illness":ti,ab,kw or insanity or "mental disorders":ti,ab,kw or "diagnosed mental disorders":ti,ab,kw or "diagnosed mental disorder":ti,ab,kw or depressed:ti,ab,kw or depression:ti,ab,kw or depressive:ti,ab,kw or "depression were":ti,ab,kw or "depression the":ti,ab,kw or "depression symptoms":ti,ab,kw or "depression severity":ti,ab,kw or "severity of depression":ti,ab,kw or "depression score":ti,ab,kw or "depression scores":ti,ab,kw or "depression rating":ti,ab,kw or "depression ratings":ti,ab,kw 63039

#8 [mh therapeutics] or therapeutics:ti,ab,kw or [mh "treatment outcome"] or "treatment outcome":ti,ab,kw 365181

#9 #6 and #7 and #8 in Trials 3462

Supportive Counseling combined topic search: (117 Results 3/7/18)

ID Search Hits

#1 ("supportive counseling":ti,ab,kw or "supportive counselling":ti,ab,kw or "supportive therapy":ti,ab,kw or "supportive therapies":ti,ab,kw or "person centered therapy":ti,ab,kw or "person centered counseling":ti,ab,kw and (supportive:ti,ab,kw and (counselling:ti,ab,kw or [mh counseling] or counseling:ti,ab))) 764

#2 [mh "behavior therapy"] or [mh behavior] 79888

#3 "behavior therapy":ti,ab,kw or "behavioral therapy":ti,ab,kw or "behavior therapies":ti,ab,kw or "behavioral therapies":ti,ab,kw 11081

#4 ACT:ti,ab,kw or "behavioral activation":ti,ab,kw or "behavior activation" or "behavioral activation therapy":ti,ab,kw or BA:ti,ab,kw or "behavioral techniques":ti,ab,kw or BATD:ti,ab,kw or "BATD R":ti,ab,kw or "Brief behavioral activation treatment":ti,ab,kw or "behavioral activity":ti,ab,kw or "behavioral activities":ti,ab,kw or "behaviour therapy":ti,ab,kw or "behaviour therapies":ti,ab,kw or "behavioural therapy":ti,ab,kw or "behavioural therapies":ti,ab,kw or "behavioural activation":ti,ab,kw or "behaviour activation":ti,ab,kw or "behavioural activation therapy":ti,ab,kw or "behaviour techniques":ti,ab,kw or "behavioural activity":ti,ab,kw or "behavioural activities":ti,ab,kw 9440

#5 ([mh "cognitive therapy"] or (cognitive:ti,ab,kw and therapy:ti,ab,kw) or "cognitive therapy":ti,ab,kw or (cognitive:ti,ab,kw and behavioral:ti,ab,kw and therapy:ti,ab,kw) or "cognitive behavioral therapy":ti,ab,kw or CBT:ti,ab,kw or "cognitive behavior therapy":ti,ab,kw or [mh cognition] or "cognitive behavior therapy":ti,ab,kw or "cognitive therapies":ti,ab,kw or "cognitive therapies":ti,ab,kw or "cognition therapy":ti,ab,kw or "cognitive psychotherapy":ti,ab,kw or "cognitive psychotherapies":ti,ab,kw or "cognition therapy":ti,ab,kw or "cognitive behaviour therapy":ti,ab,kw or "cognitive behavioural therapies":ti,ab,kw) 28928

#6 ([mh exercise] or exercise:ti,ab or "physical activity":ti,ab,kw or walking:ti,ab or running:ti,ab or sports:ti,ab or [mh sports] or athletics:ti,ab,kw or sport:ti,ab,kw or athletic:ti,ab,kw or gym:ti,ab,kw or [mh "Resistance Training"] or "resistance training":ti,ab or "exercise program":ti,ab,kw or "exercise programs":ti,ab,kw or "strength training":ti,ab,kw or "strength train":ti,ab,kw or "weight lifting":ti,ab,kw or "weight lift":ti,ab,kw or "weight bearing exercise":ti,ab,kw or "strengthening program":ti,ab,kw or "strengthening programs":ti,ab,kw or fitness:ti,ab,kw or [mh "physical fitness"] or "physical fitness":ti,ab or [mh walking] or [mh running] or [mh jogging] or jogging:ti,ab) 74737

#7 #2 or #3 or #4 or #5 or #6 167678

#8 #1 and #7 387

#9 [mh "Mental Disorders/therapy"] or "mental disorders":ti,ab or "mental disorder":ti,ab,kw or "Psychiatric Diagnosis":ti,ab,kw or "Behavior Disorders" or "severe mental disorder":ti,ab,kw or "severe mental disorders":ti,ab,kw or [mh "Depressive Disorder,

Major/therapy"] or "Major Depressive Disorders":ti,ab or "Major Depressive":ti,ab,kw or "Major Depressive Disorder":ti,ab,kw or psychosis:ti,ab,kw or Psychosis:ti,ab,kw or psychoses:ti,ab,kw or "major depression":ti,ab,kw or "severe mental illness":ti,ab,kw or insanity or "mental disorders":ti,ab,kw or "diagnosed mental disorders":ti,ab,kw or "diagnosed mental disorder":ti,ab,kw or depressed:ti,ab,kw or depression:ti,ab,kw or depressive:ti,ab,kw or "depression were":ti,ab,kw or "depression the":ti,ab,kw or "depression symptoms":ti,ab,kw or "depression severity":ti,ab,kw or "severity of depression":ti,ab,kw or "depression score":ti,ab,kw or "depression scores":ti,ab,kw or "depression rating":ti,ab,kw or "depression ratings":ti,ab,kw 63039

#10 #8 and #9 207

#11 [mh therapeutics] or therapeutics:ti,ab,kw or [mh "treatment outcome"] or "treatment outcome":ti,ab,kw 365181

#12 #10 and #11 in Trials 117

Search Strategies for Embase Database
Last date searched: 3/7/18

Search Groups:

Behavioral Activation:

('behavior therapy'/syn OR 'behavior therapy':ti,ab OR 'behavioral therapy':ti,ab OR 'behavior therapies':ti,ab OR 'behavioral therapies':ti,ab OR 'behavioral activation':ti,ab,de,tn OR 'behavior activation' OR 'behavioral activation therapy':ti,ab OR 'ba':ti,ab OR 'behavioral techniques':ti,ab OR 'batd':ti,ab OR 'batd r':ti,ab OR 'brief behavioral activation treatment':ti,ab OR 'behavioral activity':ti,ab OR 'behavioral activities':ti,ab OR 'behaviour therapy':ti,ab OR 'behaviour therapies':ti,ab OR 'behavioural therapy':ti,ab OR 'behavioural therapies':ti,ab OR 'behavioural activation':ti,ab OR 'behaviour activation':ti,ab OR 'behavioural activation therapy':ti,ab OR 'behaviour techniques':ti,ab OR 'behavioural activity':ti,ab OR 'behavioural activities':ti,ab) OR (((behavior* OR behavioral) NEXT/7 activit*):ab,ti)

Depression:

('mental disorders therapy'/syn OR 'mental disorders therapy' OR 'mental disease'/syn OR 'mental disease' OR 'mental disorder*':ti,ab OR 'psych* diagnos*':ti,ab OR 'behav* disorder*':ti,ab OR 'severe mental illness'/exp OR 'severe mental illness' OR 'severe mental disorder*':ti,ab OR 'major depression'/syn OR 'major depression' OR 'depression'/syn OR

'depression' OR 'psychosis'/syn OR 'psychosis' OR insanity:ti,ab OR 'mental disorders':ti,ab OR 'mental disorders diagnosis'/exp OR 'mental disorders diagnosis' OR 'diagnosed mental disorder*':ti,ab OR 'depression symptoms':ti,ab OR 'depression severity':ti,ab OR 'severity of depression':ti,ab OR 'depression score*':ti,ab OR 'depression rating*':ti,ab OR 'treatment resistant depression'/syn OR 'treatment resistant depression' OR 'depression in*':ti,ab OR 'depression inventor*':ti,ab OR 'depression rating scale*':ti,ab OR 'mdd':ti,ab))

Extra Limit to Depression Only:

AND ('depression'/de OR 'major depression'/de OR 'mental disease'/de)

Control Group:

'control groups'/exp OR ((control* NEAR/3 group*):ti,ab) OR ((placebo* NEAR/3 group*):ti,ab) OR 'control* group*':ti,ab OR 'placebo* group*':ti,ab OR placebo:ti,ab OR ((placebo* NEAR/3 control*):ti,ab) OR 'standard treatment*':ti,ab OR 'gold standard':ti,ab OR 'placebos'/exp OR 'sham treatment*':ti,ab

Exercise Group:

'exercise'/syn OR 'kinesiotherapy'/syn OR 'treadmill exercise'/syn OR 'aerobic exercise'/syn OR 'fitness'/syn OR 'resistance training'/syn OR 'sport'/syn OR 'physical activity'/syn OR 'walking'/syn OR 'running'/syn OR 'treadmill'/syn OR 'jogging'/syn OR exercis*:ti,ab OR ‘physical activit*’:ti,ab OR walk*:ti,ab OR run*:ti,ab OR sport*:ti,ab OR athletic:ti,ab OR gym:ti,ab OR ‘resistance train*’:ti,ab OR ‘strength* program*’:ti,ab

Cognitive Behavioral Therapy Group:

('cognitive therapy'/syn OR ((cognitive NEAR/3 therap*):ti,ab) OR (cognitive:ti,ab AND behavior*:ti,ab AND therap*:ti,ab) OR 'cognitive behavioral therap*':ti,ab OR cbt:ti,ab OR 'cognition'/syn OR 'cognitive therap*':ti,ab OR 'cognitive psychotherap*':ti,ab OR 'cognition therap*':ti,ab OR 'cognitive behaviour therap*':ti,ab OR 'cognitive behavioural':ti,ab)

Therapy Group:

(therapy:ti,ab OR treatment:ti,ab OR 'therapy'/syn OR 'treatment outcome'/syn)

Humans not Animals Filter:

Search # NOT [animals]/lim NOT 'human'/exp

RCT’s:

('randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*))

Search Strategies:

Behavioral Activation & Control & depression & RCT: (in Embase have to do Human filter separately--See above):

1,636 results date last searched: 3/7/18

#1

('exercise'/syn OR 'kinesiotherapy'/syn OR 'treadmill exercise'/syn OR 'aerobic exercise'/syn OR 'fitness'/syn OR 'resistance training'/syn OR 'sport'/syn OR 'physical activity'/syn OR 'walking'/syn OR 'running'/syn OR 'treadmill'/syn OR 'jogging'/syn OR exercis*:ti,ab OR ‘physical activit*’:ti,ab OR walk*:ti,ab OR run*:ti,ab OR sport*:ti,ab OR athletic:ti,ab OR gym:ti,ab OR ‘resistance train*’:ti,ab OR ‘strength* program*’:ti,ab) AND ('control groups'/exp OR ((control* NEAR/3 group*):ti,ab) OR ((placebo* NEAR/3 group*):ti,ab) OR 'control* group*':ti,ab OR 'placebo* group*':ti,ab OR placebo:ti,ab OR ((placebo* NEAR/3 control*):ti,ab) OR 'standard treatment*':ti,ab OR 'gold standard':ti,ab OR 'placebos'/exp OR 'sham treatment*':ti,ab) AND ('mental disorders therapy'/syn OR 'mental disorders therapy' OR 'mental disease'/syn OR 'mental disease' OR 'mental disorder*':ti,ab OR 'psych* diagnos*':ti,ab OR 'behav* disorder*':ti,ab OR 'severe mental illness'/exp OR 'severe mental illness' OR 'severe mental disorder*':ti,ab OR 'major depression'/syn OR 'major depression' OR 'depression'/syn OR 'depression' OR 'psychosis'/syn OR 'psychosis' OR insanity:ti,ab OR 'mental disorders':ti,ab OR 'mental disorders diagnosis'/exp OR 'mental disorders diagnosis' OR 'diagnosed mental disorder*':ti,ab OR 'depression symptoms':ti,ab OR 'depression severity':ti,ab OR 'severity of depression':ti,ab OR 'depression score*':ti,ab OR 'depression rating*':ti,ab OR 'treatment resistant depression'/syn OR 'treatment resistant depression' OR 'depression in*':ti,ab OR 'depression inventor*':ti,ab OR 'depression rating scale*':ti,ab OR 'mdd':ti,ab) AND (therapy:ti,ab OR treatment:ti,ab OR 'therapy'/syn OR 'therapy' OR 'treatment outcome'/syn OR 'treatment outcome') AND ('randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*))

#2

#1 AND ('depression'/de OR 'major depression'/de OR 'mental disease'/de)

#3 (5,316,247 Results)

[animals]/lim NOT 'human'/exp

#4 (1,623)

#2 NOT #3

Exercise & Behavioral Activation & depression & RCT

1,017 Results date last searched 3/7/18

#1

('behavior therapy'/syn OR 'behavior therapy':ti,ab OR 'behavioral therapy':ti,ab OR 'behavior therapies':ti,ab OR 'behavioral therapies':ti,ab OR 'behavioral activation':ti,ab,de,tn OR 'behavior activation' OR 'behavioral activation therapy':ti,ab OR 'ba':ti,ab OR 'behavioral techniques':ti,ab OR 'batd':ti,ab OR 'batd r':ti,ab OR 'brief behavioral activation treatment':ti,ab OR 'behavioral activity':ti,ab OR 'behavioral activities':ti,ab OR 'behaviour therapy':ti,ab OR 'behaviour therapies':ti,ab OR 'behavioural therapy':ti,ab OR 'behavioural therapies':ti,ab OR 'behavioural activation':ti,ab OR 'behaviour activation':ti,ab OR 'behavioural activation therapy':ti,ab OR 'behaviour techniques':ti,ab OR 'behavioural activity':ti,ab OR 'behavioural activities':ti,ab OR (((behavior* OR behavioral) NEXT/7 activit*):ab,ti)) AND ('exercise'/syn OR 'kinesiotherapy'/syn OR 'treadmill exercise'/syn OR 'aerobic exercise'/syn OR 'fitness'/syn OR 'resistance training'/syn OR 'sport'/syn OR 'physical activity'/syn OR 'walking'/syn OR 'running'/syn OR 'treadmill'/syn OR 'jogging'/syn OR exercis*:ti,ab OR ‘physical activit*’:ti,ab OR walk*:ti,ab OR run*:ti,ab OR sport*:ti,ab OR athletic:ti,ab OR gym:ti,ab OR ‘resistance train*’:ti,ab OR ‘strength* program*’:ti,ab) AND ('mental disorders therapy'/syn OR 'mental disorders therapy' OR 'mental disease'/syn OR 'mental disease' OR 'mental disorder*':ti,ab OR 'psych* diagnos*':ti,ab OR 'behav* disorder*':ti,ab OR 'severe mental illness'/exp OR 'severe mental illness' OR 'severe mental disorder*':ti,ab OR 'major depression'/syn OR 'major depression' OR 'depression'/syn OR 'depression' OR 'psychosis'/syn OR 'psychosis' OR insanity:ti,ab OR 'mental disorders':ti,ab OR 'mental disorders diagnosis'/exp OR 'mental disorders diagnosis' OR 'diagnosed mental disorder*':ti,ab OR 'depression symptoms':ti,ab OR 'depression severity':ti,ab OR 'severity of depression':ti,ab OR 'depression score*':ti,ab OR 'depression rating*':ti,ab OR 'treatment resistant depression'/syn OR 'treatment resistant depression' OR 'depression in*':ti,ab OR

'depression inventor*':ti,ab OR 'depression rating scale*':ti,ab OR 'mdd':ti,ab) AND (therapy:ti,ab OR treatment:ti,ab OR 'therapy'/syn OR 'therapy' OR 'treatment outcome'/syn OR 'treatment outcome') AND ('randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*))

#2 (5,316,247 Results)

[animals]/lim NOT 'human'/exp

#3 (1,021 Results)

#1 NOT #2

Exercise & Control Group & depression & RCT

1,586 Results date last searched 3/7/18

#1

('exercise'/syn OR 'fitness'/syn OR 'resistance training'/syn OR 'sport'/syn OR 'physical activity'/syn OR 'walking'/syn OR 'running'/syn OR 'jogging'/syn OR exercis*:ti,ab OR 'physical activit*':ti,ab OR walk*:ti,ab OR run*:ti,ab OR sport?:ti,ab OR gym:ti,ab OR 'resistance train*':ti,ab OR 'strength program*':ti,ab OR 'aerobic exercise':ti,ab) AND ('control groups'/exp OR ((control* NEAR/3 group*):ti,ab) OR ((placebo* NEAR/3 group*):ti,ab) OR 'control* group*':ti,ab OR 'placebo* group*':ti,ab OR placebo:ti,ab OR ((placebo* NEAR/3 control*):ti,ab) OR 'standard treatment*':ti,ab OR 'gold standard':ti,ab OR 'placebos'/exp OR 'sham treatment*':ti,ab) AND ('mental disorders therapy'/syn OR 'mental disorders therapy' OR 'mental disease'/syn OR 'mental disease' OR 'mental disorder*':ti,ab OR 'psych* diagnos*':ti,ab OR 'behav* disorder*':ti,ab OR 'severe mental illness'/exp OR 'severe mental illness' OR 'severe mental disorder*':ti,ab OR 'major depression'/syn OR 'major depression' OR 'depression'/syn OR 'depression' OR 'psychosis'/syn OR 'psychosis' OR insanity:ti,ab OR 'mental disorders':ti,ab OR 'mental disorders diagnosis'/exp OR 'mental disorders diagnosis' OR 'diagnosed mental disorder*':ti,ab OR 'depression symptoms':ti,ab OR 'depression severity':ti,ab OR 'severity of depression':ti,ab OR 'depression score*':ti,ab OR 'depression rating*':ti,ab OR 'treatment resistant depression'/syn OR 'treatment resistant depression' OR 'depression in*':ti,ab OR 'depression inventor*':ti,ab OR 'depression rating scale*':ti,ab OR 'mdd':ti,ab) AND (therapy:ti,ab OR treatment:ti,ab OR 'therapy'/syn OR 'therapy' OR 'treatment outcome'/syn OR

'treatment outcome') AND ('randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*))

#2

#1 AND ('depression'/de OR 'major depression'/de OR 'mental disease'/de)

#3 ((5,316,247 Results)

[animals]/lim NOT 'human'/exp

#4 (1,583 Results)

#2 NOT #3

Exercise & Cognitive Behavioral Therapy (CBT) & depression & RCT

1,336 Results date last searched: 3/7/18

#1

('cognitive therapy'/syn OR ((cognitive NEAR/3 therap*):ti,ab) OR (cognitive:ti,ab AND behavior*:ti,ab AND therap*:ti,ab) OR 'cognitive behavioral therap*':ti,ab OR cbt:ti,ab OR 'cognition'/syn OR 'cognitive therap*':ti,ab OR 'cognitive psychotherap*':ti,ab OR 'cognition therap*':ti,ab OR 'cognitive behaviour therap*':ti,ab OR 'cognitive behavioural':ti,ab) AND (('exercise'/syn OR 'kinesiotherapy'/syn OR 'treadmill exercise'/syn OR 'aerobic exercise'/syn OR 'fitness'/syn OR 'resistance training'/syn OR 'sport'/syn OR 'physical activity'/syn OR 'walking'/syn OR 'running'/syn OR 'treadmill'/syn OR 'jogging'/syn OR exercis*:ti,ab OR 'physical activit*':ti,ab OR walk*:ti,ab OR run*:ti,ab OR sport*:ti,ab OR athletic:ti,ab OR gym:ti,ab OR 'resistance train*':ti,ab OR 'strength* program*':ti,ab) AND ('mental disorders therapy'/syn OR 'mental disorders therapy' OR 'mental disease'/syn OR 'mental disease' OR 'mental disorder*':ti,ab OR 'psych* diagnos*':ti,ab OR 'behav* disorder*':ti,ab OR 'severe mental illness'/exp OR 'severe mental illness' OR 'severe mental disorder*':ti,ab OR 'major depression'/syn OR 'major depression' OR 'depression'/syn OR 'depression' OR 'psychosis'/syn OR 'psychosis' OR insanity:ti,ab OR 'mental disorders':ti,ab OR 'mental disorders diagnosis'/exp OR 'mental disorders diagnosis' OR 'diagnosed mental disorder*':ti,ab OR 'depression symptoms':ti,ab OR 'depression severity':ti,ab OR 'severity of depression':ti,ab OR 'depression score*':ti,ab OR 'depression rating*':ti,ab OR 'treatment resistant depression'/syn OR 'treatment resistant depression' OR 'depression in*':ti,ab OR 'depression inventor*':ti,ab OR 'depression

rating scale*':ti,ab OR 'mdd':ti,ab) AND (therapy:ti,ab OR treatment:ti,ab OR 'therapy'/syn OR 'therapy' OR 'treatment outcome'/syn OR 'treatment outcome') AND ('randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*)))

#2

#1 AND ('depression'/de OR 'major depression'/de OR 'mental disease'/de)

#3 (5,316,247 Results)

[animals]/lim NOT 'human'/exp

#4 (1,336 Results)

#2 NOT #3

Cognitive Behavioral Therapy (CBT) & Control Group & depression & RCT

4,076 Results date last searched: 3/1/18

#1

('cognitive therapy'/syn OR ((cognitive NEAR/3 therap*):ti,ab) OR (cognitive:ti,ab AND behavior*:ti,ab AND therap*:ti,ab) OR 'cognitive behavioral therap*':ti,ab OR cbt:ti,ab OR 'cognition'/syn OR 'cognitive therap*':ti,ab OR 'cognitive psychotherap*':ti,ab OR 'cognition therap*':ti,ab OR 'cognitive behaviour therap*':ti,ab OR 'cognitive behavioural':ti,ab) AND ('control groups'/exp OR ((control* NEAR/3 group*):ti,ab) OR ((placebo* NEAR/3 group*):ti,ab) OR 'control* group*':ti,ab OR 'placebo* group*':ti,ab OR placebo:ti,ab OR ((placebo* NEAR/3 control*):ti,ab) OR 'standard treatment*':ti,ab OR 'gold standard':ti,ab OR 'placebos'/exp OR 'sham treatment*':ti,ab) AND ('mental disorders therapy'/syn OR 'mental disorders therapy' OR 'mental disease'/syn OR 'mental disease' OR 'mental disorder*':ti,ab OR 'psych* diagnos*':ti,ab OR 'behav* disorder*':ti,ab OR 'severe mental illness'/exp OR 'severe mental illness' OR 'severe mental disorder*':ti,ab OR 'major depression'/syn OR 'major depression' OR 'depression'/syn OR 'depression' OR 'psychosis'/syn OR 'psychosis' OR insanity:ti,ab OR 'mental disorders':ti,ab OR 'mental disorders diagnosis'/exp OR 'mental disorders diagnosis' OR 'diagnosed mental disorder*':ti,ab OR 'depression symptoms':ti,ab OR 'depression severity':ti,ab OR 'severity of depression':ti,ab OR 'depression score*':ti,ab OR 'depression rating*':ti,ab OR 'treatment resistant depression'/syn OR 'treatment resistant depression' OR 'depression in*':ti,ab OR 'depression inventor*':ti,ab OR 'depression rating scale*':ti,ab OR 'mdd':ti,ab) AND

(therapy:ti,ab OR treatment:ti,ab OR 'therapy'/syn OR 'therapy' OR 'treatment outcome'/syn OR 'treatment outcome') AND ('randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*))

#2

#1 AND ('depression'/de OR 'major depression'/de OR 'mental disease'/de)

#3 (5,316,247 Results)

[animals]/lim NOT 'human'/exp

#4 (4,076 Results)

#2 NOT #3

Cognitive Behavioral Therapy (CBT) & Behavioral Activation & depression & RCT

3,297 Results date last searched: 3/7/18

#1

('behavior therapy'/syn OR 'behavior therapy':ti,ab OR 'behavioral therapy':ti,ab OR 'behavior therapies':ti,ab OR 'behavioral therapies':ti,ab OR 'behavioral activation':ti,ab,de,tn OR 'behavior activation' OR 'behavioral activation therapy':ti,ab OR 'ba':ti,ab OR 'behavioral techniques':ti,ab OR 'batd':ti,ab OR 'batd r':ti,ab OR 'brief behavioral activation treatment':ti,ab OR 'behavioral activity':ti,ab OR 'behavioral activities':ti,ab OR 'behaviour therapy':ti,ab OR 'behaviour therapies':ti,ab OR 'behavioural therapy':ti,ab OR 'behavioural therapies':ti,ab OR 'behavioural activation':ti,ab OR 'behaviour activation':ti,ab OR 'behavioural activation therapy':ti,ab OR 'behaviour techniques':ti,ab OR 'behavioural activity':ti,ab OR 'behavioural activities':ti,ab) OR (((behavior* OR behavioral) NEXT/7 activit*):ab,ti) AND ('cognitive therapy'/syn OR ((cognitive NEAR/3 therap*):ti,ab) OR (cognitive:ti,ab AND behavior*:ti,ab AND therap*:ti,ab) OR 'cognitive behavioral therap*':ti,ab OR cbt:ti,ab OR 'cognition'/syn OR 'cognitive therap*':ti,ab OR 'cognitive psychotherap*':ti,ab OR 'cognition therap*':ti,ab OR 'cognitive behaviour therap*':ti,ab OR 'cognitive behavioural':ti,ab) AND ('mental disorders therapy'/syn OR 'mental disorders therapy' OR 'mental disease'/syn OR 'mental disease' OR 'mental disorder*':ti,ab OR

'psych* diagnos*':ti,ab OR 'behav* disorder*':ti,ab OR 'severe mental illness'/exp OR 'severe mental illness' OR 'severe mental disorder*':ti,ab OR 'major depression'/syn OR 'major depression' OR 'depression'/syn OR 'depression' OR 'psychosis'/syn OR 'psychosis' OR insanity:ti,ab OR 'mental disorders':ti,ab OR 'mental disorders diagnosis'/exp OR 'mental disorders diagnosis' OR 'diagnosed mental disorder*':ti,ab OR 'depression symptoms':ti,ab OR 'depression severity':ti,ab OR 'severity of depression':ti,ab OR 'depression score*':ti,ab OR 'depression rating*':ti,ab OR 'treatment resistant depression'/syn OR 'treatment resistant depression' OR 'depression in*':ti,ab OR 'depression inventor*':ti,ab OR 'depression rating scale*':ti,ab OR 'mdd':ti,ab) AND (therapy:ti,ab OR treatment:ti,ab OR 'therapy'/syn OR 'therapy' OR 'treatment outcome'/syn OR 'treatment outcome') AND ('randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*))

#2

#1 AND ('depression'/de OR 'major depression'/de OR 'mental disease'/de)

#3 (5,316,247 Results)

[animals]/lim NOT 'human'/exp

#4 (3,297 Results)

#2 NOT #3

Topic Search: Supportive Counseling combined

86 Results date last searched: 3/7/18

#1

('behavior therapy'/syn OR 'behavior therapy':ti,ab OR 'behavioral therapy':ti,ab OR 'behavior therapies':ti,ab OR 'behavioral therapies':ti,ab OR 'behavioral activation':ti,ab,de,tn OR 'behavior activation' OR 'behavioral activation therapy':ti,ab OR 'ba':ti,ab OR 'behavioral techniques':ti,ab OR 'batd':ti,ab OR 'batd r':ti,ab OR 'brief behavioral activation treatment':ti,ab OR 'behavioral activity':ti,ab OR 'behavioral activities':ti,ab OR 'behaviour therapy':ti,ab OR 'behaviour therapies':ti,ab OR 'behavioural therapy':ti,ab OR 'behavioural therapies':ti,ab OR 'behavioural activation':ti,ab OR 'behaviour activation':ti,ab OR 'behavioural activation therapy':ti,ab OR 'behaviour techniques':ti,ab OR 'behavioural activity':ti,ab OR 'behavioural activities':ti,ab OR (((behavior* OR behavioral) NEXT/7 activit*):ab,ti) OR 'cognitive therapy'/syn OR ((cognitive

NEAR/3 therap*):ti,ab) OR (cognitive:ti,ab AND behavior*:ti,ab AND therap*:ti,ab) OR 'cognitive behavioral therap*':ti,ab OR cbt:ti,ab OR 'cognition'/syn OR 'cognitive therap*':ti,ab OR 'cognitive psychotherap*':ti,ab OR 'cognition therap*':ti,ab OR 'cognitive behaviour therap*':ti,ab OR 'cognitive behavioural':ti,ab OR 'exercise'/syn OR 'kinesiotherapy'/syn OR 'treadmill exercise'/syn OR 'aerobic exercise'/syn OR 'fitness'/syn OR 'resistance training'/syn OR 'sport'/syn OR 'physical activity'/syn OR 'walking'/syn OR 'running'/syn OR 'treadmill'/syn OR 'jogging'/syn OR exercis*:ti,ab OR 'physical activit*':ti,ab OR walk*:ti,ab OR run*:ti,ab OR sport*:ti,ab OR athletic:ti,ab OR gym:ti,ab OR 'resistance train*':ti,ab OR 'strength* program*':ti,ab) AND ('supportive counseling':ti,ab OR 'supportive counselling':ti,ab OR 'supportive therap*':ti,ab OR 'person centered therap*':ti,ab OR 'person centered counsel*':ti,ab) AND ((supportive NEAR/3 counsel*):ti,ab) AND ('mental disorders therapy'/syn OR 'mental disorders therapy' OR 'mental disease'/syn OR 'mental disease' OR 'mental disorder*':ti,ab OR 'psych* diagnos*':ti,ab OR 'behav* disorder*':ti,ab OR 'severe mental illness'/exp OR 'severe mental illness' OR 'severe mental disorder*':ti,ab OR 'major depression'/syn OR 'major depression' OR 'depression'/syn OR 'depression' OR 'psychosis'/syn OR 'psychosis' OR insanity:ti,ab OR 'mental disorders':ti,ab OR 'mental disorders diagnosis'/exp OR 'mental disorders diagnosis' OR 'diagnosed mental disorder*':ti,ab OR 'depression symptoms':ti,ab OR 'depression severity':ti,ab OR 'severity of depression':ti,ab OR 'depression score*':ti,ab OR 'depression rating*':ti,ab OR 'treatment resistant depression'/syn OR 'treatment resistant depression' OR 'depression in*':ti,ab OR 'depression inventor*':ti,ab OR 'depression rating scale*':ti,ab OR 'mdd':ti,ab) AND (therapy:ti,ab OR treatment:ti,ab OR 'therapy'/syn OR 'therapy' OR 'treatment outcome'/syn OR 'treatment outcome') AND ('randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*))

Search Strategies for PsycInfo (EBSCOhost) Database
Last date searched: 3/7/18

Behavioral Activation & Control & depression & RCT: 40 Results (3/7/18)

S9	S7 AND S8	**Search modes** - Boolean/Phrase	**View Results** (40)		
S8	MM "Clinical Trials" OR RCT OR randomized*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	71,545
S7	S5 AND S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	139
S6	(((((("Mental Disorders/therapy" OR mental disorders.ti,ab OR mental disorder.mp. OR Psychiatric Diagnosis.mp. OR Behavior Disorders OR severe mental disorder.mp. OR severe mental disorders.mp. OR "Depressive Disorder, Major/therapy" OR Major Depressive Disorders.ti,ab OR Major Depressive.mp. OR Major Depressive Disorder.mp. OR psychosis.mp. OR Psychosis.mp. OR psychoses.mp. OR major depression.mp. OR severe mental illness.mp. OR insanity OR mental disorders.mp. OR diagnosed mental disorders.mp. OR diagnosed mental disorder.mp. OR depressed.mp. OR depression.mp. OR depressive.mp. OR depression were.mp. OR depression the.mp. OR depression symptoms.mp. OR depression severity.mp. OR severity of depression.mp. OR depression score.mp. OR depression scores.mp. OR depression rating.mp. OR depression ratings.mp. OR "Depressive Disorder, Treatment-Resistant" OR Treatment resistant depressive disorder.ti,ab OR depression in.mp. OR depression inventory.mp. OR depression and.mp. OR depression rating scale.mp. OR mdd.mp. OR major depression.mp. OR "Depressive Disorder/therapy" OR Depression/therapy)))))	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	141,773
S5	S3 AND S4	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	1,849

			Search Screen - Advanced Search Database - PsycINFO	
S4	S1 OR S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	61,532
S3	((("control groups" OR ((control.mp. AND groups.mp.) OR (control.mp. AND group.mp.) OR (placebo.mp. AND group.mp.) OR (placebo.mp. AND groups.mp.)) OR control groups.ti,ab OR control group.mp. OR controlled group.mp. OR controlled groups.mp. OR controls group.mp. OR placebo group.mp. OR placebo.mp. OR placebo controlled.mp. OR standard treatment.mp. OR standard treatments.mp. OR gold standard.mp. OR Placebos OR placebos.ti,ab OR sham treatment.mp. OR sham treatments.mp.)))	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	54,813
S2	(ACT.mp. OR behavioral activation.mp. OR behavior activation OR behavioral activation therapy.mp. OR BA.mp. OR behavioral techniques.mp. OR BATD.mp. OR BATD R.mp. OR Brief behavioral activation treatment.mp. OR behavioral activity.mp. OR behavioral activities.mp. OR behaviour therapy.mp. OR behaviour therapies.mp. OR behavioural therapy.mp. OR behavioural therapies.mp. OR behavioural activation.mp. OR behaviour activation.mp. OR behavioural activation therapy.mp. OR behaviour techniques.mp. OR behavioural activity.mp. OR behavioural activities.mp.)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,765
S1	("behavior therapy" OR behavior therapy.ti,ab OR behavioral therapy.mp. OR behavior therapies.mp. OR behavioral therapies.mp. OR ((behavior OR behavior.mp. OR behavioral.mp.)) AND activation.mp. OR activational.mp. OR activations.mp. OR activity.mp. OR activities.mp.)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	59,820

Exercise & Behavioral Activation & depression & RCT: (10 Results 3/7/18)

S7	**S5 AND S6**	**Search modes - Boolean/Phrase**	**Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO**	**10**
S6	**MM "Clinical Trials" OR RCT OR randomized***	**Search modes - Boolean/Phrase**	**Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO**	**71,545**
S5	**S3 AND S4**	**Search modes - Boolean/Phrase**	**Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO**	**92**
S4	**(((((("Mental Disorders/therapy" OR mental disorders.ti,ab OR mental disorder.mp. OR Psychiatric Diagnosis.mp. OR Behavior Disorders OR severe mental disorder.mp. OR severe mental disorders.mp. OR "Depressive Disorder, Major/therapy" OR Major Depressive Disorders.ti,ab OR Major Depressive.mp. OR Major Depressive Disorder.mp. OR psychosis.mp. OR Psychosis.mp. OR psychoses.mp. OR major depression.mp. OR severe mental illness.mp. OR insanity OR mental disorders.mp. OR diagnosed mental disorders.mp. OR diagnosed mental disorder.mp. OR depressed.mp. OR depression.mp. OR depressive.mp. OR depression were.mp. OR depression the.mp. OR depression symptoms.mp. OR depression severity.mp. OR severity of depression.mp. OR depression score.mp. OR depression scores.mp. OR depression rating.mp. OR depression ratings.mp. OR "Depressive Disorder, Treatment-Resistant" OR Treatment resistant depressive disorder.ti,ab OR depression in.mp. OR depression inventory.mp. OR depression and.mp. OR depression rating scale.mp. OR mdd.mp. OR**	**Search modes - Boolean/Phrase**	**Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO**	**141,773**

	major depression.mp. OR "Depressive Disorder/therapy" OR Depression/therapy)))))			
S3	**S1 AND S2**	**Search modes - Boolean/Phrase**	**Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO**	**2,431**
S2	**((exercise OR exercise.ti,ab OR physical activity.mp. OR walking.ti,ab OR running.ti,ab OR sports.ti,ab OR sports OR athletics.mp. OR sport.mp. OR athletic.mp. OR gym.mp. OR "Resistance Training" OR resistance training.ti,ab OR exercise program.mp. OR exercise programs.mp. OR strength training.mp. OR strength train.mp. OR weight lifting.mp. OR weight lift.mp. OR weight bearing exercise.mp. OR strengthening program.mp. OR strengthening programs.mp. OR fitness.mp. OR "physical fitness" OR physical fitness.ti,ab OR walking OR running OR jogging OR jogging.ti,ab)))**	**Search modes - Boolean/Phrase**	**Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO**	**139,919**

S1	(("behavior therapy" OR behavior therapy.ti,ab OR behavioral therapy.mp. OR behavior therapies.mp. OR behavioral therapies.mp. OR ((behavior OR behavior.mp. OR behavioral.mp.)) AND activation.mp. OR activational.mp. OR activations.mp. OR activity.mp. OR activities.mp.) OR (ACT.mp. OR behavioral activation.mp. OR behavior activation OR behavioral activation therapy.mp. OR BA.mp. OR behavioral techniques.mp. OR BATD.mp. OR BATD R.mp. OR Brief behavioral activation treatment.mp. OR behavioral activity.mp. OR behavioral activities.mp. OR behaviour therapy.mp. OR behaviour therapies.mp. OR behavioural therapy.mp. OR behavioural therapies.mp. OR behavioural activation.mp. OR behaviour activation.mp. OR behavioural activation therapy.mp. OR behaviour techniques.mp. OR behavioural activity.mp. OR behavioural activities.mp.)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database	

Exercise & Control Group & depression & RCT: (6 Results 3/7/18)

S5	S3 AND S4	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6
S4	MM "Clinical Trials" OR RCT OR randomized*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	71,545
S3	S1 AND S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	24

S2	(("Mental Disorders/therapy" OR mental disorders.ti,ab OR mental disorder.mp. OR Psychiatric Diagnosis.mp. OR Behavior Disorders OR severe mental disorder.mp. OR severe mental disorders.mp. OR "Depressive Disorder, Major/therapy" OR Major Depressive Disorders.ti,ab OR Major Depressive.mp. OR Major Depressive Disorder.mp. OR psychosis.mp. OR Psychosis.mp. OR psychoses.mp. OR major depression.mp. OR severe mental illness.mp. OR insanity OR mental disorders.mp. OR diagnosed mental disorders.mp. OR diagnosed mental disorder.mp. OR depressed.mp. OR depression.mp. OR depressive.mp. OR depression were.mp. OR depression the.mp. OR depression symptoms.mp. OR depression severity.mp. OR severity of depression.mp. OR depression score.mp. OR depression scores.mp. OR depression rating.mp. OR depression ratings.mp. OR "Depressive Disorder, Treatment-Resistant" OR Treatment resistant depressive disorder.ti,ab OR depression in.mp. OR depression inventory.mp. OR depression and.mp. OR depression rating scale.mp. OR mdd.mp. OR major depression.mp. OR "Depressive Disorder/therapy" OR Depression/therapy)))	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	141,773
S1	(exercise OR exercise.ti,ab OR physical activity.mp. OR walking.ti,ab OR running.ti,ab OR sports.ti,ab OR sports OR athletics.mp. OR sport.mp. OR athletic.mp. OR gym.mp. OR "Resistance Training" OR resistance training.ti,ab OR exercise program.mp. OR exercise programs.mp. OR strength training.mp. OR strength train.mp. OR weight lifting.mp. OR weight lift.mp. OR weight bearing exercise.mp. OR strengthening program.mp. OR strengthening programs.mp. OR fitness.mp. OR "physical fitness" OR physical fitness.ti,ab OR walking OR running OR jogging OR jogging.ti,ab) AND ((("control groups" OR ((control.mp. AND groups.mp.) OR (control.mp. AND group.mp.) OR (placebo.mp. AND group.mp.) OR (placebo.mp. AND groups.mp.)) OR control groups.ti,ab OR control group.mp. OR controlled group.mp. OR controlled groups.mp. OR controls group.mp. OR placebo group.mp. OR placebo.mp. OR placebo controlled.mp. OR standard treatment.mp. OR standard treatments.mp. OR gold standard.mp. OR Placebos OR placebos.ti,ab OR sham treatment.mp. OR sham treatments.mp.)))	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,909

Exercise & Cognitive Behavioral Therapy (CBT) & depression & RCT: 10 Results 3/7/18

S3	**S1 AND S2**	**Search modes - Boolean/Phrase**	**Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO**	**10**
S2	**MM "Clinical Trials" OR RCT OR randomized***	**Search modes - Boolean/Phrase**	**Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO**	**71,677**

S1	(exercise OR exercise.ti,ab OR physical activity.mp. OR walking.ti,ab OR running.ti,ab OR sports.ti,ab OR sports OR athletics.mp. OR sport.mp. OR athletic.mp. OR gym.mp. OR "Resistance Training" OR resistance training.ti,ab OR exercise program.mp. OR exercise programs.mp. OR strength training.mp. OR strength train.mp. OR weight lifting.mp. OR weight lift.mp. OR weight bearing exercise.mp. OR strengthening program.mp. OR strengthening programs.mp. OR fitness.mp. OR "physical fitness" OR physical fitness.ti,ab OR walking OR running OR jogging OR jogging.ti,ab) AND ("cognitive therapy" OR (cognitive.mp. AND therapy.mp.) OR cognitive therapy.mp. OR (cognitive.mp. AND behavioral.mp. AND therapy.mp.) OR cognitive behavioral therapy.mp. OR CBT.mp. OR cognitive behavior therapy.mp. OR cognition OR cognitive behavior therapy.mp. OR cognitive therapies.mp. OR cognitive therapies.mp. OR cognition therapy.mp. OR cognitive psychotherapy.mp. OR cognitive psychotherapies.mp. OR cognition therapy.mp. OR cognitive behaviour therapy.mp. OR cognitive behavioural therapies.mp.) AND ((("Mental Disorders/therapy" OR mental disorders.ti,ab OR mental disorder.mp. OR Psychiatric Diagnosis.mp. OR Behavior Disorders OR severe mental disorder.mp. OR severe mental disorders.mp. OR "Depressive Disorder, Major/therapy" OR Major Depressive Disorders.ti,ab OR Major Depressive.mp. OR Major Depressive Disorder.mp. OR psychosis.mp. OR Psychosis.mp. OR psychoses.mp. OR major depression.mp. OR severe mental illness.mp. OR insanity OR mental disorders.mp. OR diagnosed mental disorders.mp. OR diagnosed mental disorder.mp. OR depressed.mp. OR depression.mp. OR depressive.mp. OR depression were.mp. OR depression the.mp. OR depression symptoms.mp. OR depression severity.mp. OR severity of depression.mp. OR depression score.mp. OR depression scores.mp. OR depression rating.mp. OR depression ratings.mp. OR "Depressive Disorder, Treatment-Resistant" OR Treatment resistant depressive disorder.ti,ab OR depression in.mp. OR depression inventory.mp. OR depression and.mp. OR depression rating scale.mp. OR mdd.mp. OR major depression.mp. OR "Depressive Disorder/therapy" OR Depression/therapy)))	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search D (94 results)

Cognitive Behavioral Therapy (CBT) & Control Group & depression & RCT: 73 Results 3/7/18

S3	**S1 AND S2**	**Search modes - Boolean/Phrase**	**View Results (73)** **View Details** **Edit**	
	S2	**MM "Clinical Trials" OR RCT OR randomized***	**Search modes - Boolean/Phrase**	**View Results (71,545)** **View Details** **Edit**
	S1	("cognitive therapy" OR (cognitive.mp. AND therapy.mp.) OR cognitive therapy.mp. OR (cognitive.mp. AND behavioral.mp. AND therapy.mp.) OR cognitive behavioral therapy.mp. OR CBT.mp. OR cognitive behavior therapy.mp. OR cognition OR cognitive behavior therapy.mp. OR cognitive therapies.mp. OR cognitive therapies.mp. OR cognition therapy.mp. OR cognitive psychotherapy.mp. OR cognitive psychotherapies.mp. OR cognition therapy.mp. OR cognitive behaviour therapy.mp. OR cognitive behavioural therapies.mp.) AND ((("Mental Disorders/therapy" OR mental disorders.ti,ab OR mental disorder.mp. OR Psychiatric Diagnosis.mp. OR Behavior Disorders OR severe mental disorder.mp. OR severe mental disorders.mp. OR "Depressive Disorder, Major/therapy" OR Major Depressive Disorders.ti,ab OR Major Depressive.mp. OR Major Depressive Disorder.mp. OR psychosis.mp. OR Psychosis.mp. OR psychoses.mp. OR major depression.mp. OR severe mental illness.mp. OR insanity OR mental disorders.mp. OR diagnosed mental disorders.mp. OR diagnosed mental disorder.mp. OR depressed.mp. OR depression.mp. OR depressive.mp. OR depression were.mp. OR depression the.mp. OR depression symptoms.mp. OR depression severity.mp. OR severity of depression.mp. OR depression score.mp. OR depression scores.mp. OR depression rating.mp. OR depression ratings.mp. OR "Depressive Disorder, Treatment-Resistant" OR Treatment resistant depressive disorder.ti,ab OR depression in.mp. OR depression inventory.mp. OR depression and.mp. OR depression rating scale.mp. OR mdd.mp. OR major depression.mp. OR "Depressive Disorder/therapy" OR Depression/therapy))) AND ((("control groups" OR ((control.mp. AND groups.mp.) OR (control.mp. AND group.mp.) OR (placebo.mp. AND group.mp.) OR (placebo.mp. AND groups.mp.)) OR control groups.ti,ab OR control group.mp. OR controlled group.mp. OR controlled groups.mp. OR controls group.mp. OR placebo group.mp. OR placebo.mp. OR placebo controlled.mp. OR standard treatment.mp. OR standard treatments.mp. OR gold standard.mp. OR Placebos OR	**Search modes - SmartText Searching**	**View Results (219)**

		placebos.ti,ab OR sham treatment.mp. OR sham treatments.mp.)))		

Cognitive Behavioral Therapy (CBT) & Behavioral Activation & depression & RCT:

(6 Results 3/7/18)

S1	("behavior therapy"[MESH] OR "behavior therapy"[tiab] OR "behavioral therapy"[tw] OR "behavior therapies"[tw] OR "behavioral therapies"[tw] OR (("behavior"[MeSH Terms] OR "behavior"[tw] OR "behavioral"[tw])) AND activation[tw] OR activational[tw] OR activations[tw] OR activity[tw] OR activities[tw]) OR (ACT[tw] OR "behavioral activation"[tw] OR "behavior activation" OR "behavioral activation therapy"[tw] OR BA[tw] OR "behavioral techniques"[tw] OR BATD[tw] OR "BATD R"[tw] OR "Brief behavioral activation treatment"[tw] OR "behavioral activity"[tw] OR "behavioral activities"[tw] OR "behaviour therapy"[tw] OR "behaviour therapies"[tw] OR "behavioural therapy"[tw] OR "behavioural therapies"[tw] OR "behavioural activation"[tw] OR "behaviour activation"[tw] OR "behavioural activation therapy"[tw] OR "behaviour techniques"[tw] OR "behavioural activity"[tw] OR "behavioural activities"[tw]) AND (("cognitive therapy"[MeSH Terms] OR ("cognitive"[tw] AND "therapy"[tw]) OR "cognitive therapy"[tw] OR ("cognitive"[tw] AND "behavioral"[tw] AND "therapy"[tw]) OR "cognitive behavioral therapy"[tw] OR CBT[tw] OR "cognitive behavior therapy"[tw] OR "cognition"[MESH] OR "cognitive behavior therapy"[tw] OR "cognitive therapies"[tw] OR "cognitive therapies"[tw] OR "cognition therapy"[tw] OR "cognitive psychotherapy"[tw] OR "cognitive psychotherapies"[tw] OR "cognition therapy"[tw] OR "cognitive behaviour therapy"[tw] OR "cognitive behavioural therapies"[tw])) AND (((((("Mental Disorders/therapy"[Mesh] OR "mental disorders"[tiab] OR "mental disorder"[tw] OR "Psychiatric Diagnosis"[tw] OR "Behavior Disorders" OR "severe mental disorder"[tw] OR "severe mental disorders"[tw] OR "Depressive Disorder, Major/therapy"[Mesh] OR "Major Depressive Disorders"[tiab] OR "Major Depressive"[tw] OR "Major Depressive Disorder"[tw] OR psychosis[tw] OR Psychosis[tw] OR psychoses[tw] OR "major depression"[tw] OR "severe mental illness"[tw] OR insanity OR "mental disorders"[tw] OR "diagnosed mental disorders"[tw] OR "diagnosed mental disorder"[tw] OR depressed[tw] OR depression[tw] OR depressive[tw] OR "depression were"[tw] OR "depression the"[tw] OR "depression symptoms"[tw] OR "depression severity"[tw] OR "severity of depression"[tw] OR "depression score"[tw] OR "depression scores"[tw] OR "depression rating"[tw] OR "depression ratings"[tw] OR "Depressive Disorder, Treatment-Resistant"/therapy[Mesh] OR "Treatment resistant depressive disorder"[tiab] OR "depression in"[tw] OR "depression inventory"[tw] OR "depression and"[tw] OR "depression rating scale"[tw] OR mdd[tw] OR "major depression"[tw] OR "Depressive Disorder/therapy"[Mesh] OR "Depression/therapy"[Mesh]))))))	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6

Supportive Counseling combined topic search: (8 Results 3/7/18)

S3	S1 AND S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	8
S2	MM "Clinical Trials" OR RCT OR randomized*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	71,545

S1	("behavior therapy"[MESH] OR "behavior therapy"[tiab] OR "behavioral therapy"[tw] OR "behavior therapies"[tw] OR "behavioral therapies"[tw] OR (("behavior"[MeSH Terms] OR "behavior"[tw] OR "behavioral"[tw])) AND activation[tw] OR activational[tw] OR activations[tw] OR activity[tw] OR activities[tw]) OR (ACT[tw] OR "behavioral activation"[tw] OR "behavior activation" OR "behavioral activation therapy"[tw] OR BA[tw] OR "behavioral techniques"[tw] OR BATD[tw] OR "BATD R"[tw] OR "Brief behavioral activation treatment"[tw] OR "behavioral activity"[tw] OR "behavioral activities"[tw] OR "behaviour therapy"[tw] OR "behaviour therapies"[tw] OR "behavioural therapy"[tw] OR "behavioural therapies"[tw] OR "behavioural activation"[tw] OR "behaviour activation"[tw] OR "behavioural activation therapy"[tw] OR "behaviour techniques"[tw] OR "behavioural activity"[tw] OR "behavioural activities"[tw]) OR ((("exercise"[MeSH Terms] OR "exercise"[tiab] OR “physical activity”[tw] OR walking[tiab] OR running[tiab] OR sports[tiab] OR “sports”[MESH] OR athletics[tw] OR sport[tw] OR athletic[tw] OR gym[tw] OR "Resistance Training"[Mesh] OR “resistance training”[tiab] OR “exercise program”[tw] OR “exercise programs”[tw] OR “strength training”[tw] OR “strength train”[tw] OR “weight lifting”[tw] OR “weight lift”[tw] OR “weight bearing exercise”[tw] OR “strengthening program”[tw] OR “strengthening programs”[tw] OR fitness[tw] OR “physical fitness”[MESH] OR “physical fitness”[tiab] OR “walking”[MESH] OR “running”[MESH] OR “jogging”[MESH] OR jogging[tiab]) OR ("cognitive therapy"[MeSH Terms] OR ("cognitive"[tw] AND "therapy"[tw]) OR "cognitive therapy"[tw] OR ("cognitive"[tw] AND "behavioral"[tw] AND "therapy"[tw]) OR "cognitive behavioral therapy"[tw] OR CBT[tw] OR “cognitive behavior therapy”[tw] OR “cognition”[MESH] OR “cognitive behavior therapy”[tw] OR “cognitive therapies”[tw] OR “cognitive therapies”[tw] OR “cognition therapy”[tw] OR “cognitive psychotherapy”[tw] OR “cognitive psychotherapies”[tw] OR “cognition therapy”[tw] OR “cognitive behaviour therapy”[tw] OR “cognitive behavioural therapies”[tw]) OR(“supportive counseling”[tw] OR “supportive counselling”[tw] OR “supportive therapy”[tw] OR “supportive therapies”[tw] OR “person centered therapy”[tw] OR “person centered counseling”[tw] AND (supportive[tw] AND ("counselling"[tw] OR "counseling"[MeSH Terms] OR "counseling"[tiab])) AND (((((“Mental Disorders/therapy"[Mesh] OR "mental disorders"[tiab] OR "mental disorder"[tw] OR "Psychiatric Diagnosis"[tw] OR "Behavior Disorders" OR "severe mental disorder"[tw] OR "severe mental disorders"[tw] OR "Depressive	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	97

Disorder, Major/therapy"[Mesh] OR "Major Depressive Disorders"[tiab] OR "Major Depressive"[tw] OR "Major Depressive Disorder"[tw] OR psychosis[tw] OR Psychosis[tw] OR psychoses[tw] OR "major depression"[tw] OR "severe mental illness"[tw] OR insanity OR "mental disorders"[tw] OR "diagnosed mental disorders"[tw] OR "diagnosed mental disorder"[tw] OR depressed[tw] OR depression[tw] OR depressive[tw] OR "depression were"[tw] OR "depression the"[tw] OR "depression symptoms"[tw] OR "depression severity"[tw] OR "severity of depression"[tw] OR "depression score"[tw] OR "depression scores"[tw] OR "depression rating"[tw] OR "depression ratings"[tw] OR "Depressive Disorder, Treatment-Resistant"/therapy[Mesh] OR "Treatment resistant depressive disorder"[tiab] OR "depression in"[tw] OR "depression inventory"[tw] OR "depression and"[tw] OR "depression rating scale"[tw] OR mdd[tw] OR "major depression"[tw] OR "Depressive Disorder/therapy"[Mesh] OR "Depression/therapy"[Mesh])))))

Search Strategies for Scopus (Elsevier) Database
Last date searched: 3/7/18

7 Total Searches

Behavioral Activation & Control & depression & RCT (1,707 Results 3/7/18)

(INDEXTERMS ("behavior therapy") OR TITLE-ABS ("behavior therapy") OR TITLE-ABS-KEY ("behavioral therapy") OR TITLE-ABS-KEY ("behavior therapies") OR TITLE-ABS-KEY ("behavioral therapies") OR ((INDEXTERMS ("behavior") OR TITLE-ABS-KEY ("behavior") OR TITLE-ABS-KEY ("behavioral"))) AND TITLE-ABS-KEY ("activation") OR TITLE-ABS-KEY ("activational") OR TITLE-ABS-KEY ("activations") OR TITLE-ABS-KEY ("activity") OR TITLE-ABS-KEY ("activities")) OR (TITLE-ABS-KEY ("ACT") OR TITLE-ABS-KEY ("behavioral activation") OR "behavior activation" OR TITLE-ABS-KEY ("behavioral activation therapy") OR TITLE-ABS-KEY ("BA") OR TITLE-ABS-KEY ("behavioral techniques") OR TITLE-ABS-KEY ("BATD") OR TITLE-ABS-KEY ("BATD R") OR TITLE-ABS-KEY ("Brief behavioral activation treatment") OR TITLE-ABS-KEY ("behavioral activity") OR TITLE-ABS-KEY ("behavioral activities") OR TITLE-ABS-KEY ("behaviour therapy") OR TITLE-ABS-KEY ("behaviour therapies") OR TITLE-ABS-KEY ("behavioural therapy") OR TITLE-ABS-KEY ("behavioural therapies") OR TITLE-ABS-KEY ("behavioural activation") OR TITLE-ABS-KEY ("behaviour activation") OR TITLE-ABS-KEY ("behavioural activation therapy") OR TITLE-ABS-KEY ("behaviour techniques") OR TITLE-ABS-KEY ("behavioural activity") OR TITLE-ABS-KEY ("behavioural activities")) AND (((INDEXTERMS ("control groups") OR ((TITLE-ABS-KEY ("control") AND TITLE-ABS-KEY ("groups")) OR (TITLE-ABS-KEY ("control") AND TITLE-ABS-KEY ("group")) OR (TITLE-ABS-KEY ("placebo") AND TITLE-ABS-KEY ("group")) OR (TITLE-ABS-KEY ("placebo") AND TITLE-ABS-KEY ("groups"))) OR TITLE-ABS ("control groups") OR TITLE-ABS-KEY ("control group") OR TITLE-ABS-KEY ("controlled group") OR TITLE-ABS-KEY ("controlled groups") OR TITLE-ABS-KEY ("controls group") OR TITLE-ABS-KEY ("placebo group") OR TITLE-ABS-KEY ("placebo") OR TITLE-ABS-KEY ("placebo controlled") OR TITLE-ABS-KEY ("standard treatment") OR TITLE-ABS-KEY ("standard treatments") OR TITLE-ABS-KEY ("gold standard") OR INDEXTERMS ("Placebos") OR TITLE-ABS ("placebos") OR TITLE-ABS-KEY ("sham treatment") OR TITLE-ABS-KEY ("sham treatments")))) AND (((((INDEXTERMS ("Mental Disorders/therapy") OR TITLE-ABS ("mental disorders") OR TITLE-ABS-KEY ("mental disorder") OR TITLE-ABS-KEY ("Psychiatric Diagnosis") OR "Behavior Disorders" OR TITLE-ABS-KEY ("severe mental disorder") OR TITLE-ABS-KEY ("severe mental disorders") OR INDEXTERMS ("Depressive Disorder, Major/therapy") OR TITLE-ABS ("Major Depressive Disorders") OR TITLE-ABS-KEY ("Major Depressive") OR TITLE-ABS-KEY ("Major Depressive Disorder") OR TITLE-ABS-KEY ("psychosis") OR TITLE-ABS-KEY ("Psychosis") OR TITLE-ABS-KEY ("psychoses") OR TITLE-ABS-KEY ("major depression") OR TITLE-ABS-KEY (

"severe mental illness") OR "insanity" OR TITLE-ABS-KEY ("mental disorders") OR TITLE-ABS-KEY ("diagnosed mental disorders") OR TITLE-ABS-KEY ("diagnosed mental disorder") OR TITLE-ABS-KEY ("depressed") OR TITLE-ABS-KEY ("depression") OR TITLE-ABS-KEY ("depressive") OR TITLE-ABS-KEY ("depression were") OR TITLE-ABS-KEY ("depression the") OR TITLE-ABS-KEY ("depression symptoms") OR TITLE-ABS-KEY ("depression severity") OR TITLE-ABS-KEY ("severity of depression") OR TITLE-ABS-KEY ("depression score") OR TITLE-ABS-KEY ("depression scores") OR TITLE-ABS-KEY ("depression rating") OR TITLE-ABS-KEY ("depression ratings") OR INDEXTERMS ("Depressive Disorder, Treatment-Resistant") OR TITLE-ABS ("Treatment resistant depressive disorder") OR TITLE-ABS-KEY ("depression in") OR TITLE-ABS-KEY ("depression inventory") OR TITLE-ABS-KEY ("depression and") OR TITLE-ABS-KEY ("depression rating scale") OR TITLE-ABS-KEY ("mdd") OR TITLE-ABS-KEY ("major depression") OR INDEXTERMS ("Depressive Disorder/therapy") OR INDEXTERMS ("Depression/therapy")))))) AND ((((INDEXTERMS ("clinical[Title") AND INDEXTERMS ("trial[Title")) OR INDEXTERMS ("clinical trials as topic") OR "clinical trial[Publication Type]" OR INDEXTERMS ("random*[Title") OR INDEXTERMS ("random allocation") OR "therapeutic use[MeSH Subheading]"))) AND ((((("therapy[Subheading]" OR TITLE-ABS ("therapy") OR TITLE-ABS-KEY ("treatment") OR INDEXTERMS ("therapeutics") OR TITLE-ABS ("therapeutics") OR INDEXTERMS ("treatment outcome") OR TITLE-ABS ("treatment outcome"))))))) AND (depres* AND diagnos*)

Exercise & Behavioral Activation & depression & RCT (463 Results 3/7/18)

((INDEXTERMS ("behavior therapy") OR TITLE-ABS ("behavior therapy") OR TITLE-ABS-KEY ("behavioral therapy") OR TITLE-ABS-KEY ("behavior therapies") OR TITLE-ABS-KEY ("behavioral therapies") OR ((INDEXTERMS ("behavior") OR TITLE-ABS-KEY ("behavior") OR TITLE-ABS-KEY ("behavioral"))) AND TITLE-ABS-KEY ("activation") OR TITLE-ABS-KEY ("activational") OR TITLE-ABS-KEY ("activations") OR TITLE-ABS-KEY ("activity") OR TITLE-ABS-KEY ("activities")) OR (TITLE-ABS-KEY ("ACT") OR TITLE-ABS-KEY ("behavioral activation") OR "behavior activation" OR TITLE-ABS-KEY ("behavioral activation therapy") OR TITLE-ABS-KEY ("BA") OR TITLE-ABS-KEY ("behavioral techniques") OR TITLE-ABS-KEY ("BATD") OR TITLE-ABS-KEY ("BATD R") OR TITLE-ABS-KEY ("Brief behavioral activation treatment") OR TITLE-ABS-KEY ("behavioral activity") OR TITLE-ABS-KEY ("behavioral activities") OR TITLE-ABS-KEY ("behaviour therapy") OR TITLE-ABS-KEY ("behaviour therapies") OR TITLE-ABS-KEY ("behavioural therapy") OR TITLE-ABS-KEY ("behavioural therapies") OR TITLE-ABS-KEY ("behavioural activation") OR TITLE-ABS-KEY ("behaviour activation") OR TITLE-ABS-KEY ("behavioural activation therapy") OR TITLE-ABS-KEY ("behaviour techniques") OR TITLE-ABS-KEY ("behavioural activity") OR TITLE-ABS-KEY ("behavioural activities")) AND ((INDEXTERMS ("exercise") OR TITLE-ABS ("exercise") OR

TITLE-ABS-KEY ("physical activity") OR TITLE-ABS ("walking") OR TITLE-ABS ("running") OR TITLE-ABS ("sports") OR INDEXTERMS ("sports") OR TITLE-ABS-KEY ("athletics") OR TITLE-ABS-KEY ("sport") OR TITLE-ABS-KEY ("athletic") OR TITLE-ABS-KEY ("gym") OR INDEXTERMS ("Resistance Training") OR TITLE-ABS ("resistance training") OR TITLE-ABS-KEY ("exercise program") OR TITLE-ABS-KEY ("exercise programs") OR TITLE-ABS-KEY ("strength training") OR TITLE-ABS-KEY ("strength train") OR TITLE-ABS-KEY ("weight lifting") OR TITLE-ABS-KEY ("weight lift") OR TITLE-ABS-KEY ("weight bearing exercise") OR TITLE-ABS-KEY ("strengthening program") OR TITLE-ABS-KEY ("strengthening programs") OR TITLE-ABS-KEY ("fitness") OR INDEXTERMS ("physical fitness") OR TITLE-ABS ("physical fitness") OR INDEXTERMS ("walking") OR INDEXTERMS ("running") OR INDEXTERMS ("jogging") OR TITLE-ABS ("jogging")))) AND (((((INDEXTERMS ("Mental Disorders/therapy") OR TITLE-ABS ("mental disorders") OR TITLE-ABS-KEY ("mental disorder") OR TITLE-ABS-KEY ("Psychiatric Diagnosis") OR "Behavior Disorders" OR TITLE-ABS-KEY ("severe mental disorder") OR TITLE-ABS-KEY ("severe mental disorders") OR INDEXTERMS ("Depressive Disorder, Major/therapy") OR TITLE-ABS ("Major Depressive Disorders") OR TITLE-ABS-KEY ("Major Depressive") OR TITLE-ABS-KEY ("Major Depressive Disorder") OR TITLE-ABS-KEY ("psychosis") OR TITLE-ABS-KEY ("Psychosis") OR TITLE-ABS-KEY ("psychoses") OR TITLE-ABS-KEY ("major depression") OR TITLE-ABS-KEY ("severe mental illness") OR "insanity" OR TITLE-ABS-KEY ("mental disorders") OR TITLE-ABS-KEY ("diagnosed mental disorders") OR TITLE-ABS-KEY ("diagnosed mental disorder") OR TITLE-ABS-KEY ("depressed") OR TITLE-ABS-KEY ("depression") OR TITLE-ABS-KEY ("depressive") OR TITLE-ABS-KEY ("depression were") OR TITLE-ABS-KEY ("depression the") OR TITLE-ABS-KEY ("depression symptoms") OR TITLE-ABS-KEY ("depression severity") OR TITLE-ABS-KEY ("severity of depression") OR TITLE-ABS-KEY ("depression score") OR TITLE-ABS-KEY ("depression scores") OR TITLE-ABS-KEY ("depression rating") OR TITLE-ABS-KEY ("depression ratings") OR INDEXTERMS ("Depressive Disorder, Treatment-Resistant") OR TITLE-ABS ("Treatment resistant depressive disorder") OR TITLE-ABS-KEY ("depression in") OR TITLE-ABS-KEY ("depression inventory") OR TITLE-ABS-KEY ("depression and") OR TITLE-ABS-KEY ("depression rating scale") OR TITLE-ABS-KEY ("mdd") OR TITLE-ABS-KEY ("major depression") OR INDEXTERMS ("Depressive Disorder/therapy") OR INDEXTERMS ("Depression/therapy")))))) AND ((((INDEXTERMS ("clinical[Title") AND INDEXTERMS ("trial[Title")) OR INDEXTERMS ("clinical trials as topic") OR "clinical trial[Publication Type]" OR INDEXTERMS ("random*[Title") OR INDEXTERMS ("random allocation") OR "therapeutic use[MeSH Subheading]"))) AND ((((("therapy[Subheading]" OR TITLE-ABS ("therapy") OR TITLE-ABS-KEY ("treatment") OR INDEXTERMS ("therapeutics") OR TITLE-ABS ("therapeutics") OR INDEXTERMS ("treatment outcome") OR TITLE-ABS ("treatment outcome")))))) AND (depres* AND diagnos*)

Exercise & Control Group & depression & RCT (802 Results 3/7/18)

(INDEXTERMS("exercise") OR TITLE-ABS("exercise") OR TITLE-ABS-KEY("physical activity") OR TITLE-ABS("walking") OR TITLE-ABS("running") OR TITLE-ABS("sports") OR INDEXTERMS("sports") OR TITLE-ABS-KEY("athletics") OR TITLE-ABS-KEY("sport") OR TITLE-ABS-KEY("athletic") OR TITLE-ABS-KEY("gym") OR INDEXTERMS("Resistance Training") OR TITLE-ABS("resistance training") OR TITLE-ABS-KEY("exercise program") OR TITLE-ABS-KEY("exercise programs") OR TITLE-ABS-KEY("strength training") OR TITLE-ABS-KEY("strength train") OR TITLE-ABS-KEY("weight lifting") OR TITLE-ABS-KEY("weight lift") OR TITLE-ABS-KEY("weight bearing exercise") OR TITLE-ABS-KEY("strengthening program") OR TITLE-ABS-KEY("strengthening programs") OR TITLE-ABS-KEY("fitness") OR INDEXTERMS("physical fitness") OR TITLE-ABS("physical fitness") OR INDEXTERMS("walking") OR INDEXTERMS("running") OR INDEXTERMS("jogging") OR TITLE-ABS("jogging")) AND (((INDEXTERMS("control groups") OR ((TITLE-ABS-KEY("control") AND TITLE-ABS-KEY("groups")) OR (TITLE-ABS-KEY("control") AND TITLE-ABS-KEY("group")) OR (TITLE-ABS-KEY("placebo") AND TITLE-ABS-KEY("group")) OR (TITLE-ABS-KEY("placebo") AND TITLE-ABS-KEY("groups"))) OR TITLE-ABS("control groups") OR TITLE-ABS-KEY("control group") OR TITLE-ABS-KEY("controlled group") OR TITLE-ABS-KEY("controlled groups") OR TITLE-ABS-KEY("controls group") OR TITLE-ABS-KEY("placebo group") OR TITLE-ABS-KEY("placebo") OR TITLE-ABS-KEY("placebo controlled") OR TITLE-ABS-KEY("standard treatment") OR TITLE-ABS-KEY("standard treatments") OR TITLE-ABS-KEY("gold standard") OR INDEXTERMS("Placebos") OR TITLE-ABS("placebos") OR TITLE-ABS-KEY("sham treatment") OR TITLE-ABS-KEY("sham treatments")))) AND (((INDEXTERMS("Mental Disorders/therapy") OR TITLE-ABS("mental disorders") OR TITLE-ABS-KEY("mental disorder") OR TITLE-ABS-KEY("Psychiatric Diagnosis") OR "Behavior Disorders" OR TITLE-ABS-KEY("severe mental disorder") OR TITLE-ABS-KEY("severe mental disorders") OR INDEXTERMS("Depressive Disorder, Major/therapy") OR TITLE-ABS("Major Depressive Disorders") OR TITLE-ABS-KEY("Major Depressive") OR TITLE-ABS-KEY("Major Depressive Disorder") OR TITLE-ABS-KEY("psychosis") OR TITLE-ABS-KEY("Psychosis") OR TITLE-ABS-KEY("psychoses") OR TITLE-ABS-KEY("major depression") OR TITLE-ABS-KEY("severe mental illness") OR "insanity" OR TITLE-ABS-KEY("mental disorders") OR TITLE-ABS-KEY("diagnosed mental disorders") OR TITLE-ABS-KEY("diagnosed mental disorder") OR TITLE-ABS-KEY("depressed") OR TITLE-ABS-KEY("depression") OR TITLE-ABS-KEY("depressive") OR TITLE-ABS-KEY("depression were") OR TITLE-ABS-KEY("depression the") OR TITLE-ABS-KEY("depression symptoms") OR TITLE-ABS-KEY("depression severity") OR TITLE-ABS-KEY("severity of depression") OR TITLE-ABS-KEY("depression score") OR TITLE-ABS-KEY("depression scores") OR TITLE-ABS-KEY("depression rating") OR TITLE-ABS-KEY("depression ratings") OR INDEXTERMS("Depressive Disorder, Treatment-Resistant") OR TITLE-ABS("Treatment resistant depressive disorder") OR TITLE-ABS-KEY("depression in") OR TITLE-ABS-KEY("depression inventory") OR TITLE-ABS-KEY("depression and") OR TITLE-ABS-KEY("depression rating scale") OR TITLE-ABS-KEY("mdd") OR TITLE-ABS-KEY("major depression") OR INDEXTERMS("Depressive Disorder/therapy") OR INDEXTERMS("Depression/therapy")))) AND ((((INDEXTERMS("clinical[Title") AND INDEXTERMS("trial[Title")) OR INDEXTERMS("clinical trials as topic") OR "clinical trial[Publication Type]" OR INDEXTERMS("random*[Title") OR INDEXTERMS("random allocation") OR "therapeutic use[MeSH Subheading"))) AND

((((("therapy[Subheading]" OR TITLE-ABS("therapy") OR TITLE-ABS-KEY("treatment") OR INDEXTERMS("therapeutics") OR TITLE-ABS("therapeutics") OR INDEXTERMS("treatment outcome") OR TITLE-ABS("treatment outcome"))))) AND (depres* AND diagnos*)

Exercise & Cognitive Behavioral Therapy (CBT) & depression & RCT (643 Results)

(INDEXTERMS("exercise") OR TITLE-ABS("exercise") OR TITLE-ABS-KEY("physical activity") OR TITLE-ABS("walking") OR TITLE-ABS("running") OR TITLE-ABS("sports") OR INDEXTERMS("sports") OR TITLE-ABS-KEY("athletics") OR TITLE-ABS-KEY("sport") OR TITLE-ABS-KEY("athletic") OR TITLE-ABS-KEY("gym") OR INDEXTERMS("Resistance Training") OR TITLE-ABS("resistance training") OR TITLE-ABS-KEY("exercise program") OR TITLE-ABS-KEY("exercise programs") OR TITLE-ABS-KEY("strength training") OR TITLE-ABS-KEY("strength train") OR TITLE-ABS-KEY("weight lifting") OR TITLE-ABS-KEY("weight lift") OR TITLE-ABS-KEY("weight bearing exercise") OR TITLE-ABS-KEY("strengthening program") OR TITLE-ABS-KEY("strengthening programs") OR TITLE-ABS-KEY("fitness") OR INDEXTERMS("physical fitness") OR TITLE-ABS("physical fitness") OR INDEXTERMS("walking") OR INDEXTERMS("running") OR INDEXTERMS("jogging") OR TITLE-ABS("jogging")) AND (INDEXTERMS("cognitive therapy") OR (TITLE-ABS-KEY("cognitive") AND TITLE-ABS-KEY("therapy")) OR TITLE-ABS-KEY("cognitive therapy") OR (TITLE-ABS-KEY("cognitive") AND TITLE-ABS-KEY("behavioral") AND TITLE-ABS-KEY("therapy")) OR TITLE-ABS-KEY("cognitive behavioral therapy") OR TITLE-ABS-KEY("CBT") OR TITLE-ABS-KEY("cognitive behavior therapy") OR INDEXTERMS("cognition") OR TITLE-ABS-KEY("cognitive behavior therapy") OR TITLE-ABS-KEY("cognitive therapies") OR TITLE-ABS-KEY("cognitive therapies") OR TITLE-ABS-KEY("cognition therapy") OR TITLE-ABS-KEY("cognitive psychotherapy") OR TITLE-ABS-KEY("cognitive psychotherapies") OR TITLE-ABS-KEY("cognition therapy") OR TITLE-ABS-KEY("cognitive behaviour therapy") OR TITLE-ABS-KEY("cognitive behavioural therapies")) AND (((INDEXTERMS("Mental Disorders/therapy") OR TITLE-ABS("mental disorders") OR TITLE-ABS-KEY("mental disorder") OR TITLE-ABS-KEY("Psychiatric Diagnosis") OR "Behavior Disorders" OR TITLE-ABS-KEY("severe mental disorder") OR TITLE-ABS-KEY("severe mental disorders") OR INDEXTERMS("Depressive Disorder, Major/therapy") OR TITLE-ABS("Major Depressive Disorders") OR TITLE-ABS-KEY("Major Depressive") OR TITLE-ABS-KEY("Major Depressive Disorder") OR TITLE-ABS-KEY("psychosis") OR TITLE-ABS-KEY("Psychosis") OR TITLE-ABS-KEY("psychoses") OR TITLE-ABS-KEY("major depression") OR TITLE-ABS-KEY("severe mental illness") OR "insanity" OR TITLE-ABS-KEY("mental disorders") OR TITLE-ABS-KEY("diagnosed mental disorders") OR TITLE-ABS-KEY("diagnosed mental disorder") OR TITLE-ABS-KEY("depressed") OR TITLE-ABS-KEY("depression") OR TITLE-ABS-KEY("depressive") OR TITLE-ABS-KEY("depression were") OR TITLE-ABS-KEY("depression the") OR TITLE-ABS-KEY("depression symptoms") OR TITLE-ABS-KEY("depression severity") OR TITLE-ABS-KEY("severity of depression") OR TITLE-ABS-KEY("depression score") OR TITLE-ABS-KEY("depression scores") OR TITLE-ABS-KEY("depression rating") OR TITLE-ABS-KEY("depression ratings") OR INDEXTERMS("Depressive Disorder, Treatment-Resistant") OR TITLE-

ABS("Treatment resistant depressive disorder") OR TITLE-ABS-KEY("depression in") OR TITLE-ABS-KEY("depression inventory") OR TITLE-ABS-KEY("depression and") OR TITLE-ABS-KEY("depression rating scale") OR TITLE-ABS-KEY("mdd") OR TITLE-ABS-KEY("major depression") OR INDEXTERMS("Depressive Disorder/therapy") OR INDEXTERMS("Depression/therapy")))) AND ((((INDEXTERMS("clinical[Title") AND INDEXTERMS("trial[Title")) OR INDEXTERMS("clinical trials as topic") OR "clinical trial[Publication Type]" OR INDEXTERMS("random*[Title") OR INDEXTERMS("random allocation") OR "therapeutic use[MeSH Subheading]"))) AND (depres* AND diagnos*)

Cognitive Behavioral Therapy (CBT) & Control Group & depression & RCT (2,463 Results 3/7/18)

(INDEXTERMS("cognitive therapy") OR (TITLE-ABS-KEY("cognitive") AND TITLE-ABS-KEY("therapy")) OR TITLE-ABS-KEY("cognitive therapy") OR (TITLE-ABS-KEY("cognitive") AND TITLE-ABS-KEY("behavioral") AND TITLE-ABS-KEY("therapy")) OR TITLE-ABS-KEY("cognitive behavioral therapy") OR TITLE-ABS-KEY("CBT") OR TITLE-ABS-KEY("cognitive behavior therapy") OR INDEXTERMS("cognition") OR TITLE-ABS-KEY("cognitive behavior therapy") OR TITLE-ABS-KEY("cognitive therapies") OR TITLE-ABS-KEY("cognitive therapies") OR TITLE-ABS-KEY("cognition therapy") OR TITLE-ABS-KEY("cognitive psychotherapy") OR TITLE-ABS-KEY("cognitive psychotherapies") OR TITLE-ABS-KEY("cognition therapy") OR TITLE-ABS-KEY("cognitive behaviour therapy") OR TITLE-ABS-KEY("cognitive behavioural therapies")) AND ((((INDEXTERMS("control groups") OR ((TITLE-ABS-KEY("control") AND TITLE-ABS-KEY("groups")) OR (TITLE-ABS-KEY("control") AND TITLE-ABS-KEY("group")) OR (TITLE-ABS-KEY("placebo") AND TITLE-ABS-KEY("group")) OR (TITLE-ABS-KEY("placebo") AND TITLE-ABS-KEY("groups"))) OR TITLE-ABS("control groups") OR TITLE-ABS-KEY("control group") OR TITLE-ABS-KEY("controlled group") OR TITLE-ABS-KEY("controlled groups") OR TITLE-ABS-KEY("controls group") OR TITLE-ABS-KEY("placebo group") OR TITLE-ABS-KEY("placebo") OR TITLE-ABS-KEY("placebo controlled") OR TITLE-ABS-KEY("standard treatment") OR TITLE-ABS-KEY("standard treatments") OR TITLE-ABS-KEY("gold standard") OR INDEXTERMS("Placebos") OR TITLE-ABS("placebos") OR TITLE-ABS-KEY("sham treatment") OR TITLE-ABS-KEY("sham treatments"))))) AND (((((INDEXTERMS("Mental Disorders/therapy") OR TITLE-ABS("mental disorders") OR TITLE-ABS-KEY("mental disorder") OR TITLE-ABS-KEY("Psychiatric Diagnosis") OR "Behavior Disorders" OR TITLE-ABS-KEY("severe mental disorder") OR TITLE-ABS-KEY("severe mental disorders") OR INDEXTERMS("Depressive Disorder, Major/therapy") OR TITLE-ABS("Major Depressive Disorders") OR TITLE-ABS-KEY("Major Depressive") OR TITLE-ABS-KEY("Major Depressive Disorder") OR TITLE-ABS-KEY("psychosis") OR TITLE-ABS-KEY("Psychosis") OR TITLE-ABS-KEY("psychoses") OR TITLE-ABS-KEY("major depression") OR TITLE-ABS-KEY("severe mental illness") OR "insanity" OR TITLE-ABS-KEY("mental disorders") OR TITLE-ABS-KEY("diagnosed mental disorders") OR TITLE-ABS-KEY("diagnosed mental disorder") OR TITLE-ABS-KEY("depressed") OR TITLE-ABS-KEY("depression") OR TITLE-ABS-KEY("depressive") OR TITLE-ABS-KEY("depression were") OR TITLE-ABS-KEY("depression the") OR TITLE-ABS-KEY("depression

symptoms") OR TITLE-ABS-KEY("depression severity") OR TITLE-ABS-KEY("severity of depression") OR TITLE-ABS-KEY("depression score") OR TITLE-ABS-KEY("depression scores") OR TITLE-ABS-KEY("depression rating") OR TITLE-ABS-KEY("depression ratings") OR INDEXTERMS("Depressive Disorder, Treatment-Resistant") OR TITLE-ABS("Treatment resistant depressive disorder") OR TITLE-ABS-KEY("depression in") OR TITLE-ABS-KEY("depression inventory") OR TITLE-ABS-KEY("depression and") OR TITLE-ABS-KEY("depression rating scale") OR TITLE-ABS-KEY("mdd") OR TITLE-ABS-KEY("major depression") OR INDEXTERMS("Depressive Disorder/therapy") OR INDEXTERMS("Depression/therapy")))))) AND ((((INDEXTERMS("clinical[Title") AND INDEXTERMS("trial[Title")) OR INDEXTERMS("clinical trials as topic") OR "clinical trial[Publication Type]" OR INDEXTERMS("random*[Title") OR INDEXTERMS("random allocation") OR "therapeutic use[MeSH Subheading]"))) AND ((((((("therapy[Subheading]" OR TITLE-ABS("therapy") OR TITLE-ABS-KEY("treatment") OR INDEXTERMS("therapeutics") OR TITLE-ABS("therapeutics") OR

INDEXTERMS("treatment outcome") OR TITLE-ABS("treatment outcome")))))))) AND (depres* AND diagnos*)

Cognitive Behavioral Therapy (CBT) & Behavioral Activation & depression & RCT (3,105 Results 3/7/18)

(INDEXTERMS("behavior therapy") OR TITLE-ABS("behavior therapy") OR TITLE-ABS-KEY("behavioral therapy") OR TITLE-ABS-KEY("behavior therapies") OR TITLE-ABS-KEY("behavioral therapies") OR ((INDEXTERMS("behavior") OR TITLE-ABS-KEY("behavior") OR TITLE-ABS-KEY("behavioral"))) AND TITLE-ABS-KEY("activation") OR TITLE-ABS-KEY("activational") OR TITLE-ABS-KEY("activations") OR TITLE-ABS-KEY("activity") OR TITLE-ABS-KEY("activities")) OR (TITLE-ABS-KEY("ACT") OR TITLE-ABS-KEY("behavioral activation") OR "behavior activation" OR TITLE-ABS-KEY("behavioral activation therapy") OR TITLE-ABS-KEY("BA") OR TITLE-ABS-KEY("behavioral techniques") OR TITLE-ABS-KEY("BATD") OR TITLE-ABS-KEY("BATD R") OR TITLE-ABS-KEY("Brief behavioral activation treatment") OR TITLE-ABS-KEY("behavioral activity") OR TITLE-ABS-KEY("behavioral activities") OR TITLE-ABS-KEY("behaviour therapy") OR TITLE-ABS-KEY("behaviour therapies") OR TITLE-ABS-KEY("behavioural therapy") OR TITLE-ABS-KEY("behavioural therapies") OR TITLE-ABS-KEY("behavioural activation") OR TITLE-ABS-KEY("behaviour activation") OR TITLE-ABS-KEY("behavioural activation therapy") OR TITLE-ABS-KEY("behaviour techniques") OR TITLE-ABS-KEY("behavioural activity") OR TITLE-ABS-KEY("behavioural activities")) AND ((INDEXTERMS("cognitive therapy") OR (TITLE-ABS-KEY("cognitive") AND TITLE-ABS-KEY("therapy")) OR TITLE-ABS-KEY("cognitive therapy") OR (TITLE-ABS-KEY("cognitive") AND TITLE-ABS-KEY("behavioral") AND TITLE-ABS-KEY("therapy")) OR TITLE-ABS-KEY("cognitive behavioral therapy") OR TITLE-ABS-KEY("CBT") OR TITLE-ABS-KEY("cognitive behavior therapy") OR INDEXTERMS("cognition") OR TITLE-ABS-KEY("cognitive behavior therapy") OR TITLE-ABS-

KEY("cognitive therapies") OR TITLE-ABS-KEY("cognitive therapies") OR TITLE-ABS-KEY("cognition therapy") OR TITLE-ABS-KEY("cognitive psychotherapy") OR TITLE-ABS-KEY("cognitive psychotherapies") OR TITLE-ABS-KEY("cognition therapy") OR TITLE-ABS-KEY("cognitive behaviour therapy") OR TITLE-ABS-KEY("cognitive behavioural therapies"))) AND (((((INDEXTERMS("Mental Disorders/therapy") OR TITLE-ABS("mental disorders") OR TITLE-ABS-KEY("mental disorder") OR TITLE-ABS-KEY("Psychiatric Diagnosis") OR "Behavior Disorders" OR TITLE-ABS-KEY("severe mental disorder") OR TITLE-ABS-KEY("severe mental disorders") OR INDEXTERMS("Depressive Disorder, Major/therapy") OR TITLE-ABS("Major Depressive Disorders") OR TITLE-ABS-KEY("Major Depressive") OR TITLE-ABS-KEY("Major Depressive Disorder") OR TITLE-ABS-KEY("psychosis") OR TITLE-ABS-KEY("Psychosis") OR TITLE-ABS-KEY("psychoses") OR TITLE-ABS-KEY("major depression") OR TITLE-ABS-KEY("severe mental illness") OR "insanity" OR TITLE-ABS-KEY("mental disorders") OR TITLE-ABS-KEY("diagnosed mental disorders") OR TITLE-ABS-KEY("diagnosed mental disorder") OR TITLE-ABS-KEY("depressed") OR TITLE-ABS-KEY("depression") OR TITLE-ABS-KEY("depressive") OR TITLE-ABS-KEY("depression were") OR TITLE-ABS-KEY("depression the") OR TITLE-ABS-KEY("depression symptoms") OR TITLE-ABS-KEY("depression severity") OR TITLE-ABS-KEY("severity of depression") OR TITLE-ABS-KEY("depression score") OR TITLE-ABS-KEY("depression scores") OR TITLE-ABS-KEY("depression rating") OR TITLE-ABS-KEY("depression ratings") OR INDEXTERMS("Depressive Disorder, Treatment-Resistant") OR TITLE-ABS("Treatment resistant depressive disorder") OR TITLE-ABS-KEY("depression in") OR TITLE-ABS-KEY("depression inventory") OR TITLE-ABS-KEY("depression and") OR TITLE-ABS-KEY("depression rating scale") OR TITLE-ABS-KEY("mdd") OR TITLE-ABS-KEY("major depression") OR INDEXTERMS("Depressive Disorder/therapy") OR INDEXTERMS("Depression/therapy")))))) AND ((((INDEXTERMS("clinical[Title") AND INDEXTERMS("trial[Title")) OR INDEXTERMS("clinical trials as topic") OR "clinical trial[Publication Type]" OR INDEXTERMS("random*[Title") OR INDEXTERMS("random allocation") OR "therapeutic use[MeSH Subheading]"))) AND (((((("therapy[Subheading]" OR TITLE-ABS("therapy") OR TITLE-ABS-KEY("treatment") OR INDEXTERMS("therapeutics") OR TITLE-ABS("therapeutics") OR INDEXTERMS("treatment outcome") OR TITLE-ABS("treatment outcome")))))) AND (depres* AND diagnos*)

Supportive Counseling combined topic search: (13 Results 3/1/18)

(((INDEXTERMS ("exercise") OR TITLE-ABS ("exercise") OR TITLE-ABS-KEY ("physical activity") OR TITLE-ABS ("walking") OR TITLE-ABS ("running") OR TITLE-ABS ("sports") OR INDEXTERMS ("sports") OR TITLE-ABS-KEY ("athletics") OR TITLE-ABS-KEY ("sport") OR TITLE-ABS-KEY ("athletic") OR TITLE-ABS-KEY ("gym") OR INDEXTERMS ("resistance training") OR TITLE-ABS ("resistance training") OR TITLE-ABS-KEY ("exercise program") OR TITLE-ABS-KEY ("exercise programs") OR TITLE-ABS-KEY ("strength training") OR TITLE-ABS-KEY (

"strength train") OR TITLE-ABS-KEY ("weight lifting") OR TITLE-ABS-KEY ("weight lift") OR TITLE-ABS-KEY ("weight bearing exercise") OR TITLE-ABS-KEY ("strengthening program") OR TITLE-ABS-KEY ("strengthening programs") OR TITLE-ABS-KEY ("fitness") OR INDEXTERMS ("physical fitness") OR TITLE-ABS ("physical fitness") OR INDEXTERMS ("walking") OR INDEXTERMS ("running") OR INDEXTERMS ("jogging") OR TITLE-ABS ("jogging")) AND (INDEXTERMS ("cognitive therapy") OR (TITLE-ABS-KEY ("cognitive") AND TITLE-ABS-KEY ("therapy")) OR TITLE-ABS-KEY ("cognitive therapy") OR (TITLE-ABS-KEY ("cognitive") AND TITLE-ABS-KEY ("behavioral") AND TITLE-ABS-KEY ("therapy")) OR TITLE-ABS-KEY ("cognitive behavioral therapy") OR TITLE-ABS-KEY ("CBT") OR TITLE-ABS-KEY ("cognitive behavior therapy") OR INDEXTERMS ("cognition") OR TITLE-ABS-KEY ("cognitive behavior therapy") OR TITLE-ABS-KEY ("cognitive therapies") OR TITLE-ABS-KEY ("cognitive therapies") OR TITLE-ABS-KEY ("cognition therapy") OR TITLE-ABS-KEY ("cognitive psychotherapy") OR TITLE-ABS-KEY ("cognitive psychotherapies") OR TITLE-ABS-KEY ("cognition therapy") OR TITLE-ABS-KEY ("cognitive behaviour therapy") OR TITLE-ABS-KEY ("cognitive behavioural therapies")) AND (((INDEXTERMS ("Mental Disorders/therapy") OR TITLE-ABS ("mental disorders") OR TITLE-ABS-KEY ("mental disorder") OR TITLE-ABS-KEY ("Psychiatric Diagnosis") OR "Behavior Disorders" OR TITLE-ABS-KEY ("severe mental disorder") OR TITLE-ABS-KEY ("severe mental disorders") OR INDEXTERMS ("Depressive Disorder, Major/therapy") OR TITLE-ABS ("Major Depressive Disorders") OR TITLE-ABS-KEY ("Major Depressive") OR TITLE-ABS-KEY ("Major Depressive Disorder") OR TITLE-ABS-KEY ("psychosis") OR TITLE-ABS-KEY ("Psychosis") OR TITLE-ABS-KEY ("psychoses") OR TITLE-ABS-KEY ("major depression") OR TITLE-ABS-KEY ("severe mental illness") OR "insanity" OR TITLE-ABS-KEY ("mental disorders") OR TITLE-ABS-KEY ("diagnosed mental disorders") OR TITLE-ABS-KEY ("diagnosed mental disorder") OR TITLE-ABS-KEY ("depressed") OR TITLE-ABS-KEY ("depression") OR TITLE-ABS-KEY ("depressive") OR TITLE-ABS-KEY ("depression were") OR TITLE-ABS-KEY ("depression the") OR TITLE-ABS-KEY ("depression symptoms") OR TITLE-ABS-KEY ("depression severity") OR TITLE-ABS-KEY ("severity off depression") OR TITLE-ABS-KEY ("depression score") OR TITLE-ABS-KEY ("depression scores") OR TITLE-ABS-KEY ("depression rating") OR TITLE-ABS-KEY ("depression ratings") OR INDEXTERMS ("Depressive Disorder, Treatment-Resistant") OR TITLE-ABS ("Treatment resistant depressive disorder") OR TITLE-ABS-KEY ("depression in") OR TITLE-ABS-KEY ("depression inventory") OR TITLE-ABS-KEY ("depression and") OR TITLE-ABS-KEY ("depression rating scale") OR TITLE-ABS-KEY ("mdd") OR TITLE-ABS-KEY ("major depression") OR INDEXTERMS ("Depressive Disorder/therapy") OR INDEXTERMS ("Depression/therapy")))) AND ((((INDEXTERMS ("clinical[title") AND INDEXTERMS ("trial[Title")) OR INDEXTERMS ("clinical trials as topic") OR "clinical trial[publication type]" OR INDEXTERMS ("random*[Title") OR INDEXTERMS ("random allocation") OR "therapeutic use[mesh subheading]")))) OR (((INDEXTERMS ("behavior therapy") OR TITLE-ABS ("behavior therapy") OR TITLE-ABS-KEY ("behavioral therapy") OR TITLE-ABS-KEY ("behavior therapies") OR TITLE-ABS-KEY ("behavioral therapies") OR ((INDEXTERMS ("behavior") OR TITLE-ABS-KEY ("behavior") OR TITLE-ABS-KEY ("behavioral"))) AND TITLE-ABS-KEY ("activation") OR TITLE-ABS-KEY ("activation") OR TITLE-ABS-KEY (

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Search Strategies for Clinical Trials.gov
Last date searched: 3/8/18

Date last searched: 3/8/18

clinicaltrials.gov

Search #1:

13 Studies found for: **Behavioral Activation AND Control AND depression | Completed Studies | Studies With Results | Interventional Studies**
Also searched for **Depressive Disorders** and **Controlled**. See Search Details

Applied Filters: Completed With Results Interventional

Search #2

8 Studies found for: **Exercise AND Cognitive Behavioral Therapy AND depression | Studies With Results | Interventional Studies**
Also searched for **Treatment**. See Search Details

Applied Filters: With Results Interventional

Search #3

7 Studies found for: **Counseling AND Exercise AND depression | Studies With Results | Interventional Studies**
Also searched for **Physical Activities**. See Search Details

Applied Filters: With Results Interventional

Search #4

21 Studies found for: **Behavioral Activation | Studies With Results | Interventional Studies | depression**
Also searched for **Depressive Disorders** and **Behavior**. See Search Details

Applied Filters: With Results Interventional

Search #5

5 Studies found for:

Supportive Counseling

| Studies With Results | Interventional Studies | depression
Also searched for **Depressive Disorders** and **Behavior**. See Search Details

Applied Filters: With Results Interventional

Search #6

50 Studies found for:

Cognitive Behavioral Therapy

| Studies With Results | Interventional Studies | depression
Also searched for **Depressive Disorders** and **Behavior**. See Search Details

Applied Filters: With Results Interventional

Search #7

20 Studies found for:

Exercise

| Studies With Results | Interventional Studies | depression
Also searched for **Depressive Disorders** and **Behavior**. See Search Details
Applied Filters: With Results Interventional

Search Strategies for PsychiatryOnline.org
Last date searched: 3/2/18

Search #1

3 Results Date last searched 3.2.18

Search: Behavioral Activation AND Control AND depression AND Randomized
Searched Within: Depressive Disorders Articles American Journal of Psychiatry

Search #2:
11 Results Date last searched 3.2.18

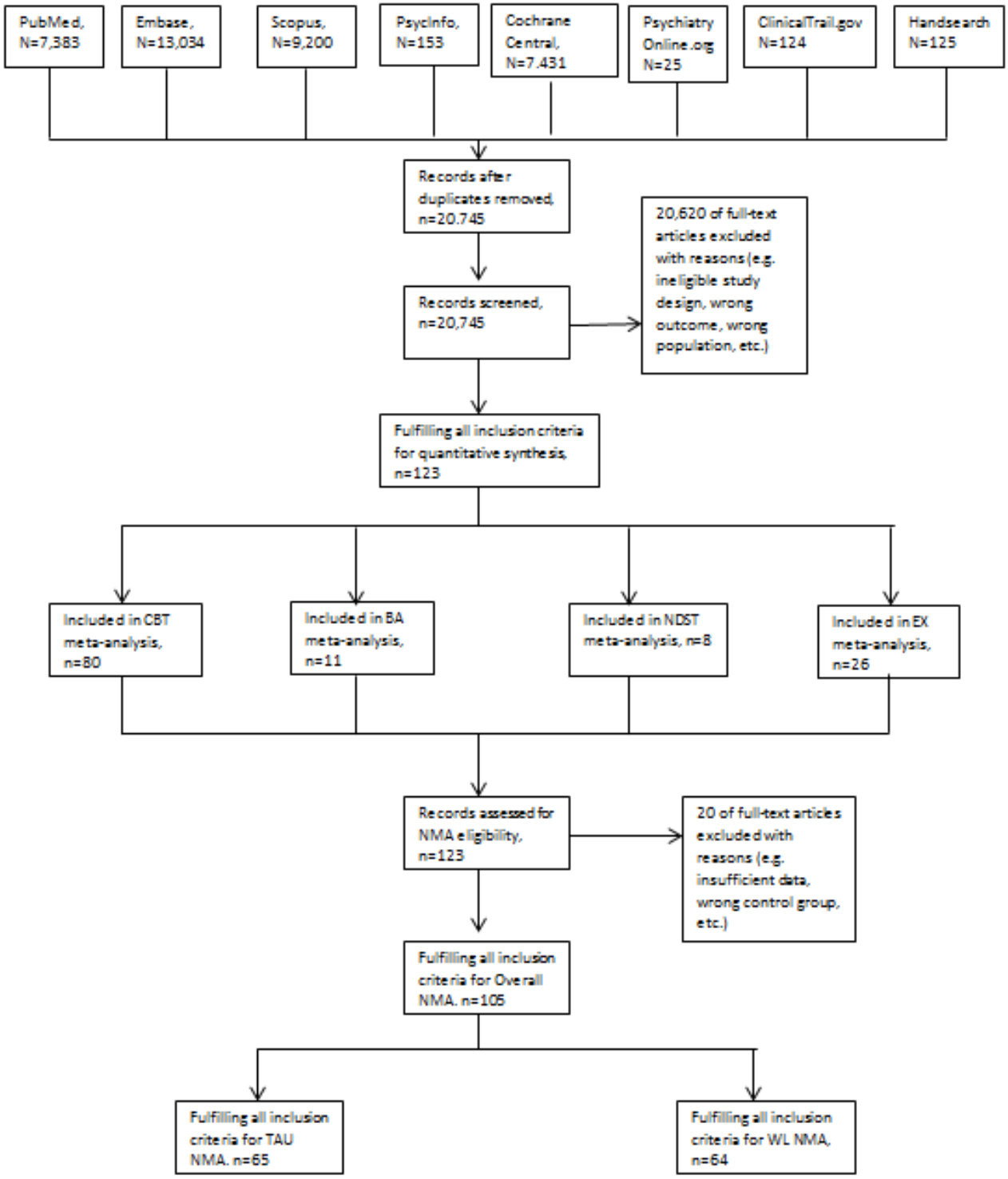
Search: Exercise AND Cognitive Behavioral Therapy AND depression AND randomized
Searched within: Cognitive-Behavioral Therapy American Journal of Psychiatry Since 2011

Search #3:

11 Results Date last searched 3.2.18
Search: Supportive AND Exercise AND depression AND randomized
Searched within: Depressive Disorders American Journal of Psychiatry Since 2011

APPENDIX C

STUDY FLOW DIAGRAM



APPENDIX D

CHARACTERISTICS OF INCLUDED STUDIES

Author, year	**Diagnosis**	**Total Number of patients**	**Total Number of patients per group**	**Intervention**	**Assessments, frequency, time/session**	**Outcome Assessment**
Andersson et al.,2005	Mild to Moderate Depression	117	CBT: 57 PLC: 60	T: Cognitive Behavioral Therapy C: Placebo	Baseline, 10 weeks, 6 months (follow up)	BDI and MADRS-S
Ayen et al., 2004	Depression	41	NDST: 20 CBT:11 WL: 10	T: Non-directive supportive therapy T2: Cognitive Behavioral Therapy C: Wl	Baseline, 3 months, and 6 and 12 months (follow-up)	BDI
Beach et al., 1992	Dysthymia or MDD	45	CBT: 15 WL: 15	T: Cognitive Behavioral Therapy C: WL	Baseline, post-treatmennt (appx. 15 weeks)	BDI
Berger et al., 2011	Dysthymia or MDD	76	Unguided self-help CBT: 25 Guided self-help CBT: 25 WL: 26	T: Unguided self-help CBT T2: Guided self-help CBT C: WL	Baseline, 10 weeks, and 6 months (follow up)	BDI-II
Bernard et al., 2015	Depression	121	EX: 61 WL: 60	T: Aerobic Exercise C: WL	Baseline, 6 months	BDI
Blumenthal et al., 2007	Major Depression	202	Supervised EX: 51 Home-based EX: 53 PLC: 49	T: Supervised aerobic exercise T2: Home-based aerobic exercise C: PLC	Baseline, 16 weeks; Aerobic exercise (walking or jogging) based on HR	HAMD
Bombardier et al., 2013	MDD or Dysthymia in individuals with MS	92	BA: 44 WL: 48	T: Behavioral Activation Therapy C: WL	Baseline, 12 weeks, 24 weeks (follow up)	HAMD

Bright et al., 1999	Depression	98	CBT: 27 CBT: 21 NDST:28 NDST: 22	T: CBT administered by professionals or paraprofessionals T2: NDST administered by professionals or paraprofessionals	Baseline, 10 weeks, 2 months (follow up)	HAMD and BDI
Brown et al., 1984	Depression	63	CBT: 13 CBT: 14 CBT: 25 WL: 11	T: Individual, telephone or group CBT C: WL	Baseline, posttreatment, and 1 and 6 months (follow ups)	BDI and CES-D
Carta et al., 2012	Depression	64	CBT: 34 TAU: 30	T: Cognitive Behavioral Therapy C: TAU	Baseline, 3 months and 6 months	BDI
Chen et al., 2000	Postnatal depression	60	NDST: 30 TAU: 30	T: Non-directive Supportive Therapy C: TAU	Baseline, 4 weeks	BDI
Choi et al., 2012	Depression	63	i-CBT: 32 WL: 31	T: Internet Cognitive Behavioral Therapy C: WL	Baseline, 8 weeks, and 3 month (follow up)	BDI (Chinese Version) and PHQ-9
Christensen et al., 2004	Depression	525	CBT: 182 PLC: 178	T: Cognitive Behavioral Therapy C: Placebo	Baseline, 6 weeks	CES-D
Collado et al., 2016	MDD	46	BA: 23 NDST: 23	T: Behavioral Activation T2: Non-Directive supportive Therapy	Baseline, 10 weeks, 1 month (follow up)	BDI
Comas-Diaz, 1981	Depression	26	CBT: 8 BA: 8 WL: 10	T: Cognitive Behavioral Therapy T2: Behavioral Activation Therapy C: WL	Baseline, 4 weeks, 5 weeks (follow up)	BDI and HAMD

Cooper et al., 2003	Post-Partum Depression	190	NDST 48 CBT: 42 TAU: 52	T: Non-directive supportive Therapy T2: Cognitive Behavioral Therapy C: TAU	Baseline, 4.5 months, and 9 months, 18 months and 5 years (follow ups)	EPDS
Cullen, 2003	Depression	17	Behavioral Activation: 8 WL: 9	T: Behavioral Activation C: WL	Baseline, posttreatment, and 3 months (follow up)	BDI-II
Dobkin et al., 2011	Depression	80	CBT: 41 TAU: 39	T: Cognitive Behavioral Therapy C: TAU	Baseline, 5 weeks, 10 weeks, and 14 weeks; CBT over 10 weeks	HAMD and BDI
Doering et al., 2016	Depression	53	CBT: 33 TAU: 20	T: Cognitive Behavioral Therapy C: TAU	Baseline, 8 weeks	BDI
Duarte et al., 2009	Major Depressive Disorder	85	CBT: 41 TAU: 44	T: Group Cognitive Behavioral Therapy C: TAU	Baseline, 3 months, 9 month (follow up)	BDI
Dwight-Johnson et al., 2011	Probable MDD	101	CBT: 50 TAU:51	T: Cognitive Behavioral Therapy C: TAU	Baseline, 6 weeks, 3 months, and 6 months; 8 sessions	PHQ-9
Embling, 2002	Unipolar Depression	38	CBT: 19 WL: 19	T: Cognitive Behavioral Therapy C: WL	Baseline, 6 weeks, 12 weeks; 12 sessions over 8 weeks	BDI-II
Fann et al., 2015	MDD	100	CBT-T: 40 CBT-IP: 18 TAU: 42	T: Telephone Administered CBT T2: In persons CBT C: TAU	Baseline, 8 weeks, 16 weeks, and 24 weeks	HAMD-17

Faramarzi et al., 2008	Mild to Moderate Depression	89	CBT: 29 TAU: 30	T: Cognitive Behavioral Therapy C: TAU	Baseline, 3 months; Weekly sessions over 10 weeks	BDI
Freedland et al., 2009	Minor or Major Depression	123	CBT: 41 TAU: 40	T: Cognitive Behavioral Therapy C: TAU	Baseline, 3 months, 6 months, 9 months; weekly, individual sessions	HAMD and BDI
Freire et al., 2015	Depression	36	CBT: 17 NDST: 19	T: Cognitive Behavioral Therapy T2: Non-Directive Supportive Therapy	Baseline, 3 months, 6 months (follow up)	GRID, HAMD-17, and PHQ-9
Furukawa et al., 2012	Depression	118	CBT: 58 TAU: 60	T: Telephone administered CBT C: TAU	Baseline, 4 months, 8 month (follow up)	BDI-II
Gallagher et al., 1982	Depression	30	CBT: 10 BA: 10	T: Cognitive Behavioral Therapy T2: Behavioral Activation Therapy	Baseline, 12 weeks, and 1 year (follow up)	HAMD and BDI
Hallgren et al., 2015	Depression	947	EX: 317 CBT: 317 TAU: 317	T: Physical Exercise T2: internet based Cognitive Behavioral Therapy C: TAU	Baseline, 12 weeks, 3 months (follow up)	MADRS
Hamdan-Mansour et al., 2009	Severe Depressive Symptoms	84	CBT: 44 WL: 40	T: Cognitive Behavioral Therapy C: WL	Baseline, 10 weeks, 3 months (follow up); 1 weekly session over 10 weeks	BDI (Arabic Version)
Haringsma et al., 2006	Depression	119	CBT: 61 WL: 58	T: Cognitive Behavioral Therapy C: WL	Baseline, 10 weeks, 2 and 14 months (follow up)	CES-D (Dutch Version)

Hautzinger & Welz, 2004	Depression	85	CBT: 55 WL: 30	T: Cognitive Behavioral Therapy C: WL	Baseline, posttreatment, 6 months (follow up)	GDS, IDS and SCLD
Hayden et al., 2012	Depression	34	CBT: 20 NDST: 14	T: Cognitive Behavioral Therapy T2: Non-directive Supportive Therapy	Baseline, 10 weeks	BDI
Hegerl et al., 2009	Depression	368	CBT: 61 NDST: 59 PLC: 83	T: Cognitive Behavioral Therapy T2: Non-Directive Supportive Therapy	Baseline, 10 weeks	HAMD and IDS
Helgadottir et al., 2017	Moderate Depression	620	Light EX: 106 Mod EX: 105 High EX: 99 TAU: 310	T: Light Aerobic Exercise T2: Moderate Aerobic Exercise T3: Vigorous Aerobic Exercise C: TAU	Baseline, post-treatment, 12 month (follow up)	MADRS
Hess-Homeier, 1981	Depression	17	CBT: 6 EX: 5 WL: 6	T: Cognitive Behavioral Therapy T2: Aerobic Exercise C: WL	Baseline, 5 weeks, 8 weeks and 6, 9 and 12 months (follow up)	BDI
Ho et al., 2014	Mild to Moderate Depression	52	EX: 26 TAU: 26	T: Exercise C: TAU	Baseline, 3 weeks	MADRS and BDI (Chinese Version)
Horrell et al., 2014	Depression	452	CBT: 228 WL: 231	T: Cognitive Behavioral Therapy C: WL	Baseline, 12 weeks	BDI-II
Huang et al., 2015	Depression	57	EX: 19 CBT: 18 TAU: 20	T: Physical Exercise T2: Cognitive Behavioral Therapy C: TAU	Baseline, 12 weeks, 3 months, and 6 months	GDS

Hummel et al., 2017	Depression	155	CBT: 56 TAU: 99	T: Cognitive Behavioral Therapy C: TAU	Baseline, 4 months; 15-90 min sessions	HAMD
Hunter et al., 2012	Depression	73	CBT: 47 TAU: 26	T: Cognitive Behavioral Therapy C: TAU	Baseline, 3 months, and 6 months (follow up)	BDI-II
Jacobson et al., 1996	Depression	151	BA: 57 CBT: 50	T: Behavioral Activation Therapy T2: Cognitive Behavioral Therapy	Baseline, post-treatment, 6,12,18, and 24 months (follow ups)	HAMD and BDI
Jamison et al., 1995	Minor to Moderate Depression	80	CBT: 40 WL:40	T: Cognitive Behavioral Therapy C: WL	Baseline, 4 weeks, 3 months (follow up)	HAMD and BDI
Jarrett et al., 1999	Depression	108	CBT: 36 PLC: 36	T: Cognitive Behavioral Therapy C: PLC	Baseline, 4 weeks, 7 weeks, 10 weeks	HAMD and BDI
Kanter et al., 2015	Depression	43	BA: 21 TAU: 22	T: Behavioral Activation for Latinos C: TAU	Baseline, post treatment, 9 months (follow up)	HAMD and BDI-II
Kelly et al., 1993	Depression	68	CBT: 27 NDST: 14 TAU: 27	T: Cognitive Behavioral Therapy T2: Supportive Therapy C: TAU	Baseline, 8 weeks, 3 months (follow up)	CES-D
King et al., 2000	Depression	197	CBT: 63 NDST: 67 TAU: 67	T: Cognitive Behavioral Therapy T2: Non-Directive Supportive Therapy C: TAU	Baseline, posttreatment	BDI

King et al., 2014	Depression	316	CBT: 129 NDST: 122 TAU: 65	T: Cognitive Behavioral Therapy T2: Non-Directive Supportive Therapy C: TAU	Baseline, 4 months, 12 months	BDI
Kivi et al., 2014	Mild to Moderate Depression	90	CBT: 44 TAU: 46	T: Internet Based CBT C: TAU	Baseline, 12 weeks	BDI-II
Klein et al., 1985	Depression	74	EX: 27 CBT: 24	T: Aerobic Exercise T2: Group Cognitive Behavioral Therapy	Baseline, 12 weeks, and 1, 3, and 9 months (follow ups)	SCL depression
Laidlaw, 2008	Depression	40	CBT: 20 TAU: 20	T: Cognitive Behavioral Therapy C: TAU	Baseline, 18 weeks, 3 and 6 months (follow up)	GDS, BDI, and HAMD
Lamers et al., 2010	Minor to moderate depression	361	CBT: 183 TAU: 178	T: Cognitive Behavioral Therapy C: TAU	Baseline, 13 weeks, and 3 and 9 months (follow up)	BDI
Landreville et al., 1997	Depression	23	CBT: 10 WL: 13	T: Cognitive Behavioral Bibliotherapy C: WL	Baseline, post-treatment, 6 months (follow up)	IDD, GDS, and BDI
Larcombe et al., 2984	Depressed patients w/ MS	19	CBT: 9 WL: 10	T: Cognitive Behavioral Therapy C: WL	Baseline, post-treatment, 4 weeks (follow up)	BDI and HAMD
Legrand, 2014	Depression	44	EX: 22 WL: 22	T: Aerobic Exercise Training C: WL	Baseline, 2 week, 4 week, 7 weeks	BDI-II

Lincoln et al., 2003	Depression	123	CBT: 39 TAU: 41	T: Cognitive Behavioral Therapy C: TAU	Baseline, 3 months and 6 months	BDI
Lustman et al., 1998	Depression	42	CBT: 20 TAU: 22	T: Cognitive Behavioral Therapy C: TAU	Baseline, 10 weeks, 6 months (follow up)	BDI
Martin et al., 2015	Depression	66	CBT: 36 TAU: 30	T: Cognitive Behavioral Therapy C: TAU	Baseline, during treatment, 12 weeks, and 4 months (follow up)	BDI-II
Mather et al., 2002	Depression	86	EX: 43 TAU: 43	T: Mixed aerobic and strengthening exercise C: TAU	Baseline, 10 weeks and 34 weeks	GDS and HAMD-17
McCann et al., 1984	Depression	47	EX: 16 WL: 16	T: Aerobic Exercise C: WL	Baseline, 5 weeks and 10 weeks	BDI
McIndoo et al., 2016	Depression	50	BA: 16 WL: 14	T: Behavioral Activation Therapy C: WL	Baseline, 4 weeks, and 1 month (follow up)	BDI-II and HAMD
McNeil et al., 1981	Depression	30	EX: 10 WL: 10	T: Exercise C: WL	Baseline, Posttreatment	BDI
Milgrom et al., 2005	Depression	192	CBT: 46 NDST: 113 TAU: 33	T: Cognitive Behavioral Therapy T2: Non-Directive Supportive Therapy C: TAU	Baseline, Posttreatment	BDI

Milgrom et al., 2011	Postnatal Depression	68	CBT: 23 TAU: 23	T: Cognitive Behavioral Therapy with Psychologist C: TAU	Baseline, 3 weeks, and 6 weeks	BDI-II
Milgrom et al., 2016	Depression	43	CBT: 21 TAU: 22	T: Internet Cognitive Behavioral Therapy C: TAU	Baseline, 12 weeks	BDI-II and PHQ-9
Miranda et al., 2003	Depression	267	CBT: 90 TAU: 89	T: Cognitive Behavioral Therapy C: TAU	Baseline, 1 month, 3 months, and 6 months	HAMD
Mohr et al., 2000	Depressed patients with MS	32	CBT: 16 TAU: 16	T: Telephone administered CBT C: TAU	Baseline and 8 weeks	POMS depression scale
Mohr et al., 2005	Depression	122	CBT: 60 NDST: 62	T: Cognitive Behavioral Therapy T2: Non-directive Supportive Therapy	Baseline, posttreatment	HAMD and BDI-II
Mota-Pereira et al., 2011	Treatment Resistant MDD	33	EX: 22 TAU: 11	T: Aerobic Exercise C: TAU	Baseline, 4 weeks, 8 weeks, 12 weeks	HAMD-17 and BDI- II
Mukhter, 2011	MDD or Dysthymia	113	CBT: 58 TAU: 55	T: Group Cognitive Behavioral Therapy C: TAU	Baseline, 4 weeks	BDI
Naeem et al., 2014	Depression	183	CBT: 94 TAU: 89	T: Culturally adapted CBT C: TAU	Baseline, 12 weeks	Hospital Anxiety and Depression Scale

Naik & Cully	Depression	255	N/A	T: Cognitive Behavioral Therapy C: TAU	Baseline, 6 months, and 12 months (follow up)	PHQ-9
Newby et al., 2017	Depression	90	iCBT: 41 TAU: 49	T: Internet Cognitive Behavioral Therapy C: TAU	Baseline, 10 weeks, 3 months (follow up)	PHQ-9
Ngai et al., 2015	Post-Natal Depression	397	CBT: 197 TAU: 200	T: Telephone based CBT C: TAU	Baseline, 6 weeks, 6 months	EPDS
Noroozi et al., 2017	Depression	30	CBT: 15 WL: 15	T: Cognitive Behavioral Therapy C: WL	Baseline, 10 weeks	BDI
Nystrom et al., 2017	Mild to Moderate Depression	286	PA w/o rational: 59 PA w/ rational: 62 BAM: 49 BAL: 63 WL: 53	T: Physical Activity with or without rational T2: Behavioral Activation Therapy C: WL	Baseline, 12 weeks; Internet Administration	PHQ-9
O'Mahen et al., 2013	Perinatal Depression	55	CBT: 30 TAU: 25	T: Modified Cognitive Behavioral Therapy C: TAU	Baseline, 16 weeks, 3 months (follow up)	BDI-II
Omidi et al., 2013	MDD	90	CBT: 30 TAU: 30	T: Cognitive Behavioral Therapy C: TAU	Baseline, 8 weeks	BSI (Depression Subscale)
Peden et al., 2000	Depression	92	CBT: 46 TAU: 46	T: Cognitive Behavioral Therapy C: TAU	Baseline, 1 month, 6 months (follow up)	BDI and CES-D

Prendergast et al., 2001	Post-natal Depression	37	CBT: 17 TAU: 20	T: Cognitive Behavioral Therapy C: TAU	Baseline, 6 weeks, 6 month (follow up)	EPDS
Propst et al., 1992	Depression	59	RCT: 10 RCT-NT: 9 RCT-RT: 10 NRCT-RT: 9 NRCT-NT: 10 WL: 11	Multiple groups with either religious CBT or non-religious CBT with a either religious therapist or non-religious therapist C: WL	Baseline, 3 months (post treatment), 3 months and 2 years (follow ups)	BDI and HAMD
Qiu et al., 2013	Major Depression in Breast Cancer Patients	62	CBT: 31 WL: 31	T: Group Cognitive Behavioral Therapy C: WL	Baseline, 12 weeks	HAMD-17
Rahman et al., 2008	Perinatal depression	903	CBT: 463 PLC: 440	T: Cognitive Behavioral Therapy C: PLC	Baseline, 6 months, 12 months	HAMD
Rethorst et al., 2010	Depression	171	EX: 70 WL: 101	T: Aerobic Exercise C: WL	Baseline, 5 weeks	BDI
Richards et al., 2015	Depression	188	iCBT: 96 WL: 92	T: Internet delivered CBT C: WL	Baseline, Post-Treatment	BDI-II
Richards et al., 2016	Depression	440	BA: 221 CBT: 219	T: Cognitive Behavioral Therapy T2: Behavioral Activation Therapy	Baseline, 6 months, 12 months, and 18 months	PHQ-9
Robledo-Colonia et al., 2012	Prenatal depression	80	EX: 40 WL: 40	T: Supervised aerobic exercise C: WL	Baseline, 3 months	CES-D

Ross et al., 1985	Depression	51	ICBT: 21 GCBT: 9 WL: 21	T: Individual Cognitive Behavioral Therapy T2: Group Cognitive Behavioral Therapy C: WL	Baseline, 3 months (post-treatment), 3-, 6-, 12 months (follow ups)	BDI and MARDS
Roy et al., 2018	Moderate or Severe Depression	40	EX: 20 TAU: 20	T: Aerobic Exercise C: TAU	Baseline, 10 days; Daily session over 10 days	HAMD
Ruwaard et al., 2009	Moderate Depression	54	CBT: 36 WL: 18	T: Web based Cognitive Behavioral Therapy C: WL	Baseline, 11 weeks, 18 months (follow up)	BDI
Sadeghi et al., 2016	Depression	46	CBT: 16 EX: 16 WL: 14	T: Cognitive Behavioral Therapy T2: Physical Activity C: WL	Baseline, Post-Treatment	BDI-II
Saravanan et al., 2017	Depression	65	CBT: 21 PLC: 22	T: Cognitive Behavioral Therapy C: Placebo	Baseline and post-treatment	BDI-II
Savard et al., 2006	Depression in women with breast cancer	37	CBT: 21 WL: 16	T: Cognitive Behavioral Therapy C: WL	Baseline, 8 weeks, 3 and 6 month (follow up)	BDI and HAMD
Schuch et al., 2011	Severe depression	26	EX: 15 TAU: 11	T: Aerobic Exercise C: TAU	Baseline, 2 weeks, at discharge from hospital	HAMD
Scott et al., 1997	MDD	48	CBT: 24 TAU: 24	T: Cognitive Behavioral Therapy C: TAU	Baseline, 7 weeks, and 19, 32,and 58 weeks (follow ups)	BDI and HAMD

Selmi et al., 1990	Major or Minor Depression	36	Computer CBT: 12 Therapist CBT: 12 WL: 12	T1: Computer Assisted CBT T2: Therapist Assisted CBT C: WL	Baseline, Post-Treatment, 2 months (follow up)	BDI, HAMD, and SCL-90-R
Sims et al., 2006	Depression	32	EX: 14 TAU: 18	T: Progressive Resistance training C: TAU	Baseline, 10 weeks, and 6 month; 3 sessions/week	GDS
Sims et al., 2009	Depressed Stroke Survivors	45	EX: 23 TAU: 22	T: Progressive Resistance training C: TAU	Baseline, 10 weeks, and 6 month; PRT program under trainer	CES-D
Singh et al., 1997	Depression	32	EX: 17 TAU: 15	T: Progressive Resistance Training C: TAU	Baseline, 10 weeks	BDI, HAMD, and GDS
Singh et al., 2001	Minor Depression	29	EX: 15 WL: 14	T: Progressive Resistance Training C: WL	Baseline, 6 weeks, 10 weeks, 20 weeks, and 26 months (follow up)	BDI
Singh et al., 2005	Minor and Major Depression	60	High EX: 20 Low EX: 20 TAU: 20	T: High Intensity PRT T2: Low intensity PRT C: TAU	Baseline, 8 weeks	HAMD

Smith et al., 2017	Depression	270	iCBT: 61 bCBT: 77 WL: 68	T: Internet delivered CBT T2: Cognitive Behavioral Bibliotherapy C: WL	Baseline, mid-point, post-treatment, and 3 month (follow up)	PHQ-9
Soucy et al., 2017	Mild to Moderate Depression	59	BA: 20 EX: 19 WL: 20	T: Behavioral Activation T2: Physical Activity C: WL	Baseline, 4 weeks, 8 weeks, 2 months (follow up)	PHQ-9
Spek et al., 2007	Depression	301	Internet CBT: 102 Group CBT: 99 WL: 100	T: Internet CBT T2: Group CBT C: WL	Baseline, 10 weeks	BDI-II
Taylor et al., 1977	Mild to Moderate Depression	28	CBT:N/A BA:N/A WL:N/A	T: Cognitive Behavioral Therapy T2: Behavioral Activation Therapy C: WL	Baseline, 4 weeks, 5 weeks (follow up)	BDI
Teasdale et al., 1984	MDD	44	CBT: 24 TAU: 20	T: Cognitive Behavioral Therapy C: TAU	Baseline, end of treatment, 3 months (follow up)	BDI, MADS, HAMD
Thapinta et al., 2014	Depression	60	CBT: 33 TAU: 27	T: Cognitive Behavioral Therapy C: TAU	Baseline, 3 weeks, 7 weeks (follow up)	9Q

Titov et al., 2010	Depression	127	Technician-assisted CBT: 41 Clinician assisted CBT: 46 WL: 40	T: Technician-assisted CBT T2: Clinician assisted CBT C: WL	Baseline, 8 weeks, 4 months (follow up)	BDI-II and PHQ-9
Tulbure et al., 2017	Depression	79	CBT:34 WL:26	T: Cognitive Behavioral therapy C: WL	Baseline, post-assessment, 6 months (follow-up)	BDI-II
Van Bastelaar et al., 2011	Elevated Depressive Symptomology	255	CBT: 125 WL: 130	T: Cognitive Behavioral Therapy C: WL	Baseline, 12 weeks, 1 month (follow up)	CES-D
Valsaraj et al., 2016	Depression	67	CBT: 33 NDST: 34	T: Cognitive Behavioral Therapy T2: Non-Directive Supportive Therapy	Baseline, 3 months, and 6 months (follow up)	HAMD
Vazquez et al., 2017	Depression	61	CBT: 20 BA: 22 TAU: 19	T: Telephone based CBT T2: Telephone based BA C: TAU	Baseline and 5 weeks	CES-D
Vernmark et al., 2010	Depression	88	Email CBT: 30 Self- help: 29 WL: 29	T: Email Cognitive Behavioral Therapy T2: Self-help Cognitive Behavioral Therapy C: WL	Baseline, 8 weeks, and 6 months (follow up)	BDI and MADRS-S
Wiersma et al., 2014	Depression	139	CBT: 67 TAU: 72	T: Cognitive Behavioral Therapy C: TAU	Baseline, 8 weeks, 16 weeks, 32 weeks, 52 weeks	IDS
Williams et al., 2013	Depression	281	CBT: 141 TAU: 140	T: Cognitive Behavioral guided self-help book C: TAU	Baseline, 4 months, 12 months (follow up)	BDI-II

Williams & Tappen, 2008	Depression w/ Alzheimer's disease	45	Comprehensive EX: 16 Supervised walking: 17 TAU: 12`	T: Comprehensive Exercise T2: Supervised walking C: TAU	Baseline, 16 weeks;	CSDD
Wilson et al., 1983	Depression	25	BA: 8 CBT: 8 WL: 9	T: Behavioral Activation Therapy T2: Cognitive Behavioral Therapy C: WL	Baseline, midtreatment, 8 weeks, 5 months (follow up)	BDI and HAMD
Wong et al., 2008	Major Depressive Disorder	322	CBT: 163 WL: 159	T: Cognitive Behavioral Therapy C: WL	Baseline, 10 weeks; Group CBT program	C-BDI
Wright et al., 2005	Depression	45	CBT: 15 Computer CBT: 15 WL: 15	T: Cognitive Behavioral Therapy T2: Computer – assisted CBT C: WL	Baseline, 4 weeks, 8 weeks, 3 and 5 months (follow up)	HAMD and BDI
Zu et al., 2014	Moderate to Severe Depression	96	CBT: 12 TAU: 16	T: Cognitive Behavioral Therapy C: TAU	Baseline, 3 months, 6 months (follow up)	HAMD

APPENDIX E

NMA CODES

Overall NMA codes 6-31-18.do - Printed on 2018/6/1 21:49:25

```
*** Overall NMA

use "C:\Users\Administrator\Dropbox\Academic Life\01 Data Analysis\NMA Analysis for Nick\Data from Nick\Final Data\Overall NMA 6-1-18.dta", clear

//prepare the data in the appropriate format
network setup SMD SD n, study(ID) trt(T) numcodes // armvars( drop)
network convert pairs

/*produce a network plot in which nodes are weighted according to the number of studies evaluating each treatment
and edges according to the precision of the direct estimate for each pairwise comparison*/
gen invvarES=1/(  stderr^2)
networkplot _t1 _t2, edgew(invvarES) edgecol(by blinding mean) edgesc(1.2) asp(0.8) lab(WL CBT BA NDST EX)

***3.Producing the contribution plot***

//produce the contribution plot
netweight _y _stderr _t1 _t2,asp(0.7)


***4.Producing the inconsistency plot***

//produce the inconsistency plot assuming loop-specific heterogeneity estimate
ifplot _y _stderr _t1 _t2 ID

//assume a common heterogeneity estimate 0.02 in the entire network (derived from network meta)
ifplot _y _stderr _t1 _t2 ID, tau2(0.02)


***5.Running network meta-analysis with network meta***

//prepare the data in the appropriate format
network convert augment
edit

//perform network meta-analysis assuming consistency a common heterogeneity across all comparisons in the network
network meta c


***6.Producing the predictive interval plot***

//produce the predictive interval plot
intervalplot,pred null(0) lab(WL CBT BA NDST EX)  marg(10 40 5 5) xlab(-2 -1.5 -1 -0.5 0 0.5 1)

***7.Producing the league table***

/*produce the league table of the network estimates and sort the treatments according to their relative effects
against placebo*/
netleague, lab(WL CBT BA NDST EX) sort(WL CBT BA NDST EX)


***8.Producing ranking plots for a single outcome using probabilities***

//estimate the ranking probabilities using network rank command
network rank min, all zero reps(5000) gen(prob)

//produce the rankograms for all treatments
sucra prob*, rankog lab(WL CBT BA NDST EX)

//produce the cumulative ranking curve plots for all treatments
sucra prob*, lab(WL CBT BA NDST EX)


***9.Producing the comparison-adjusted%funnel plot***

//prepare again the data in the pairs format
network convert pairs

```

Page 1

Overall NMA codes 8-31-18.do - Printed on 2018/6/1 21:49:25

```
68   //produce the comparison-adjusted funnel plot for all comparisons of an active treatment
     vs. placebo
69   netfunnel  y  stderr  t2  t1 if  t1~="1", wlab(0 0.1 0.2 0.3) bycomparison random
70
71   netfunnel  y  stderr  t2  t1 if  t1~="1", wlab(0 0.1 0.2 0.3) bycomparison random add(lfit
       stderr  ES CEN)
72
73
74
75
76
77
78
79
80
```

WL NMA codes.do - Printed on 2018/6/24 0:52:14

```
  1  *** WL NMA
  2
  3  //prepare the data in the appropriate format
  4  network setup SMD SD n, study(ID) t(T) ref(codes
  5  network convert pairs
  6
  7  /*produce a network plot in which nodes are weighted according to the number of studies
     evaluating each treatment
  8  and edges according to the precision of the direct estimate for each pairwise comparison*/
  9  gen invvarES=1/(  stderr^2)
 10  networkplot _t1 _t2, edgew(invvarES) edgecol(by blinding mean) edgesc(1.2) asp(0.8) lab(WL
      CBT BA NDST EX)
 11
 12  ***3.Producing the contribution plot***
 13
 14  //produce the contribution plot
 15  netweight _y _stderr _t1 _t2,asp(0.7)
 16
 17
 18  ***4.Producing the inconsistency plot***
 19
 20  //produce the inconsistency plot assuming loop-specific heterogeneity estimate
 21  ifplot _y _stderr _t1 _t2 ID
 22
 23  //assume a common heterogeneity estimate 0.02 in the entire network (derived from network
     meta)
 24  ifplot _y _stderr _t1 _t2 ID, tau2(0.02)
 25
 26
 27  ***5.Running network meta-analysis with network meta***
 28
 29  //prepare the data in the appropriate format
 30  network convert augment
 31  edit
 32
 33  //perform network meta-analysis assuming consistency a common heterogeneity across all
     comparisons in the network
 34  network meta c
 35
 36
 37  ***6.Producing the predictive interval plot***
 38
 39  //produce the predictive interval plot
 40  intervalplot,pred null(0) lab(WL CBT BA NDST EX)  marg(10 40 5 5) xlab(-2 -1.5 -1 -0.5 0
     0.5 1)
 41
 42  ***7.Producing the league table***
 43
 44  /*produce the league table of the network estimates and sort the treatments according to
     their relative effects
 45  against placebo*/
 46  netleague, lab(WL CBT BA NDST EX) sort(WL CBT BA NDST EX)
 47
 48
 49  ***8.Producing ranking plots for a single outcome using probabilities***
 50
 51  //estimate the ranking probabilities using network rank command
 52  network rank min, all sucra reps(5000) gen(prob)
 53
 54  //produce the rankogram for all treatments
 55  sucra prob*, rankog lab(WL CBT BA NDST EX)
 56
 57  //produce the cumulative ranking curve plots for all treatments
 58  sucra prob*, lab(WL CBT BA NDST EX)
 59
 60
 61  ***9.Producing the comparison-adjusted funnel plot***
 62
 63  //prepare again the data in the pairs format
 64  network convert pairs
 65
```

TAU NMA codes 8-31-18.do - Printed on 2018/8/31 1:56:42

```
1   *** TAU NMA
2
3   use "C:\Users\Administrator\Dropbox\Academic Life\01 Data Analysis\NMA Analysis for
    Nick\Data from Nick\Final Data\TAU NMA.dta", clear
4
5   //prepare the data in the appropriate format
6   network setup SMD SD n, study(ID) trt(T) ref(codes
7   network convert pairs
8
9   /*produce a network plot in which nodes are weighted according to the number of studies
    evaluating each treatment
10  and edges according to the precision of the direct estimate for each pairwise comparison*/
11  gen invvarES=1/(  stderr^2)
12  networkplot _t1 _t2, edgev(invvarES) edgecol(by blinding mean) edgesc(1.2) asp(0.8) lab(WL
     CBT BA NDST EX)
13
14  ***3.Producing the contribution plot***
15
16  //produce the contribution plot
17  netweight _y _stderr _t1 _t2,asp(0.7)
18
19
20  ***4.Producing the inconsistency plot***
21
22  //produce the inconsistency plot assuming loop-specific heterogeneity estimate
23  ifplot _y _stderr _t1 _t2 ID
24
25  //assume a common heterogeneity estimate 0.02 in the entire network (derived from network
    meta)
26  ifplot _y _stderr _t1 _t2 ID, tau2(0.02)
27
28
29  ***5.Running network meta-analysis with network meta***
30
31  //prepare the data in the appropriate format
32  network convert augment
33  edit
34
35  //perform network meta-analysis assuming consistency a common heterogeneity across all
    comparisons in the network
36  network meta c
37
38
39  ***6.Producing the predictive interval plot***
40
41  //produce the predictive interval plot
42  intervalplot,pred null(0) lab(WL CBT BA NDST EX)  marg(10 40 5 5) xlab(-2 -1.5 -1 -0.5 0
    0.5 1)
43
44  ***7.Producing the league table***
45
46  /*produce the league table of the network estimates and sort the treatments according to
    their relative effects
47  against placebo*/
48  netleague, lab(WL CBT BA NDST EX) sort(WL CBT BA NDST EX)
49
50
51  ***8.Producing ranking plots for a single outcome using probabilities***
52
53  //estimate the ranking probabilities using network rank command
54  network rank min, all rare reps(5000) gen(prob)
55
56  //produce the rankogramm for all treatments
57  sucra prob*, rankog lab(WL CBT BA NDST EX)
58
59  //produce the cumulative ranking curve plots for all treatments
60  sucra prob*, lab(WL CBT BA NDST EX)
61
62
63  ***9.Producing the comparison-adjusted funnel plot***
64
65  //prepare again the data in the pairs format
```

TAU NMA codes 8-31-18.do - Printed on 2018/8/31 1:06:42

```
68   //produce the comparison-adjusted funnel plot for all comparisons of an active treatment
     vs. placebo
69   ~~netfunnel~~  y  ~~stderr~~  t2  t1 if  t1~="1", ~~vlab~~(0 0.1 0.2 0.3) ~~bycomparison~~ random
70
71   ~~netfunnel~~  y  ~~stderr~~  t2  t1 if  t1~="1", ~~vlab~~(0 0.1 0.2 0.3) ~~bycomparison~~ random add(lfit
       ~~stderr~~  ES CEN)
72
73
74
75
76
77
78
79
80
```

APPENDIX F

NMA OUTPUTS

```
      Friday June 1 21:50:15 2018    Page 1

                                                  ___  ____  ____  ____  ____(R)
                                                 /__    /   ____/   /   ____/
                                                ___/   /   /___/   /   /___/
                                                  Statistics/Data Analysis

1 . 
         name:  <unnamed>
          log:  C:\Users\Administrator\Dropbox\Academic Life\01 Data Analysis\NMA Analysis for Nick
     log type:  smcl
    opened on:  1 Jun 2018,  21:42:22

2 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

3 . //prepare the data in the appropriate format
4 . network setup SMD SD n, study(ID) trt(T) ncovcodes // covvars( drop)
  Treatments used
      1 (reference):                      1
      2:                                  2
      3:                                  3
      4:                                  4
      5:                                  5
      6:                                  6

  Measure                                 Mean difference
      Standard deviation pooling:         off

  Studies
      ID variable:                        ID
      Number used:                        104
      IDs with augmented reference arm:   1 2 5 7 10 12 16 17 18 19 20 21 22 23 24 25 66 67 68 69 7
  > 105
      - observations added:               0.001
      - mean in augmented observations:   study-specific mean
      - SD in augmented observations:     study-specific within-arms SD

  Network information
      Components:                         1 (connected)
      D.f. for inconsistency:             18
      D.f. for heterogeneity:             94

  Current data
      Data format:                        augmented
      Design variable:                    _design
      Estimate variables:                 _y*
      Variance variables:                 _S*
      Command to list the data:           list ID _y* _S*, nop sepby(_design)

5 . network convert pairs
  Converting augmented to pairs ...

6 . 
7 . /*produce a network plot in which nodes are weighted according to the number of studies evaluating e
  > ach edges according to the precision of the direct estimate for each pairwise comparison*/
8 . gen invvarSS=1/(_stderr^2)

9 . networkplot _t1 _t2, edgew(invvarSS) edgecol(by blinding mean) edgesc(1.2) sep(0.5) lab(NL CBT BA ND

10 . 
  end of do-file

11 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

12 . ***3.Producing the contribution plot***
13 . 
14 . //produce the contribution plot
15 . networkgbt _y _stderr _t1 _t2,sep(0.7)

  Direct comparisons and number of included studies:
```

1.	1-2	35
2.	1-3	3
3.	1-4	6
4.	1-5	14
5.	2-3	6
6.	2-4	11
7.	2-5	5
8.	2-6	32
9.	3-4	1
10.	3-5	2
11.	3-6	7
12.	5-6	10

Indirect comparisons:

1.	1-6
2.	4-5
3.	4-6

Direct relative effects:

	y
1-2	0.85
1-3	0.96
1-4	0.55
1-5	0.99
2-3	-0.20
2-4	-0.30
2-5	-0.01
2-6	-1.52
3-4	-0.75
3-5	0.48
3-6	-1.88
5-6	-1.19

Variances of direct relative effects:

	1-2	1-3	1-4	1-5	2-3	2-4	2-5	2-6	3-4	3-5	3-6	5-6
1-2	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1-3	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1-4	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1-5	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-3	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-4	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00
2-5	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00
2-6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
3-4	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00
3-5	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.19	0.00	0.00
3-6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00
5-6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01

Basic contrasts:

1-2	1-3	1-4	1-5	2-6

Design matrix:

	1-2	1-3	1-4	1-5	2-6
1-2	1	0	0	0	0
1-3	0	1	0	0	0
1-4	0	0	1	0	0
1-5	0	0	0	1	0
2-3	-1	1	0	0	0
2-4	-1	0	1	0	0
2-5	-1	0	0	1	0
2-6	0	0	0	0	1
3-4	0	-1	1	0	0
3-5	0	-1	0	1	0
3-6	1	-1	0	0	1

Friday June 1 21:50:18 2018 Page 3

Mat matrix:

	1-2	1-3	1-4	1-5	2-3	2-4	2-5	2-6	3-4	3-5	3-6	5-6
1-2	0.74	0.03	0.11	0.13	-0.06	-0.06	-0.04	-0.10	-0.05	0.00	0.01	0.09
1-3	0.44	0.11	0.36	0.09	0.29	0.15	-0.02	0.05	-0.50	-0.00	-0.10	0.07
1-4	0.39	0.08	0.46	0.08	0.17	0.22	-0.02	0.00	0.31	-0.00	-0.06	0.06
1-5	0.47	0.02	0.08	0.43	-0.03	-0.03	0.16	0.37	-0.05	0.00	0.04	-0.41
2-3	-0.30	0.09	0.25	-0.04	0.35	0.21	0.02	0.13	-0.45	-0.00	-0.11	-0.02
2-4	-0.35	0.05	0.35	-0.05	0.25	0.29	0.02	0.10	0.36	-0.00	-0.07	-0.03
2-5	-0.27	-0.01	-0.03	0.30	0.03	0.03	0.20	0.47	0.00	0.00	0.02	-0.30
2-6	-0.10	0.00	0.00	0.10	0.03	0.02	0.07	0.79	-0.02	0.00	0.05	0.17
3-4	-0.06	-0.04	0.11	-0.01	-0.11	0.08	0.00	-0.02	0.81	0.00	0.04	-0.01
3-5	0.03	-0.09	-0.28	0.34	-0.31	-0.18	0.18	0.35	0.46	0.01	0.13	-0.48
3-6	0.19	-0.08	-0.25	0.14	-0.32	-0.19	0.04	0.66	0.44	0.00	0.16	0.19
5-6	0.16	0.01	0.03	-0.20	-0.01	-0.01	-0.13	0.31	-0.02	-0.00	0.02	0.66
1-6	0.65	0.03	0.11	0.23	-0.05	-0.04	0.03	0.68	-0.07	0.00	0.06	0.26
4-5	0.08	-0.06	-0.38	0.35	-0.20	-0.26	0.17	0.37	-0.36	0.01	0.10	-0.47
4-6	0.25	-0.05	-0.33	0.15	-0.21	-0.27	0.04	0.68	-0.38	0.00	0.12	0.20

Percentage contribution of each direct comparison in each pairwise summary effect:

	1-2	1-3	1-4	1-5	2-3	2-4	2-5	2-6	3-4	3-5	3-6	5-6
1-2	78.59	1.35	4.59	4.89	2.44	3.16	1.91	3.52	1.43	0.00	0.34	2.98
1-3	19.45	11.32	17.76	2.96	14.27	4.86	0.38	0.71	22.62	0.19	3.10	2.39
1-4	16.56	3.82	46.26	1.91	5.72	11.18	0.37	0.04	11.11	0.08	1.50	1.46
1-5	18.33	0.73	1.85	43.02	0.55	0.86	7.99	11.74	0.99	0.15	1.02	12.77
2-3	11.28	4.31	7.80	0.83	34.31	10.44	0.67	5.87	18.24	0.19	5.51	0.36
2-4	17.54	1.08	17.62	1.16	11.73	28.68	0.61	3.08	15.35	0.08	2.46	0.62
2-5	13.30	0.22	0.99	14.51	1.11	0.96	19.80	25.75	0.03	0.15	0.72	24.47
2-6	3.37	0.05	0.01	3.32	1.28	0.62	3.36	78.73	0.63	0.02	1.93	6.69
3-4	1.66	1.84	3.88	0.38	4.98	3.90	0.00	0.58	81.48	0.04	0.91	0.33
3-5	0.58	4.64	8.81	12.86	15.35	4.50	8.76	9.67	15.30	0.68	6.59	16.26
3-6	5.35	2.83	5.91	3.41	15.98	6.34	0.89	26.76	12.25	0.23	15.55	4.53
5-6	5.48	0.27	0.73	6.48	0.13	0.26	6.54	12.42	0.47	0.11	0.71	66.39
1-6	51.72	1.42	5.23	11.96	0.71	1.49	0.58	55.54	1.74	0.02	2.43	11.96
4-5	1.84	1.12	18.43	17.71	5.06	11.51	8.75	9.66	9.62	0.27	5.17	12.84
4-6	8.51	1.20	11.75	4.64	6.60	15.41	1.10	27.22	13.86	0.11	5.95	5.85

Percentage contribution of each direct comparison in the entire network:

	1-2	1-3	1-4	1-5	2-3	2-4	2-5	2-6	3-4	3-5	3-6	5-6
network	15.22	2.41	9.97	8.65	7.89	6.81	4.11	16.46	13.54	0.15	3.46	11.33

. end of do-file

. do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

. ***4.Producing the inconsistency plot***

. //produce the inconsistency plot assuming loop-specific heterogeneity estimate

. ifplot _y _stderr _t1 _t2 ID

* 10 triangular loops found

Evaluation of inconsistency using loop-specific heterogeneity estimates:

Loop	IF	seIF	z_value	p_value	CI_95	Loop_Heterog_tau2
3 5 6	0.762	0.825	0.924	0.356	(0.00,2.38)	0.150
2 3 4	0.727	0.699	1.041	0.298	(0.00,2.10)	0.267
2 5 6	0.672	0.579	1.162	0.245	(0.00,1.81)	0.147
1 2 3	0.394	0.578	0.682	0.495	(0.00,1.53)	0.169
1 3 4	0.306	0.777	0.393	0.694	(0.00,1.83)	0.191
1 3 5	0.176	1.377	0.128	0.899	(0.00,2.87)	0.252
1 2 5	0.140	0.583	0.240	0.810	(0.00,1.28)	0.228
1 2 4	0.104	0.394	0.264	0.792	(0.00,0.88)	0.181
2 5 6	0.090	0.532	0.169	0.866	(0.00,1.15)	0.152
2 3 5	0.068	0.833	0.082	0.935	(0.00,1.70)	0.216

```
Friday June 1 21:50:15 2015    Page 4

22...
    end of do-file

23 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

24 . //assume a common heterogeneity estimate 0.02 in the entire network (derived from network meta)
25 . ifplot _y _stderr _t1 _t2 ID, tau2(0.02)

    * 10 triangular loops found
```

Loop	IF	seIF	z_value	p_value	CI_95
2 3 5	0.667	0.191	3.488	0.000	(0.29,1.04)
1 3 5	0.622	0.172	3.609	0.000	(0.28,0.96)
1 3 4	0.464	0.197	2.360	0.018	(0.08,0.85)
2 3 4	0.412	0.192	2.147	0.032	(0.04,0.79)
2 3 6	0.346	0.126	2.744	0.006	(0.10,0.59)
2 5 6	0.295	0.118	2.500	0.012	(0.06,0.53)
3 5 6	0.066	0.176	0.375	0.708	(0.00,0.41)
1 2 5	0.062	0.112	0.556	0.578	(0.00,0.28)
1 2 3	0.039	0.129	0.302	0.763	(0.00,0.29)
1 2 4	0.014	0.087	0.160	0.873	(0.00,0.18)

```
26...
    end of do-file

27 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

28 . ***5.Running network meta-analysis with network meta***
29...
30 . //prepare the data in the appropriate format
31 . network convert augment
    Converting pairs to augmented ...

32...
    end of do-file

33 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

34 . //perform network meta-analysis assuming consistency a common heterogeneity across all comparisons i
35 . network meta c
    Command is: mvmeta _y _S   , bscovariance(exch 0.5) longparm suppress(uv mm)   vars(_y_2 _y_3 _y_4 _y_5
    Note: using method   reml
    Note: using variables   _y_2 _y_3 _y_4 _y_5  _y_6
    Note:   104 observations on   5 variables
    Note: variance-covariance matrix is    proportional to .5*I(5)+.5*J(5,5,1)

    initial:        log likelihood =   -472.79146
    rescale:        log likelihood =   -472.79146
    rescale eq:     log likelihood =   -472.79146
    Iteration 0:    log likelihood =   -472.79146
    Iteration 1:    log likelihood =   -472.44156
    Iteration 2:    log likelihood =   -472.43253
    Iteration 3:    log likelihood =   -472.43253

    Multivariate meta-analysis
    Variance-covariance matrix =   proportional .5*I(5)+.5*J(5,5,1)
    Method =  reml                                  Number of dimensions     =        5
    Restricted log likelihood =   -472.43253        Number of observations   =      104
```

	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
_y_2						
_cons	-.9227929	.1473739	-6.26	0.000	-1.21164	-.6339454
_y_3						
_cons	-1.010333	.2743179	-3.68	0.000	-1.547986	-.4726801
_y_4						

Friday June 1 21:50:18 2018 Page 5

_y_5	_cons	-.943724	.2023911	-4.66	0.000	-1.340403	-.5470446
_y_6	_cons	.4912576	.1968686	2.50	0.013	.1054022	.8771131

Estimated between-studies SDs and correlation matrix:

	SD	_y_2	_y_3	_y_4	_y_5	_y_6
_y_2	.93995411	1	.	.	.	.
_y_3	.93995411	.5	1	.	.	.
_y_4	.93995411	.5	.5	1	.	.
_y_5	.93995411	.5	.5	.5	1	.
_y_6	.93995411	.5	.5	.5	.5	1

mymeta command stored as F9

```
36...
    end of do-file

37 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

38 . ***6.Producing the predictive interval plot***
39...
40 . //produce the predictive interval plot
41 . intervalplot,pred null(0) lab(WL CBT BA NDST EX)   marg(10 40 5 5) xlab(-2 -1.5 -1 -0.5 0 0.5 1)
```

The intervalplot command assumes that the saved results from mymeta or network meta commands hav

Comparison	Effect_Size	LCI	UCI	LPrI	UPrI
CBT vs WL	-.9227929	-1.21164	-.6339453	-2.809964	.9643784
BA vs WL	-1.010333	-1.547987	-.4726801	-2.952502	.9318358
NDST vs WL	-.5345386	-1.057697	-.0113806	-2.472649	1.403572
EX vs WL	-.943724	-1.340403	-.5470446	-2.850848	.9634002
vs WL	.4912576	.1054022	.8771131	-1.413591	2.396106
BA vs CBT	-.0875404	-.5934644	.4183836	-2.020959	1.845879
NDST vs CBT	.3882543	-.1047486	.8812572	-1.541743	2.318252
EX vs CBT	-.0209311	-.4272802	.3854179	-1.930139	1.888277
vs CBT	1.41405	1.114992	1.713109	-.474749	3.30285
NDST vs BA	.4757947	-.1943964	1.145986	-1.508134	2.459723
EX vs BA	.0666093	-.5233027	.6565214	-1.891034	2.024253
vs BA	1.501591	.9819148	2.021267	-.43556	3.438742
EX vs NDST	-.4091854	-1.022541	.2041702	-2.374194	1.555823
vs NDST	1.025796	.459888	1.591704	-.9245769	2.976169
vs EX	1.434982	1.009638	1.860325	-.4784589	3.348422

```
42...
    end of do-file

43 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

44 . ***7.Producing the league table***
45...
46 . /"produce the league table of the network estimates and sort the treatments according to their relat
   > against placebo"/
47 . netleague, lab(WL CBT BA NDST EX) sort(WL CBT BA NDST EX)
```

The netleague command assumes that the saved results from mymeta or network meta commands have b

The league table has been stored at the end of the dataset

```
Friday June 1 21:50:18 2018    Page 6

48...
    end of do-file

49 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

50 . """5.Producing ranking plots for a single outcome using probabilities"""
51...
52 . //estimate the ranking probabilities using network rank command
53 . network rank min, all zero reps(5000) gen(prob)
    Command is: mvmeta, noest pbest(min  in 1, zero id(ID) all reps(5000) gen(prob) stripprefix(_y_) zeron

    Estimated probabilities (%) of each treatment being the best (and other ranks)
    - assuming the minimum parameter is the best
    - using 5000 draws
    - allowing for parameter uncertainty
```

ID and Rank	Treatment 1	2	3	4	5	6
1						
Best			49.5	2.1	29.7	0.0
2nd	0.0	41.5	21.7	4.2	32.5	0.0
3rd	0.0	37.1	22.6	10.0	30.3	0.0
4th	2.0	2.8	6.1	81.6	7.5	0.0
5th	97.3	0.0	0.0	2.0	0.0	0.7
Worst	0.7	0.0	0.0	0.0	0.0	99.3

```
    mvmeta command is stored in F9

54...
    end of do-file

55 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

56 . //produce the rankograms for all treatments
57 . sucra prob", rankog lab(WL CBT BA NDST EX)

    Treatment Relative Ranking of Model 1
```

Treatm~t	SUCRA	PrBest	MeanRank
WL	20.3	00.0	05.0
CBT	75.2	18.6	02.2
BA	82.9	49.5	01.9
NDST	44.6	02.1	03.8
EX	76.9	29.7	02.2
	00.1	00.0	06.0

```
58...
    end of do-file

59 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

60 . //produce the cumulative ranking curve plots for all treatments
61 . sucra prob", lab(WL CBT BA NDST EX)

    Treatment Relative Ranking of Model 1
```

Treatm~t	SUCRA	PrBest	MeanRank
WL	20.3	00.0	05.0
CBT	75.2	18.6	02.2
BA	82.9	49.5	01.9
NDST	44.6	02.1	03.8
EX	76.9	29.7	02.2
	00.1	00.0	06.0

```
     Friday June 1 21:50:19 2018    Page 7

62.
    end of do-file

63  . do "C:\Users\AIMINI~1\AppData\Local\Temp\STD00000000.tmp"

64  . ***9.Producing the comparison-adjusted funnel plot***
65.
66  . //prepare again the data in the pairs format
67  . network convert pairs
    Converting augmented to pairs ...

68.
    end of do-file

69  . do "C:\Users\AIMINI~1\AppData\Local\Temp\STD00000000.tmp"

70  . //produce the comparison-adjusted funnel plot for all comparisons of an active treatment vs. placebo
71  . netfunnel _y _stderr _t2 _t1 if _t1=="1", ylab(0 0.1 0.2 0.3) bycomparison random

    Comparisons in the plot:

      1.        1 - 5
      2.        1 - 4
      3.        1 - 3
      4.        1 - 2

72.
    end of do-file

73  . do "C:\Users\AIMINI~1\AppData\Local\Temp\STD00000000.tmp"

74  . netfunnel _y _stderr _t2 _t1 if _t1=="1", ylab(0 0.1 0.2 0.3) bycomparison random add(ifit _stderr _

    Comparisons in the plot:

      1.        1 - 5
      2.        1 - 4
      3.        1 - 3
      4.        1 - 2

75.
    end of do-file

76. log close
          name:  <unnamed>
           log:  C:\Users\Administrator\Dropbox\Academic Life\01 Data Analysis\NMA Analysis for Nick
      log type:  smcl
     closed on:   1 Jun 2018,  21:45:43
```

```
      name:  <unnamed>
       log:  C:\Users\Administrator\Dropbox\Academic Life\01 Data Analysis\NMA Analy
> MA Output 5-24-18.smcl
  log type:  smcl
 opened on:  24 May 2018, 00:41:01

1 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

2 . //prepare the data in the appropriate format
3 . network setup SMD SD n, study(ID) trt(T) numcodes
  Treatments used
     1 (reference):                    1
     2:                                2
     3:                                3
     4:                                4
     5:                                5

  Measure                              Mean difference
     Standard deviation pooling:       off

  Studies
     ID variable:                      ID
     Number used:                      64
     IDs with augmented reference arm: 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59
     - observations added:             0.001
     - mean in augmented observations: study-specific mean
     - SD in augmented observations:   study-specific within-arms SD

  Network information
     Components:                       1 (connected)
     D.f. for inconsistency:           9
     D.f. for heterogeneity:           56

  Current data
     Data format:                      augmented
     Design variable:                  _design
     Estimate variables:               _y*
     Variance variables:               _S*
     Command to list the data:         list ID _y* _S*, noo sepby(_design)

4 . network convert pairs
  Converting augmented to pairs ...

5 .
6 . /*produce a network plot in which nodes are weighted according to the number of st
  > and edges according to the precision of the direct estimate for each pairwise comp
7 . gen invvarES=1/( _stderr^2)
```

```
 8 . networkplot _t1 _t2, edgew(invvarE3) edgecol(by blinding mean) edgesc(1.2) asp(0.8

 9 .
10 . ***3.Producing the contribution plot***
11 .
12 . //produce the contribution plot
13 . netweight _y _stderr _t1 _t2,asp(0.7)

   Direct comparisons and number of included studies:

     1.         1-2          32
     2.         1-3           7
     3.         1-5          10
     4.         2-3           6
     5.         2-4          11
     6.         2-5           5
     7.         3-4           1
     8.         3-5           2

   Indirect comparisons:

     1.         1-4
     2.         4-5

   Direct relative effects:

            y
1-2    1.32
1-3    1.88
1-5    1.13
2-3   -0.20
2-4   -0.50
2-5   -0.01
3-4   -0.73
3-5    0.48

   Variances of direct relative effects:

       1-2   1-3   1-5   2-3   2-4   2-5   3-4   3-5
1-2   0.01  0.00  0.00  0.00  0.00  0.00  0.00  0.00
1-3   0.00  0.08  0.00  0.00  0.00  0.00  0.00  0.00
1-5   0.00  0.00  0.01  0.00  0.00  0.00  0.00  0.00
2-3   0.00  0.00  0.00  0.03  0.00  0.00  0.00  0.00
2-4   0.00  0.00  0.00  0.00  0.05  0.00  0.00  0.00
2-5   0.00  0.00  0.00  0.00  0.00  0.04  0.00  0.00
3-4   0.00  0.00  0.00  0.00  0.00  0.00  0.01  0.00
3-5   0.00  0.00  0.00  0.00  0.00  0.00  0.00  2.19

   Basic contrasts:
```

User: Lin Zhu

```
          1-2         1-3         1-5         2-4
```

Design matrix:

	1-2	1-3	1-5	2-4
1-2	1	0	0	0
1-3	0	1	0	0
1-5	0	0	1	0
2-3	-1	1	0	0
2-4	0	0	0	1
2-5	-1	0	1	0
3-4	1	-1	0	1
3-5	0	-1	1	0
1-4	1	0	0	1
4-5	-1	0	1	-1

Hat matrix:

	1-2	1-3	1-5	2-3	2-4	2-5	3-4	3-5
1-2	0.86	0.05	0.10	-0.03	-0.02	-0.10	0.02	-0.00
1-3	0.69	0.22	0.08	0.51	0.26	-0.08	-0.26	-0.01
1-5	0.18	0.01	0.81	-0.00	-0.00	0.19	0.00	0.00
2-3	-0.16	0.18	-0.01	0.54	0.27	0.02	-0.27	-0.01
2-4	-0.14	0.15	-0.01	0.48	0.36	0.02	0.64	-0.01
2-5	-0.68	-0.04	0.71	0.03	0.01	0.28	-0.01	0.00
3-4	0.02	-0.02	0.00	-0.07	0.09	-0.00	0.91	0.00
3-5	-0.51	-0.21	0.73	-0.52	-0.26	0.26	0.26	0.01
1-4	0.71	0.20	0.09	0.44	0.35	-0.08	0.65	-0.01
4-5	-0.53	-0.19	0.72	-0.45	-0.35	0.27	-0.65	0.01

Percentage contribution of each direct comparison in each pairwise summary effect:

	1-2	1-3	1-5	2-3	2-4	2-5	3-4	3-5
1-2	85.57	2.13	4.80	1.62	0.53	4.77	0.53	0.03
1-3	31.61	22.38	2.27	25.55	7.96	1.90	7.96	0.37
1-5	9.02	0.39	80.90	0.16	0.06	9.24	0.06	0.16
2-3	8.15	8.59	0.44	54.35	13.70	0.75	13.70	0.31
2-4	4.77	5.06	0.29	23.84	36.30	0.47	29.08	0.18
2-5	33.77	1.11	34.88	0.99	0.35	28.32	0.35	0.22
3-4	0.67	0.71	0.04	3.33	4.06	0.07	91.10	0.03
3-5	14.91	10.66	25.57	21.59	6.50	13.18	6.50	1.07
1-4	29.54	10.11	2.18	14.16	17.33	1.96	24.50	0.22
4-5	14.00	6.38	20.39	11.23	16.07	13.30	18.12	0.50

Percentage contribution of each direct comparison in the entire network:

	1-2	1-3	1-5	2-3	2-4	2-5	3-4	3-5
network	23.20	6.75	17.18	15.68	10.29	7.40	19.19	0.31

User: Lin Zhu

```
14. 
    end of do-file

15 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

16 . ***4.Producing the inconsistency plot***
17. 
    end of do-file

18 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

19 . //assume a common heterogeneity estimate 0.02 in the entire network (derived from
20 . ifplot _y _stderr _t1 _t2 ID, tau2(0.02)

     * 5 triangular loops found
```

Loop	IF	seIF	z_value	p_value	CI_95
2 3 5	0.667	0.191	3.488	0.000	(0.29,1.04)
1 2 3	0.346	0.126	2.744	0.006	(0.10,0.59)
1 2 5	0.295	0.118	2.500	0.012	(0.06,0.53)
2 3 4	0.229	0.192	1.194	0.232	(0.00,0.60)
1 3 5	0.066	0.176	0.375	0.708	(0.00,0.41)

```
21. 
    end of do-file

22 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

23 . ***5.Running network meta-analysis with network meta***
24. 
25 . //prepare the data in the appropriate format
26 . network convert augment
    Converting pairs to augmented ...

27. 
    end of do-file

28 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

29 . //perform network meta-analysis assuming consistency a common heterogeneity across
30 . network meta c
    Command is: mvmeta _y _S  , bscovariance(exch 0.5) longparm suppress(uv mm)  vars(_y
    Note: using method reml
    Note: using variables  y 2  y 3  y 4  y 5
    Note: 64 observations on 4 variables
```

User: Lin Zhu

```
Note: variance-covariance matrix is proportional to .5*I(4)+.5*J(4,4,1)

initial:       log likelihood = -207.73404
rescale:       log likelihood = -207.73404
rescale eq:    log likelihood = -207.73404
Iteration 0:   log likelihood = -207.73404
Iteration 1:   log likelihood = -207.49926
Iteration 2:   log likelihood = -207.49171
Iteration 3:   log likelihood =  -207.4917

Multivariate meta-analysis
Variance-covariance matrix = proportional .5*I(4)+.5*J(4,4,1)
Method = reml                                   Number of dimensions    =      4
Restricted log likelihood = -207.4917           Number of observations  =     64
```

		Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
_y_2	_cons	-1.434243	.1566505	-9.16	0.000	-1.741272	-1.127213
_y_3	_cons	-1.524405	.2805209	-5.43	0.000	-2.074216	-.9745943
_y_4	_cons	-.9260656	.310265	-2.98	0.003	-1.534174	-.3179574
_y_5	_cons	-1.347274	.2550033	-5.28	0.000	-1.847071	-.8474767

```
Estimated between-studies SDs and correlation matrix:
              SD        _y_2        _y_3        _y_4        _y_5
_y_2   .93289248           1           .           .           .
_y_3   .93289248          .5           1           .           .
_y_4   .93289248          .5          .5           1           .
_y_5   .93289248          .5          .5          .5           1
mvmeta command stored as F9

31 .
end of do-file

32 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

33 . ***6.Producing the predictive interval plot***
34 .
35 . //produce the predictive interval plot
36 . intervalplot,pred null(0) lab(WL CBT BA NDST EX)  marg(10 40 5 5) xlab(-2 -1.5 -1

  The intervalplot command assumes that the saved results from mvmeta or network meta
```

User: Lin Zhu

```
> the current dataset
```

Comparison	Effect_Size	LCI	UCI	LPrI	UPrI
CBT vs WL	-1.434243	-1.741272	-1.127213	-3.325177	.456691
BA vs WL	-1.524405	-2.074216	-.9745944	-3.471716	.4229053
NDST vs WL	-.9260656	-1.534174	-.3179574	-2.891323	1.039192
EX vs WL	-1.347274	-1.847072	-.8474767	-3.280513	.585965
BA vs CBT	-.0901624	-.6387702	.4584453	-2.03712	1.856795
NDST vs CBT	.5081772	-.024072	1.040426	-1.434051	2.450406
EX vs CBT	.0869687	-.4400859	.6140234	-1.853786	2.027723
NDST vs BA	.5983396	-.1324116	1.329091	-1.409903	2.606582
EX vs BA	.1771312	-.5085289	.8627912	-1.814502	2.168765
EX vs NDST	-.4212084	-1.164177	.32176	-2.434108	1.591692

```
37 . 
   end of do-file

38 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

39 . ***7.Producing the league table***
40 . 
41 . /*produce the league table of the network estimates and sort the treatments accord
   > against placebo*/
42 . netleague, lab(WL CBT BA NDST EX) sort(WL CBT BA NDST EX)

     The netleague command assumes that the saved results from mvmeta or network meta co
   > e current dataset



43 . 
   end of do-file

44 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

45 . ***8.Producing ranking plots for a single outcome using probabilities***
46 . 
47 . //estimate the ranking probabilities using network rank command
48 . network rank min, all sucra reps(5000) gen(prob)
   Command is: mvmeta, noest pbest(min  in 1, zero id(ID) all reps(5000) gen(prob) stri
   > 1 = 1, 2 = 2, 3 = 3, 4 = 4, 5 = 5))

   Estimated probabilities (%) of each treatment being the best (and other ranks)
   - assuming the minimum parameter is the best
   - using 5000 draws
   - allowing for parameter uncertainty
```

User: Lin Zhu

ID and Rank	Treatment 1	2	3	4	5
1					
Best	0.0	25.3	53.1	1.2	20.4
2nd	0.0	47.1	24.0	3.0	26.0
3rd	0.0	26.6	19.4	12.9	41.1
4th	0.1	1.0	3.5	82.8	12.6
Worst	99.9	0.0	0.0	0.1	0.0

sucra command is stored in F9

```
49
50 . //produce the rankograms for all treatments
51 . sucra prob*, rankog lab(WL CBT BA NDST EX)
```

Treatment Relative Ranking of Model 1

Treatment	SUCRA	PrBest	MeanRank
WL	00.0	00.0	05.0
CBT	74.2	25.3	02.0
BA	81.7	53.1	01.7
NDST	30.6	01.2	03.8
EX	63.5	20.4	02.5

```
52
```
end of do-file

```
53 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

54 . //produce the cumulative ranking curve plots for all treatments
55 . sucra prob*, lab(WL CBT BA NDST EX)
```

Treatment Relative Ranking of Model 1

Treatment	SUCRA	PrBest	MeanRank
WL	00.0	00.0	05.0
CBT	74.2	25.3	02.0
BA	81.7	53.1	01.7
NDST	30.6	01.2	03.8
EX	63.5	20.4	02.5

User: Lin Zhu

```
56 . 
   end of do-file

57 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

58 . ***9.Producing  the Hcomparison-adjustedKfunnel  plot***
59 . 
60 . //prepare again the data in the pairs format
61 . network convert pairs
   Converting augmented to pairs ...

62 . 
63 . //produce the comparison-adjusted funnel plot for all comparisons of an active trt
64 . netfunnel _y _stderr _t2 _t1 if _t1=="1", ylab(0 0.1 0.2 0.3) bycomparison

   Comparisons in the plot:

     1.      1 - 5
     2.      1 - 3
     3.      1 - 2

65 . 
   end of do-file

66 . log close
          name:  <unnamed>
           log:  C:\Users\Administrator\Dropbox\Academic Life\01 Data Analysis\NMA Analy
   > MA Output 5-24-18.smcl
     log type:  smcl
    closed on:  24 May 2018, 00:42:24
```

```
Thursday May 31 01:43:23 2018   Page 1

                                                  ___  ____  ____  ____  ____(R)
                                                 /_   /   ____/  /   ____/
                                                ___/   /   /___/  /   /___/
                                                  Statistics/Data Analysis

      name:  <unnamed>
       log:  C:\Users\Administrator\Dropbox\Academic Life\01 Data Analysis\NMA Analysis for Nick
  log type:  smcl
 opened on:  31 May 2018, 01:39:15

1 . do "C:\Users\ADMINI-1\AppData\Local\Temp\STD00000000.tmp"

2 . //prepare the data in the appropriate format
3 . network setup SMD SD n, study(ID) trt(T) numcodes
  Treatments used
     1 (reference):                        1
     2:                                    2
     3:                                    3
     4:                                    4
     5:                                    5

  Measure                                  Mean difference
     Standard deviation pooling:           off

  Studies
     ID variable:                          ID
     Number used:                          65
     IDs with augmented reference arm:     1 2 5 7 10 12 16 17 18 19 20 21 22 23 24 25 66
     - observations added:                 0.001
     - mean in augmented observations:     study-specific mean
     - SD in augmented observations:       study-specific within-arms SD

  Network information
     Components:                           1 (connected)
     D.f. for inconsistency:               11
     D.f. for heterogeneity:               58

  Current data
     Data format:                          augmented
     Design variable:                      _design
     Estimate variables:                   _y*
     Variance variables:                   _S*
     Command to list the data:             list ID  y*  S*, noo sepby( design)

4 . network convert pairs
  Converting augmented to pairs ...

5 .
  end of do-file

6 . do "C:\Users\ADMINI-1\AppData\Local\Temp\STD00000000.tmp"

7 . /*produce a network plot in which nodes are weighted according to the number of studies evaluating e
  > and edges according to the precision of the direct estimate for each pairwise comparison*/
8 . gen invvarFS-1/( _stderr^2)

9 . networkplot _t1 _t2, edgew(invvarFS) edgecol(by blinding mean) edgesc(1.2) asp(0.8) lab(WL CBT BA ND

10 .
  end of do-file

11 . do "C:\Users\ADMINI-1\AppData\Local\Temp\STD00000000.tmp"

12 . ***3.Producing the contribution plot***
13 .
```

Thursday May 31 01:43:24 2018 Page 2

```
14 . //produce the contribution plot
15 . netweight _y _stderr _t1 _t2,asp(0.7)

   Direct comparisons and number of included studies:

     1.          1-2           33
     2.          1-3            3
     3.          1-4            6
     4.          1-5           14
     5.          2-3            6
     6.          2-4           11
     7.          2-5            5
     8.          3-4            1
     9.          3-5            2

   Indirect comparisons:

     1.          4-5

   Direct relative effects:

          y
1-2    0.85
1-3    0.96
1-4    0.53
1-5    0.99
2-3   -0.20
2-4   -0.30
2-5   -0.01
3-4   -0.73
3-5    0.48

   Variances of direct relative effects:

       1-2   1-3   1-4   1-5   2-3   2-4   2-5   3-4   3-5
1-2   0.01  0.00  0.00  0.00  0.00  0.00  0.00  0.00  0.00
1-3   0.00  0.09  0.00  0.00  0.00  0.00  0.00  0.00  0.00
1-4   0.00  0.00  0.02  0.00  0.00  0.00  0.00  0.00  0.00
1-5   0.00  0.00  0.00  0.02  0.00  0.00  0.00  0.00  0.00
2-3   0.00  0.00  0.00  0.00  0.03  0.00  0.00  0.00  0.00
2-4   0.00  0.00  0.00  0.00  0.00  0.03  0.00  0.00  0.00
2-5   0.00  0.00  0.00  0.00  0.00  0.00  0.04  0.00  0.00
3-4   0.00  0.00  0.00  0.00  0.00  0.00  0.00  0.01  0.00
3-5   0.00  0.00  0.00  0.00  0.00  0.00  0.00  0.00  2.19

   Basic contrasts:

          1-2         1-3         1-4         1-5

   Design matrix:

     1-2  1-3  1-4  1-5
1-2    1    0    0    0
1-3    0    1    0    0
1-4    0    0    1    0
1-5    0    0    0    1
2-3   -1    1    0    0
2-4   -1    0    1    0
2-5   -1    0    0    1
3-4    0   -1    1    0
3-5    0   -1    0    1
4-5    0    0   -1    1

   Hat matrix:
```

Thursday May 31 01:43:24 2018 Page 3

	1-2	1-3	1-4	1-5	2-3	2-4	2-5	3-4	3-5
1-2	0.79	0.03	0.11	0.07	-0.07	-0.07	-0.07	-0.04	-0.00
1-3	0.44	0.12	0.39	0.04	0.32	0.17	-0.04	-0.55	-0.00
1-4	0.39	0.08	0.48	0.04	0.20	0.24	-0.04	0.28	-0.00
1-5	0.27	0.01	0.04	0.68	-0.02	-0.02	0.32	-0.02	0.01
2-3	-0.34	0.10	0.27	-0.03	0.39	0.24	0.03	-0.51	-0.00
2-4	-0.39	0.06	0.37	-0.04	0.26	0.31	0.04	0.32	-0.00
2-5	-0.51	-0.02	-0.07	0.60	0.05	0.05	0.39	0.02	0.01
3-4	-0.05	-0.04	0.10	-0.01	-0.12	0.07	0.00	0.83	0.00
3-5	-0.17	-0.11	-0.35	0.63	-0.34	-0.19	0.36	0.53	0.01
4-5	-0.12	-0.07	-0.44	0.64	-0.22	-0.26	0.35	-0.30	0.01

Percentage contribution of each direct comparison in each pairwise summary effect:

	1-2	1-3	1-4	1-5	2-3	2-4	2-5	3-4	3-5
1-2	78.65	1.36	4.91	3.70	2.76	3.53	3.69	1.39	0.01
1-3	20.14	12.38	19.35	1.23	15.98	5.17	1.00	24.52	0.23
1-4	17.07	4.16	48.33	1.00	6.22	11.75	0.90	10.48	0.10
1-5	13.65	0.43	1.21	67.62	0.58	0.78	15.01	0.44	0.28
2-3	13.01	4.83	8.92	0.74	38.88	11.78	0.94	20.70	0.21
2-4	19.25	1.58	18.56	0.88	13.23	30.56	0.96	14.89	0.09
2-5	25.68	0.57	2.18	28.43	1.48	1.58	39.18	0.60	0.31
3-4	1.67	2.03	3.85	0.16	5.27	3.50	0.10	83.37	0.05
3-5	4.29	5.69	11.54	21.51	17.08	4.85	17.64	16.39	1.02
4-5	3.04	2.44	22.12	27.60	6.23	12.92	16.11	9.11	0.43

Percentage contribution of each direct comparison in the entire network:

	1-2	1-3	1-4	1-5	2-3	2-4	2-5	3-4	3-5
network	19.65	3.55	14.10	15.29	10.77	8.64	9.55	18.19	0.27

```
16 . 
    end of do-file

17 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

18 . ***4.Producing the inconsistency plot***
19 . 
20 . //produce the inconsistency plot assuming loop-specific heterogeneity estimate
21 . ifplot _y _stderr _t1 _t2 ID

     * 7 triangular loops found

     Evaluation of inconsistency using loop-specific heterogeneity estimates:
```

Loop	IF	seIF	z_value	p_value	CI_95	Loop_Heterog_tau2
2 3 4	0.727	0.699	1.041	0.298	(0.00,2.10)	0.287
1 2 3	0.394	0.578	0.682	0.495	(0.00,1.53)	0.169
1 3 4	0.306	0.777	0.393	0.694	(0.00,1.83)	0.191
1 3 5	0.176	1.377	0.128	0.899	(0.00,2.87)	0.252
1 2 5	0.140	0.583	0.240	0.810	(0.00,1.28)	0.228
1 2 4	0.104	0.394	0.264	0.792	(0.00,0.88)	0.181
2 3 5	0.068	0.833	0.082	0.935	(0.00,1.70)	0.216

```
22 . 
    end of do-file

23 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"
```

Thursday May 31 01:43:24 2018 Page 4

```
24  . //assume a common heterogeneity estimate 0.02 in the entire network (derived from network meta)
25  . ifplot _y _stderr _t1 _t2 ID, tau2(0.02)

     * 7 triangular loops found
```

Loop	IF	seIF	z_value	p_value	CI_95
2 3 5	0.667	0.191	3.488	0.000	(0.29,1.04)
1 3 5	0.622	0.172	3.609	0.000	(0.28,0.96)
1 3 4	0.464	0.197	2.360	0.018	(0.08,0.85)
2 3 4	0.412	0.192	2.147	0.032	(0.04,0.79)
1 2 5	0.062	0.112	0.556	0.578	(0.00,0.28)
1 2 3	0.039	0.129	0.302	0.763	(0.00,0.29)
1 2 4	0.014	0.087	0.160	0.873	(0.00,0.18)

```
26  . ***
    end of do-file

27  . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

28  . ***5.Running network meta-analysis with network meta***
29  . ***
30  . //prepare the data in the appropriate format
31  . network convert augment
    Converting pairs to augmented ...

32  . ***
    end of do-file

33  . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

34  . //perform network meta-analysis assuming consistency a common heterogeneity across all comparisons i
35  . network meta c
    Command is: nwmeta _y _S , bscovariance(exch 0.5) longparm suppress(ux mm)  vars(_y_2 _y_3 _y_4 _y_5
    Note: using method  reml
    Note: using variables  _y_2 _y_3 _y_4 _y_5
    Note:  65 observations on  4 variables
    Note: variance-covariance matrix is  proportional to  .5*I(4)+.5*J(4,4,1)

    initial:       log likelihood =   -192.22418
    rescale:       log likelihood =   -192.22418
    rescale eq:    log likelihood =   -192.22418
    Iteration 0:   log likelihood =   -192.22418
    Iteration 1:   log likelihood =   -191.79084
    Iteration 2:   log likelihood =   -191.75726
    Iteration 3:   log likelihood =   -191.75715
    Iteration 4:   log likelihood =   -191.75715

    Multivariate meta-analysis
    Variance-covariance matrix =  proportional .5*I(4)+.5*J(4,4,1)
    Method = reml                                 Number of dimensions    =       4
    Restricted log likelihood =  -191.75715       Number of observations  =      65
```

	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
_y_2						
_cons	-.9271258	.1486131	-6.24	0.000	-1.218402	-.6358494
_y_3						
_cons	-.6956455	.2987628	-2.33	0.020	-1.28121	-.1100813
_y_4						
_cons	-.5157603	.2613259	-1.97	0.048	-1.02795	-.0035709

Thursday May 31 01:43:24 2018 Page 5

Estimated between-studies SDs and correlation matrix:

	SD	_y_2	_y_3	_y_4	_y_5
_y_2	.91640611	1	.	.	.
_y_3	.91640611	.5	1	.	.
_y_4	.91640611	.5	.5	1	.
_y_5	.91640611	.5	.5	.5	1

nwmeta command stored as F9

```
36 . 
```
end of do-file

```
37 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

38 . ***6.Producing the predictive interval plot***
39 . 
40 . //produce the predictive interval plot
41 . intervalplot,pred null(0) lab(WL CBT BA NDST EX)  marg(10 40 5 5) xlab(-2 -1.5 -1 -0.5 0 0.5 1)
```

The intervalplot command assumes that the saved results from nwmeta or network meta commands hav

Comparison	Effect_Size	LCI	UCI	LPrI	UPrI
CBT vs WL	-.9271258	-1.218402	-.6358494	-2.782341	.9280899
BA vs WL	-.6956455	-1.28121	-.1100812	-2.6218	1.23051
NDST vs WL	-.5157603	-1.02795	-.0035709	-2.420056	1.388535
EX vs WL	-1.004138	-1.432377	-.5759	-2.886761	.8784843
BA vs CBT	.2314803	-.3411348	.8040953	-1.690623	2.153584
NDST vs CBT	.4113655	-.070771	.8935019	-1.484756	2.307487
EX vs CBT	-.0770126	-.5481143	.3940891	-1.970248	1.816223
NDST vs BA	.1798852	-.5235999	.8833703	-1.786861	2.146631
EX vs BA	-.3084929	-.9688637	.3518779	-2.259637	1.642651
EX vs NDST	-.4883781	-1.128788	.1520317	-2.432593	1.455837

```
42 . 
```
end of do-file

```
43 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

44 . ***7.Producing the league table***
45 . 
46 . /*produce the league table of the network estimates and sort the treatments according to their relat
   > against placebo*/
47 . netleague, lab(WL CBT BA NDST EX) sort(WL CBT BA NDST EX)
```

The netleague command assumes that the saved results from nwmeta or network meta commands have b

The league table has been stored at the end of the dataset

```
48 . 
```
end of do-file

```
49 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

50 . ***8.Producing ranking plots for a single outcome using probabilities***
51 . 
52 . //estimate the ranking probabilities using network rank command
53 . network rank min, all nsim reps(5000) gen(prob)
```

Command is: nwmeta, mvmeta pbest(min in 1, nsim id(ID) all reps(5000) gen(prob) stripprefix(_y_) mvmn

Estimated probabilities (%) of each treatment being the best (and other ranks)
- assuming the minimum parameter is the best
- using 5000 draws
- allowing for parameter uncertainty

ID and Rank	Treatment 1	2	3	4	5

```
Thursday May 31 01:43:24 2018   Page 6

      4th |  3.2   1.1  28.8  64.0   2.9
    Worst |  96.7   0.0   0.9   2.4   0.0
-------------------------------------------
mvmeta command is stored in F9

54...
end of do-file

55 . do "C:\Users\ADMINI-1\AppData\Local\Temp\STD00000000.tmp"

56 . //produce the rankograms for all treatments
57 . sucra prob*, rankog lab(WL CBT BA NDST EX)

Treatment Relative Ranking of Model 1
```

Treatm-t	SUCRA	PrBest	MeanRank
WL	00.8	00.0	05.0
CBT	77.8	30.7	01.9
BA	52.0	11.5	02.9
NDST	35.1	01.9	03.6
EX	84.2	55.9	01.6

```
58...
end of do-file

59 . do "C:\Users\ADMINI-1\AppData\Local\Temp\STD00000000.tmp"

60 . //produce the cumulative ranking curve plots for all treatments
61 . sucra prob*, lab(WL CBT BA NDST EX)

Treatment Relative Ranking of Model 1
```

Treatm-t	SUCRA	PrBest	MeanRank
WL	00.8	00.0	05.0
CBT	77.8	30.7	01.9
BA	52.0	11.5	02.9
NDST	35.1	01.9	03.6
EX	84.2	55.9	01.6

```
62...
end of do-file

63 . do "C:\Users\ADMINI-1\AppData\Local\Temp\STD00000000.tmp"

64 . ***9.Producing the comparison-adjusted%funnel plot***
65...
66 . //prepare again the data in the pairs format
67 . network convert pairs
Converting augmented to pairs ...

68...
end of do-file

69 . do "C:\Users\ADMINI-1\AppData\Local\Temp\STD00000000.tmp"
```

```
      Thursday May 31 01:43:24 2018   Page 7

70 . //produce the comparison-adjusted funnel plot for all comparisons of an active treatment vs. placebo
71 . netfunnel _y _stderr _t2 _t1 if _t1=="1", ylab(0 0.1 0.2 0.3) bycomparison random

   Comparisons in the plot:

     1.       1 - 5
     2.       1 - 4
     3.       1 - 3
     4.       1 - 2

J2...
   end of do-file

73 . do "C:\Users\ADMINI~1\AppData\Local\Temp\STD00000000.tmp"

74 . netfunnel _y _stderr _t2 _t1 if _t1=="1", ylab(0 0.1 0.2 0.3) bycomparison random add(lfit _stderr _

   Comparisons in the plot:

     1.       1 - 5
     2.       1 - 4
     3.       1 - 3
     4.       1 - 2

J5...
   end of do-file

J6... log close
          name:  <unnamed>
           log:  C:\Users\Administrator\Dropbox\Academic Life\01 Data Analysis\NMA Analysis for Nick
     log type:  smcl
    closed on:  31 May 2018, 01:42:50
-------------------------------------------------------------------------------
```