ABSTRACT

Title of dissertation: ENVIRONMENTAL REWARD, GOAL-DIRECTED ACTIVATION, AND DEPRESSIVE SYMPTOMS AS PREDICTORS OF TRANSDERMAL NICOTINE PATCH ADHERENCE IN A RANDOMIZED CONTROLLED TRIAL OF BEHAVIORAL ACTIVATION TREATMENT FOR SMOKING

Elana M. Hoffman, Doctor of Philosophy, 2018

Dissertation directed by: Professor Andrea Chronis-Tuscano
Department of Psychology

Cigarette smoking remains the leading cause of morbidity and mortality in the U.S., and smoking rates are high. Nicotine Replacement Therapy (NRT) is sold over-the-counter and often distributed in smoking cessation clinical trials. With proper use, the nicotine patch is effective at helping individuals quit smoking and stay quit. However, rates of NRT adherence are low, and there is little research on the psychological predictors of compliance. Drawing from the larger medication adherence literature, we know that depressive symptoms predict poor medication adherence, though this has never been studied as it relates to NRT use. Furthermore, Behavioral Activation Treatment for Smoking (BATS) is hypothesized to reduce depressive symptoms

through increases in both positive reinforcement from the environment and goal-directed activation. Thus, it is possible that individuals who receive this treatment may exhibit increased compliance to the patch first through increases in environmental rewards or goal-directed activation, and subsequently though decreases in depressive symptoms. Using data from a stage-II randomized controlled trial (RCT) examining BATS compared to standard smoking cessation treatment (ST), we utilized a serial mediation model to examine this question. The aims of the study were: (1) to examine a serial mediation model in which BATS would affect NRT adherence through increases in environmental reward at mid-treatment and decreases in end-of-treatment depressive symptoms; and (2) to examine a serial mediation model in which BATS would affect NRT adherence through increases in goal-directed activation mid-treatment and decreases in end-of-treatment depressive symptoms. We hypothesized that BATS would produce increases in environmental reward, which in turn would decrease depressive symptoms, which in turn would predict greater patch use. Our second model examined goal-directed activation as a mediator, and we hypothesized that BATS would predict increases in goal-directed activation, which in turn would predict decreases in depressive symptoms, which in turn would predict increases in NRT adherence. We examined these models using Structural Equation Modeling (SEM). Our serial mediation model examining treatment condition→environmental rewards→depressive symptoms→NRT adherence was not supported, and neither was our model examining treatment condition→goal-directed activation→depressive symptoms→NRT adherence. However, we found significant pathways from mid-treatment goal-directed activation and NRT adherence, and end-of-treatment depressive symptoms to NRT adherence in our model examining goal-directed activation. Changes in both goal-directed activation and depressive

symptoms may be key when predicting NRT adherence in a sample of adult smokers enrolled in smoking cessation treatment.

ENVIORNMENTAL REWARD, GOAL-DIRECTED ACTIVATION, AND DEPRESSIVE SYMPTOMS AS PREDICTORS OF TRANSDERMAL NICOTINE PATCH ADHERENCE IN A RANDOMIZED CONTROLLED TRIAL OF BEHAVIORAL ACTIVATION TREATMENT FOR SMOKING

By

Elana M. Hoffman

Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, College Park in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
2018

Advisory Committee:
Dr. Andrea Chronis-Tuscano, Chair
Dr. Julia Felton
Dr. Jessica Magidson
Dr. Andres De Los Reyes
Dr. Eric Wish (Dean's Representative)

Acknowledgements

I would like to express my gratitude to my Dissertation committee: Drs. Andrea Chronis-Tuscano, Julia Felton, Jessica Magidson, Andres De Los Reyes, and Eric Wish. Your insight, feedback, and flexibility helped me make this project what it is today. To my mentor, Dr. Andrea-Chronis Tuscano, thank you for your immense guidance, wisdom and support as this milestone progressed. I could not have completed this Dissertation without you. I would also like to thank Drs. Laura MacPherson and Carl Lejuez for their support and guidance throughout my doctoral training.

Thank you also to the entire Center for Addictions, Personality, and Emotions Research (CAPER lab) for all of your hard work in the designing, recruiting and running of study assessments. I want to convey special thanks to the staff who recruited and ran participants through this study, as well as my fellow graduate students who participated as study therapists. Thank you also to my fellow graduate students for your support and friendship throughout our years at CAPER, and especially this past year. I could not have done this without you.

Final and very special thanks go to my family and friends, both across the country and here at UMD, and a very special thank you to my wonderful husband Ben Bresee. Your love, support and friendship are the reason I am who I am today.

Table of Contents

Acknowledgements ii
List of Tables iv
List of Figures v
List of Appendices vi
Chapter 1: Introduction 1
Chapter 2: Methods 17
Chapter 3: Results 26
Chapter 4: Discussion 29
Figures 44
Tables 48
Appendices 55
References 63

List of Tables

Table 1: Demographics and smoking history variables for total sample and baseline differences by treatment condition (BATS vs. ST)
Table 2: Descriptive Statistics for key study variables and comparisons between treatment conditions
Table 3: Bivariate correlations among NRT adherence, environmental reward, goal-directed activation, depressive symptoms, cigarettes per day, lifetime quit attempts, and age

List of Figures

Figure 1: Conceptual multiple mediation model
Figure 2: Consort Diagram
Figure 3: Study Timeline
Figure 4: Timeline of Study Measures
Figure 5: The association between treatment and NRT adherence with each pathway in the multiple mediation model examining environmental rewards as a mediator
Figure 6: The association between treatment and NRT adherence with each pathway in the multiple mediation model examining goal-directed activation as a mediator
Figure 7: Mediation model with environmental reward as MI, including all paths and covariates
Figure 8: Mediation model with goal-directed activation as MI, including all paths and covariates

List of Appendices

Appendix A: Time-Line Follow Back
Appendix B: Smoking History Questionnaire
Appendix C: Beck Depression Inventory-II
Appendix D: Reward Probability Index
Appendix E: Behavioral Activation for Depression Scale

Chapter 1: Introduction

Cigarette smoking and Nicotine Replacement Therapy

Cigarette smoking remains the leading cause of morbidity and mortality in the United States (CDC, 2016). Despite this, rates of smoking in the U.S. are approximately 16.8% (CDC, 2016). Though 70% of smokers report interest in quitting, only a small percentage (2-3%) are successful (Moore, Aveyard, Connock, WangDechao, Fry-Smith, Barton, et al., 2009). To this end, there have been numerous clinical trials conducted to treat cigarette smoking and nicotine dependence, and the number of evidence-based treatments continues to grow. The vast majority of evidence-based treatments for cigarette smoking involve nicotine replacement therapy (NRT).

NRT is a type of treatment that uses special products that provide small doses of nicotine in order to stop cravings and relieve withdrawal symptoms that occur when an individual attempts to quit smoking (National Cancer Institute, 2016). The Food and Drug Administration has approved five NRT products: nicotine gum, nicotine inhalers, nicotine nasal spray, nicotine lozenges, and the transdermal nicotine patch. The nicotine patch, in which nicotine is delivered to the body through the skin in the form of an adhesive patch, is easy to use, has extensive empirical support regarding effectiveness and safety, and has a relatively benign side effect profile that led to its approval as an over-the-counter medication. Though the number of people who purchase the nicotine patch over the counter is unclear, we know that there is a huge market for this product, with annual sales in the Unites States around $2.4 billion (Partnership for Drug-Free Kids, 2015).

The transdermal nicotine patch is highly effective in helping individuals quit smoking, both by itself and also in conjunction with smoking cessation counseling (Brown, Niaura, Lloyd-Richardson, Strong, Kahler, 2007; Stead, Perera, Bullen, Mant, Hartmann- Boyce, Cahill, et al.,

2008). Standard smoking cessation includes different components, but typically involves relapse prevention, setting a quit-date, self-monitoring, and strategies to avoid smoking behaviors (Brown, Lichtenstein, McIntyre, & Harrington-Kostur, 1984; Brown et al., 2007; Fiore & Baker, 2008).

Regarding effectiveness of the nicotine patch, a 1994 meta-analysis of 17 randomized controlled trials that compared the active nicotine patch to a placebo patch showed that overall abstinence rates for those using an active nicotine patch were 27% vs. 13% for those using the placebo patch, and the rates of abstinence at 6 months were 22% for those using the nicotine patch vs. 9% for those using placebo. Additionally, the odds ratios for the efficacy of the active nicotine patch vs. the placebo patch were 2.6 at the end of treatment and 3.0 at 6 months. The authors found that the active patch was superior to the placebo patch regardless of patch type, patch treatment duration, weaning, counseling format, or counseling intensity (Fiore, Smith, Jorenby, & Baker, 1994). Additionally, Silagy and colleagues (2004) conducted a meta-analysis in which they examined the effectiveness of different forms of NRT in achieving abstinence from cigarettes at six months. They analyzed data from 103 trials comparing NRT to placebo or no treatment, and found that, regardless of treatment setting, the odds ratio (OR) of any form of NRT compared to control was 1.77 (95% confidence intervals (CI): 1.66 to 1.88), and 1.81 (95% CI: 1.63 to 2.02) for nicotine patches (Silagy, Lancaster, Stead, Mant, & Fowler, 2004). Thus, the nicotine patch is clearly an effective way to help those who wish to quit smoking.

Despite the wealth of evidence to support the effectiveness of the patch, major gaps in the literature remain regarding patterns of patch use, measurement of patch use, and predictors of patch adherence. It is imperative to gain a fuller understanding of predictors and processes

related to nicotine patch adherence in order to maximize its effectiveness and deliver targeted smoking cessation interventions to individuals at high risk for non-adherence.

Measuring and defining adherence to the nicotine patch

Regarding patch use, individuals typically start with a high dosage and taper off as they are weaned off of the nicotine. The latest guidelines from the U.S. public health service recommend that individuals wear the nicotine patch for eight weeks or less, though some brands are designed to be used for ten weeks (National Cancer Institute, 2016). After the individual is weaned off of nicotine by way of the patch, their body does not crave the drug and, if the treatment is successful, the individual remains smoke-free.

Due to the paucity of literature regarding medication adherence in the context of smoking cessation, there is no consensus on what defines adequate adherence to NRT (Raupach, Brown, Herbec, Brose, & West, 2014). As a consequence, studies have used a variety of definitions, including "taking at least one dose of medication for 80% of the recommended days' (Hays, Leischow, Lawrence & Lee, 2010), 'chewing at least 10 pieces of nicotine gum per day' (Fagerstrom, 1984), and proportion of prescribed doses to doses actually taken (Goldstein, Niaura, Follick, & Abrams, 1989; Schmitz, Stotts, Mooney, Delaune, & Moeller, 2007). In the larger medication adherence literature, "good adherence" to oral medication for chronic diseases is defined as taking the medication for at least 80% of the recommended duration (DiMatteo et al., 2014). Along these lines, given that the transdermal nicotine patch is recommended for 24 hours, perfect NRT adherence (24 hour use) is important for cessation outcomes.

Adherence to NRT has been measured in numerous ways. For example, NRT adherence has been measured using total days per week of patch use, both continuously and chunking days of the week into segments (e.g. less than 7 days, 7-27 days, and at least 28 days), by a ratio of

days used to total days recommended (Fish, Peterson, Brouwer, Lyna, Oncken, Swamy, et al., 2009; Shaw, Ferry, Pethica, Brenner, & Tucker, 1998; Scherpof, van den Eijnden, Lugtig, Engels, & Vollebergh, 2014), and by number of weeks participants reported wearing the patch (Lam, Abdullah, Chan, & Hedley, 2005, Roddy, Romilly, Challenger, Lewis, & Britton, 2006). In addition to measuring adherence continuously, several studies have examined adherence dichotomously (i.e. adherent or not) according to various cutoff points (Shiffman et al., 2008; Wiggers, Smets, Oort, de Haes, Storm-Versloot,….& Peters, 2006; Swartz, Ellsworth, Curry, & Boyko, 1995). For example, Ehrman and colleagues (1994) used the Time-Line Follow Back (TLFB) method for measuring adherence, and defined adherence as wearing the patch for 24 hours a day. Though most studies examining NRT adherence have used retrospective reporting, there have been a few that used daily dairy methods and Ecological Momentary Assessment (EMA; Shiffman et al., 2008; Ma, Kendzor, Poonawalla, Balis, & Businelle, 2016), though these studies have important limitations such as short follow-up duration (during which patch use was measured) or measuring adherence dichotomously.

NRT Adherence Rates

Overall NRT adherence rates vary widely depending on the approach to measurement. For example, when measured dichotomously, adherence rates range from 55%-96% (Shiffman et al., 2008; Swartz et al., 1995; Ehrman et al., 1994). However, other studies show that daily adherence may be much lower (29%; Fish et al., 2009). When Lam and colleagues (2005) measured adherence by weekly retrospective reports, they found that adherence rates were 16%, and Roddy and colleagues (2006) found that the mean duration of adherence in low-income young adults smokers was one week out of six. Wiggers and colleagues (2006) also found weekly adherence to be low (36%) when they measured according to retrospective reports.

Balmford and colleagues (2011) found that 71.4% of NRT users discontinued the patch prematurely.

NRT adherence in the context of smoking cessation trials is also low. In a trial for smoking cessation among HIV positive African Americans, Matthews and colleagues (2013) found that daily adherence to NRT was 39%. In a controlled trial examining a three-group randomized design (varenicline vs. placebo, in comparison with NRT plus ad libitum rescue) for smoking cessation among methodone-maintained smokers, adherence to the nicotine patch was 48.8% in the first 30 days of follow-up (Stein & Anderson, 2003). In a smoking cessation trial for HIV positive smokers, the rates of daily NRT adherence were 62% after 1 month, and 37% after 3 months (Ingersoll, Cropsey, & Heckman, 2009). Overall, based on a multitude of studies taking different approaches to the measurement of adherence, it appears that rates of NRT adherence are quite low. Low NRT adherence rates undermine the success of smoking cessation interventions, and thus is a critically important construct to study (Raupach et al., 2014).

Who exhibits poor patch adherence?

The literature regarding predictors of adherence and characteristics of those who initiate patch use is quite limited. Fu and colleagues (2008) examined patch use and abstinence rates among 9,216 Caucasian, African-American, Asian, and Latino adult lifetime smokers. Results showed that Caucasians were most likely to initiate patch use compared to all other groups. When multivariate analyses were conducted with all racial/ethnic groups in the same model, only African-Americans (relative to the Caucasian reference group) significantly predicted having never used the nicotine patch to assist in smoking cessation. These differences persisted after controlling for demographic factors such as socioeconomic status. Additional studies have identified demographic characteristics associated with increased patch adherence and found that

older age, male gender, higher education, and non-Latino minority status predicted greater patch adherence (Lam et al., 2004; Burns and Levinson, 2008).

In addition to demographic characteristics, several studies have examined smoking history and study variables in relation to NRT adherence. This research has shown that smoking history variables including experience with NRT, motivation to quit, number of cigarettes per day, and more previous quit attempts were associated with increased NRT adherence (Alterman, Gariti, Cook, & Cnaan, 1999; Lam et al., 2004; Cooper, DeBon, Stockton, Klesges, Steenbergh, ... & Johnson, 2004). Regarding study variables, more intensive concurrent treatment (compared to standard care), and continued study participation were also associated with greater NRT adherence (Cooper et al., 2004).

In addition to studies investigating demographic variables, smoking history variables, and study variables, to our knowledge, there has only been one study to investigate personality traits associated with NRT adherence. Scherphof and colleagues (2014) assessed whether different NRT compliance trajectories could be distinguished among adolescent smokers. They found that individuals who demonstrated the highest level of compliance were characterized by high levels of conscientiousness and agreeableness as well as lower levels of extraversion compared with those whose compliance to the patch decreased over time. In addition to investigating personality variables, it is critically important to investigate psychological predictors of patch utilization in order to gain a more complete understanding of factors that contribute to patch adherence given the dearth of literature on this topic, widespread use of the patch, and high comorbidity rates among individuals who are attempting to quit smoking.

Depressive symptoms, smoking, and adherence

Although depression has been found to predict adherence to medication for a variety of health problems, it has never been studied in relation to NRT adherence. This is surprising given the high comorbidity between smoking and Major Depressive Disorder (MDD), with estimates as high as 30% (Grant, Hasin, Chou, Stinson, & Dawson, 2004). Indeed, lifetime history and prevalence of MDD in the past year have been consistently associated with increased smoking prevalence in community samples (Lasser, Boyd, Woolhandler, Himmelstein, McCormick, & Bor, 2000; Leventhal, Japuntich, Piper, Jorenby, Schlam, & Baker, 2012; Morris, Giese, Turnball, Dickinson, & Johnson-Nagel, 2006). In addition showing a strong connection between smoking and diagnosis of MDD, the literature to date has shown that smokers with elevated depressive symptoms smoke more than their non-depressed counterparts (Anda, Williamson, Escobedo, Mast, Giovino, & Remington, 1990; Brown et al., 2000) and have poorer cessation outcomes, regardless of use of NRT, compared to smokers without elevated depressive symptoms (MacPherson, Tull, Matusiewicz, Rodman, Strong, Kahler,... & Lejuez, 2010; Catley et al., 2005; Cinciripini et al., 2003; Niaura et al., 2001). For example, in a randomized controlled trial testing a Behavioral Activation Treatment for Smokers (BATS) among community adults with elevated depressive symptoms, MacPherson and colleagues (2010) found that higher baseline depressive symptoms were associated with lower odds of smoking abstinence. Leventhal and colleagues (2008) investigated the differential effects of depressive symptoms and positive and negative motivations for cigarette smoking, as well as the effect of depressive symptoms on smoking cessation. They found that baseline depressive symptoms including negative affect, somatic complaints, and anhedonia (i.e., low interest in pleasurable activities) each predicted relapse to smoking. Furthermore, Berlin and Covey (2006) found that individuals with elevated depressive symptoms at baseline indicated by a BDI score of ≥ 10 had

a decreased likelihood of cessation in a large multisite smoking cessation trial. Findings suggesting that elevated depressive symptoms are associated with poor smoking cessation outcomes highlights the vulnerability of this population in regards to successful cessation efforts. Though it is established that elevated depressive symptoms are associated with poor cessation outcomes, to our knowledge, no study to date has examined poor adherence to the nicotine patch as a function of depressive symptoms.

In addition to the aforementioned vulnerabilities, individuals with elevated depressive symptoms have increased difficulty adhering to their medication for a variety of conditions. For instance, a study conducted examining the impact of depressive symptoms on multiple aspects of diabetes management found that compared to participants with low levels of depressive symptoms, participants with moderate to high levels of depressive symptoms had a higher percentage of days on which they were non-adherent to hypoglycemic regimens (15% to 7%; Ciechanowski, Katon, & Russo, 2000). Numerous additional studies have found significant associations between depressive symptoms and compromised medication adherence among individuals with diabetes (Lin, Katon, Von Korff, Rutter, Simon, Oliver, & Young 2004; Gonzalez, Safren, Cagliero, Wexler, Delahanty, Wittenberg, & Grant, 2007). Depressive symptoms have also been associated with poor medication adherence among patients with cardiovascular disease, HIV/AIDS, and hypertension (Bane, Hughes, & McElnay, 2006; Safren, Otto, & Worth, 1999; Ammassari, Antinori, Aloisi, Trotta, Murri, Bartoli, L., ... & Starace, 2004). A 2003 review by Katon suggested that depressive symptoms account for increased rates of morbidity and mortality among individuals with chronic illness due in part to poor medication adherence.

Taken together, individuals with elevated depressive symptoms are more likely to smoke cigarettes, have an increased difficulty quitting smoking when they try, and have increased difficulty adhering to their medications for a variety of conditions. Thus, depressive symptoms as they relate specifically to poor nicotine patch adherence are a critically important area of research.

Theoretical Framework for the Link between Smoking, Environmental Reward, Goal-Directed Activation, Depressive Symptoms, and Poor Adherence

Behavioral theory (Skinner, 1953: Bandura and Walters, 1963; Bandura, 1969) provides a useful framework for conceptualizing predictors of poor adherence to NRT. Lack of reinforcement from the environment (Ferster, 1973; Lewinsohn, 1974; Skinner, 1953) has been linked to both depression and various forms of substance use, including smoking (Higgins, Heil, & Lussier, 2004; Daughters, Braun, Sargeant, Reynolds, Hopko, Blanco, & Lejuez, 2008). Smokers who experience a lack of access to positive reinforcement in the environment may be less motivated to use NRT as suggested because they may be less likely to access the rewards from a healthy and active lifestyle, which may include a successful quit attempt. Additionally, smokers who experience a lack of environmental reinforcement may exhibit increased depressive symptoms, which may affect NRT adherence.

Indeed, there is evidence to suggest that smokers do not benefit from positive reinforcement in the environment at the same rate as their non-smoking counterparts. For example, studies have shown depressed responses to rewarding stimuli both when smokers are abstinent, as well as when they are not abstinent (Powell, Dawkins, & Davis, 2002; Perkins, Lerman, Grottenthaler, Ciccocioppo, Milanak, Conklin, 2008; Martin-Sölch et al., 2001; Martin-Sölch, Missimer, Leenders, & Schultz, 2003). Specifically, Martin- Sölch and colleagues

investigated regional cerebral blood flow (rCBF) in smokers and nonsmokers during a monetary reward task. The investigators found a cortico-subcortical loop involved in processing increasing monetary reward. The loop consisted of the dorsolateral prefrontal cortex, the orbitofrontal cortex, the cingulate gyrus and the thalamus. Results of this study indicated that the striatal response to reward differentiates smokers from nonsmokers, in that there were significant associations between rCBF increases in striatum and increasing monetary reward and between striatal rCBF increases and mood in nonsmokers, but not in smokers. This shows that smokers do not exhibit the same reward processing as nonsmokers. Furthermore, Powell and colleagues (2001) showed that, independent of withdrawal severity, smokers who were abstinent exhibited decreased pleasure expectancies and responsiveness to financial incentives. This is important because it shows that even when smokers are not experiencing withdrawal (i.e., when low positive affect cannot be attributed to withdrawal symptoms), they derive less reward from the environment.

A related concept to environmental reward is goal-directed activation. This construct represents focused, goal-directed completion of scheduled activities, which is in line with Lewinsohn's behavioral theory of depression. This theory states that depressed individuals engage in fewer activities, increased withdrawal behaviors, and fail to complete activities that result in pleasure or mastery, thereby maintaining depression (Ferster, 1973; Lewinsohn, 1974; Skinner, 1953). As with environmental reward, goal-directed activation is important to consider when discussing mechanisms that serve to maintain depressive symptoms and smoking behavior. Indeed, in response to this blunted reward system among smokers, treatments for smoking cessation have been developed to incorporate rewarding activities in order to increase positive

reinforcement in the environment and goal-directed activation, and decrease depressive symptoms to aid in smoking cessation (e.g., MacPherson et al., 2010).

Environmental Reinforcement, Goal-Directed Activation, Depression, and Medication Adherence

There is also literature to support an association between lack of environmental reward and poor medication adherence for a variety of medical conditions. Magidson and colleagues (2015) investigated behavioral predictors of poor medication adherence among HIV positive individuals in residential treatment for substance use. The authors found that an important aspect of reinforcement from the environment, environmental punishment, or perceived negative consequences in the environment (i.e., the belief that bad things happen and choices will not lead to positive reinforcement) significantly predicted poor medication adherence. Individuals may be less motivated to take their medication as prescribed if they believe that the environment is punishing regardless of their choices, that is, that even if they choose to take their medication as instructed, the environment will not positively reinforce this behavior. Furthermore, goal-directed activation might affect medication adherence. Research has identified that an element of goal-directed activation, participation in regular activities (i.e. changes in daily routine) is related to medication adherence (Chesney, 2000). Additionally, because a lack of goal-directed activation is known to contribute to the development and maintenance of depressive symptoms (Lewinsohn, 1974), it may also affect adherence indirectly through depressive symptoms.

Though neither environmental reinforcement nor goal-directed activation has been studied with smokers attempting to quit using NRT, the behavioral principles underlying these results may be useful in conceptualizing predictors of poor adherence to the nicotine patch. If individuals are not engaging in meaningful activities and therefore not accessing rewards from

their environment, and are instead receiving much of their positive reinforcement from cigarette smoking, they may be less inclined to utilize the recommended agents to quit smoking (e.g., the nicotine patch) because they are not motivated to live a healthy and active lifestyle complete with multiple sources of positive reinforcement.

Lack of access to environmental rewards and goal-directed activation is central to many models of depression (Lewinsohn, 1974), and there is a wealth of literature to support the relationship between depressive symptoms and lack of access to environmental reward in adults. Evidence suggests that depressed individuals engage in fewer pleasant activities (Lewinsohn & Graf, 1973). Additionally, Hopko and colleagues found that individuals who are depressed engage in fewer interpersonal behaviors, suggesting a lack of social reinforcement (Hopko, Bell, Armento, Hunt, & Lejuez, 2005; Lewinsohn & Shaffer, 1971; Libet & Lewinsohn, 1973). Smokers with elevated depressive symptoms may be experiencing a lack of positive reinforcement from the environment for non-smoking activities because they are not accessing rewards from living a healthy and active life, due to their depressive symptoms and smoking being a primary source of reward. Furthermore, it is likely that the lack of positive reinforcement in the environment and goal-directed activation may precede depressive symptoms because individuals who do not engage in positive activities in the environment can develop depressive symptoms (Lewinson 1974; Hopko et al., 2011). The resulting increases in depressive symptoms may lead to poor NRT adherence.

Behavioral Activation

Given the connection between low mood and medication adherence, it follows that effective treatment for depressive symptoms may also be effective for medication adherence, and specifically, NRT adherence. Brief Behavioral Activation Treatment for Depression (BATD;

Lejuez, 2001; 2011) is rooted in Lewinsohn's behavioral theory of depression (Lewinsohn 1974), which states that depression and depressive symptoms are developed and maintained as a result of a low rate of response-contingent positive reinforcement in the environment. BA targets this lack of response-contingent positive reinforcement in the patient's environment by brainstorming and scheduling value-driven activities with various life areas. For example, if a person values being a good spouse, they may schedule the activity of going out to dinner once per week with their partner (Lejuez et al., 2011). Theoretically, due to the increase in goal-directed, rewarding activities, depressive symptoms are reduced. BATD has been effective in reducing depressive symptoms in a wide range of populations including patients within an inpatient psychiatric hospital (Hopko, Lejuez, LePage, Hopko, and McNeil (2003), university students (Gawrysiak, Nicholas, and Hopko (2009), obese individuals, (Pagoto et al., 2008), cancer patients (Hopko, Bell, Armento, Hunt, & Lejuez, 2005), older adults (Egede et al., 2009; Snarski et al., 2011), depressed primary care patients (Ekers et al., 2011), substance users (Daughters et al., 2008), and HIV positive substance users when coupled with Life-Steps (Safren et al., 2001; Daughters et al., 2008; Magidson et al., 2014).

MacPherson and colleagues (2010) extended this treatment to community smokers with elevated depressive symptoms. A sample of 68 adult smokers were randomized to receive either Behavioral Activation Treatment for Smoking (BATS), or Standard Treatment (ST). Results showed that at the 26-week follow-up, participants in BATS reported greater smoking abstinence (adjusted odds ratio=3.59, 95% CI [1.22, 10.53], p =.02), as well as greater reduction in depressive symptoms (*B*=1.99, *SE* _ 0.86, *p* =.02) than those in the ST condition. Though this study was the first to examine BA as a treatment for smoking, it did not address predictors of

adherence to the nicotine patch, nor did it address mechanisms through which depression or adherence might be affected.

Current Study

Given the widespread use of NRT, and particularly the nicotine patch for smoking cessation, it is imperative to understand affective and environmental factors that contribute to patch adherence among treatment-seeking individuals. There are significant gaps in the literature regarding the use of the nicotine patch. First, while the literature shows that patterns of adherence to the nicotine patch varies widely (Shaw et al., 1998; Swartz et al., 1995; Fish et al., 2009; Shiffman et al., 2008), the predictors of inconsistent adherence are not well documented.

Moreover, although it is apparent that NRT adherence is generally low across methods of measuring adherence, we know little about the psychological factors that predict adherence. Furthermore, many studies measure adherence by the month, week, or day, but there may be important information lost with these methods since the patch is typically recommended for 24-hour use. Measuring adherence by the hour is critical in order to gain a clear picture of adherence because we know that the patch is most effective when it is worn according to the recommended length of time (Ma et al., 2016).

Additionally, while we know that depressive symptoms contribute to poor medication adherence among individuals with various medical conditions (Bane et al., 2006; Safren et al., 1999; Ammassari, et al., 2004), depressive symptoms have never been studied as a predictor of poor nicotine patch adherence. Moreover, low levels of environmental reward has also been shown to contribute to poor medication adherence among individuals taking highly active antiretroviral medication (Magidson et al., 2015). Indeed, the effect of increased environmental reward and increased goal-directed activation on depressive symptoms are well known

(Lewinsohn, 1974; Lejuez et al., 2001, 2011), but more research is needed regarding these constructs and their effects on medication adherence through changes in depressive symptoms. Finally, environmental reward and goal-directed activation are a major treatment target for behavioral activation studies (Lejuez et al., 2011; Daughters et al., 2008; MacPherson et al., 2010), but they have not been investigated as mechanisms through which depressive symptoms may be decreased and NRT adherence may be increased. Behavioral Activation Treatment for Smoking (BATS) may address NRT adherence through increasing positive reinforcement in the environment and goal-directed activation, therefore decreasing depressive symptoms.

This study will address the gaps in the literature by examining the hypothesized mechanisms of Behavioral Activation Treatment for Smoking (BATS) (e.g., environmental reward, goal-directed activation, and depressive symptoms) as predictors of NRT adherence in the context of an RCT comparing BATS to standard smoking cessation treatment (ST). We will use data from a large RCT which examined BATS vs. ST as a treatment for smoking cessation and depressive symptoms. We will investigate the effect of BATS vs. ST on changes in environmental reward and goal-directed activation, respectively, and the effect of these changes on depressive symptoms and ultimately NRT adherence. We will use precise measurements of hourly patch use, which has not been examined previously in this context. Results of this study hold potential to yield valuable information regarding mechanisms that may explain the relationship between environmental rewards, goal-directed activation, depressive symptoms, and NRT adherence among treatment-seeking adult smokers from the community.

Aims and Hypotheses

Primary Aim: To examine two separate serial mediation models examining the effect of two distinct treatment targets of Behavioral Activation Treatment for Smoking (BATS) on NRT adherence: (1) environmental reward; and (2) goal-directed activation.

Aim 1a: Our first model will examine the effect of treatment condition (BATS vs. ST) on NRT adherence through changes in environmental reward leading to changes in depressive symptoms leading to changes in patch adherence.

Aim 1b: Our second model will examine the effect of treatment condition on NRT adherence through changes in goal-directed activation leading to changes in depression leading to changes in patch adherence.

Hypothesis 1a: In line with the theoretical underpinnings of Behavioral Activation, we hypothesize that BATS (relative to standard treatment) will significantly increase positive reinforcement in the environment, which will significantly predict decreases in depressive symptoms (Lewinsohn, 1974; Lejuez et al., 2001; 2011), which will ultimately predict increases in NRT adherence. Though depressive symptoms have not been examined in relation to NRT adherence, we rely on extant literature in the medical field to justify these hypotheses (Bane et al., 2006; Safren et al., 1999; Ammassari et al., 2004).

Hypothesis 1b: We hypothesize that BATS will significantly increase goal-directed activation, which will significantly predict decreases in depressive symptoms (Lewinsohn, 1974; Lejuez et al., 2001; 2011), which will ultimately predict increases in NRT adherence. See Figure 1 for an illustration of our multiple serial mediation models.

Chapter 2: Methods

Participants

Participants in the study included adult smokers with elevated depressive symptoms enrolled in a stage II Randomized Controlled Trial (RCT) investigating Behavioral Activation Treatment for Smoking (BATS) compared to standard smoking cessation treatment (ST). Participants were recruited from the Washington, D.C. area via online and print flyers, in addition to radio and newspaper ads for a study advertising group therapy for smoking cessation. Advertisements did not mention depressive symptoms, and participants were blinded to study goals and hypotheses. Participants were eligible for the larger treatment study (see below for description of treatment conditions) if they met the following inclusion criteria: Were between 18 and 65 years of age; were a regular smoker for at least one year; were willing to use the patch; were currently smoking an average of at least 5 cigarettes per day; reported motivation to quit smoking in the next month (≥5 on a scale of 1-10); reported current elevated depressive symptoms on the Beck Depression Inventory (BDI-II ≥ 10); and were English speaking with reading comprehension of at least an eighth grade level. Participants were excluded based on evidence of: any current Axis I disorder; psychoactive substance dependence (excluding nicotine dependence) within the past 6 months; current use of psychotropic medication or participation in any form of psychotherapy; a history of a significant medical condition (e.g., cardiovascular, neurological, gastrointestinal), pregnancy and/or breast feeding, or other systemic illness and/or be deemed as currently unhealthy in the context of a complete physical examination due to the use of NRT during the study; limited mental competency and/or the inability to give informed, voluntary, written consent to participate; and current use of any pharmacotherapy for smoking cessation not provided by the researchers. Participants were included in the current study if they attended the baseline assessment, and were randomized to a treatment condition (n=184). See

Figure 2 for the consort diagram. Data were collected from 184 participants that were randomized to receive either BATS (*n*=96), or ST (*n*=88). Participants smoked an average of 14.29 cigarettes per day since starting smoking (*SD*=7.69). See Table 1 for descriptions of participant demographics and smoking history variables.

Procedures

Participants who were eligible after the phone screen completed a battery of measures at the baseline assessment. Participants were randomized into one of two treatment groups that received either BATS or ST. Participants attended weekly sessions for 8 consecutive weeks. Participants were given one patch to apply the night before their assigned quit day, which was at session 4. They were instructed to place the patch on a clean, dry, hairless part of the body and leave it on for 24 hours, and then apply a new one. Unless participants smoked significantly less than the amount equivalent to the highest dosage of the nicotine patch, participants began with the full strength 21mg patch for 4 weeks, then tapered down to 14mg for 2 weeks, then finally 7mg for the remaining 2 weeks, for a total of an 8-week patch regimen. Participants were instructed to continue to wear the patch if they lapsed, unless their smoking reached 4 cigarettes per day for 4 consecutive days. At this point, they reset their quit day and re-committed to quit. Participants were given 7 days of patches at each treatment session, and then 4 weeks of patches following treatment (to last until the one month follow up assessment). See Figure 3 for the study timeline.

Participants completed questionnaires at each visit, including patch use for the previous week (following quit-day). Specifically, participants were asked how many hours (out of 24 hours) they used the patch each day since the previous visit. Thus, during the week 5, 6, 7, and 8 visits, participants reported hourly patch use for the previous week. Following treatment,

participants attended a one-month follow-up session, which occurred 8 weeks after their quit-date (4 weeks after the final treatment session). At the follow-up visit, participants reported on hourly patch use for the previous 4 weeks. Perfect patch adherence, for the purpose of this study, was defined as wearing the patch for 24 hours per day per the instructions participants were given[1].

Treatments

Participants in the trial were randomized to receive either Standard Treatment (ST) for smoking cessation or Behavioral Activation for Smoking (BATS; MacPherson et al., 2016). Both treatments were delivered in 60-minute weekly group sessions over a period of 8 weeks. Participants in both groups received 8 weeks of the nicotine patch and were given the same instructions for use.

ST was consistent with the standard smoking cessation treatment utilized in stage 1 of the study (MacPherson et al., 2010), and the standard behavioral treatment components have been well established (e.g., Brown et al., 1984; Brown et al., 2007). Session 1 consisted of discussing support for quitting, past quit experiences, benefits of quitting, setting a quit date, monitoring smoking behaviors, and the distribution of self-help materials (Clearing the Air, USDHHD, 1995). Sessions 2-3 consisted of identifying high-risk situations, discussing the abstinence violation effect, developing coping strategies, discussing alcohol use, enlisting social support, distribution and explanation of the nicotine patch (to put on right before session 4), and preparation for quitting, including cutting down smoking as much as possible in the weeks leading up to quit date. Quit week (session 4) and beyond (sessions 5-8) consists of discussing quit experiences, providing support, anticipating high-risk situations, developing social support,

[1] Updated guidelines for use of the nicotine patch recommend 10 weeks or even longer, but the majority of published clinical trials to date utilize an 8 week regimen as previously recommended.

and discussing lifestyle changes that promote staying quit. Participants in the ST condition were also asked to keep a written journal discussing topics of their choosing (thoughts, feelings, activities, etc.) as a means to equate for time spent on daily activity monitoring in the BATS condition.

BATS (MacPherson et al., 2010, 2016) consisted of the ST strategies described above, as well as integrating Behavioral Activation. BATS was focused on identifying life areas, values, and value-based activity scheduling in order to live a meaningful life according to one's values. The aims of this treatment was to reduce smoking and depressed mood though increasing access to positive reinforcement in the environment by the scheduling and executing of value-driven activities. Session 1 consisted of discussing the rationale for the BA treatment (helping the individual structure a variety of reinforcing activities that comprise a more rewarding nonsmoking lifestyle, which may help people manage negative emotions and improve positive affect, thus reducing the motivation to smoke), and assigning homework, which consisted of monitoring daily activities in addition to smoking. Sessions 2-3 consisted of discussing values and goals within a variety of life areas. Then, participants and therapists collaborated to brainstorm activities that were observable and measurable, and in line with the values identified. The activities were then scheduled in for the days until the next session. Sessions 4-8 (Quit week and beyond) consisted of checking in about daily activities, adding social support for said activities, and troubleshooting (i.e. difficulties completing activities, use of the patch). These last sessions consisted of continuing to schedule value-driven activities, discussing quit attempts, and modifying activities as necessary.

Measures

Psychopathology

The Structured Clinical Interview for the DSM-IV (SCID-IV; First & Gibbon, 2004) was used to assess lifetime and current DSM-IV Axis-I psychopathology to determine study eligibility (individuals with current disorders were excluded). The SCID-IV was conducted by trained interviewers (graduate students and post-baccalaureate research assistants) supervised by a clinical psychologist during the baseline assessment. Assessors attended weekly supervision meetings to review SCID and to confirm diagnoses with the supervisor. See figure 4 for timeline of measures.

Demographics

The Demographics form assessed age, race/ethnicity, education level, marital status, employment status, and annual household income.

Nicotine Patch Adherence

Time Line Follow-Back (TLFB) is a measure in the form of a calendar that was used for assessing hours that participants wore the patch. At each weekly visit post-quit (i.e., beginning in session 5), and at the one month follow-up, participants were asked how many hours they wore the patch each day out of a possible 24 hours. Thus, participants reported on 7 days of patch use at each weekly visit, and for a one-month period at the 8-week follow-up to assess patch adherence since the previous assessment. Participants kept all the patches they were given, regardless of their use. This self-report method of TLFB has been used to assess patch adherence previously (Alterman et al., 1999; Stein et al., 2005; A. de Dios et al., 2014; Matthews et al., 2013), and one prior study asked participants about hourly use using the TLFB (Ehrman et al., 1994), though the authors measured adherence dichotomously. The TLFB has demonstrated good reliability and validity with adult alcoholics (Sobell & Sobell, 1978; 1980; 1996) and has been validated for the assessment of adult daily cigarette use (Brown et al., 1998; MacPherson et

al., 2010). Several studies have used this method of retrospective reporting on NRT adherence, for duration longer than 4 weeks, though they did not use the TLFB (Fish et al., 2009; Balmford et al., 2011; Wiggers et al., 2006).

To quantify our dependent variable, patch adherence, we totaled the hours participants wore the patch according to the TLFB starting on quit day until their one-month follow-up (8 weeks total). The maximum number of hours was 1,344 (24 hours*7 days a week*8 weeks). This method of measurement is in line with literature suggesting that hourly use is recommended for optimal outcomes; thus, it is critical to measure adherence by the hour (Ma et al., 2016). See Appendix A.

Cigarette Smoking

Smoking History: Smoking history was assessed at baseline using the smoking history and current status questionnaire (Proceedings of the National Working Conference on Smoking Relapse, 1986). This questionnaire has been used in previous studies (MacPherson et al., 2010) and measures smoking variables including: smoking rate, brand, nicotine content, previous quit attempts and duration, household smokers, and onset age. We used relevant smoking history variables in our analyses. See Appendix B.

Depressive Symptoms

Beck Depression Inventory (BDI-II; Beck, Steer, Ball, & Ranieri, 1996) is a 21-item self-report measure of depressive symptoms. Items are scored on a 0-3 scale, where higher scores reflect increased depressive symptoms. Sample items include "sadness" and "loss of pleasure." The instrument has excellent internal consistency (α =.90 in the current sample) with depressed younger and older adults (Beck et al., 1996; Nezu, Ronan, Meadows, & McClure, 2000). We

used the total score in all our analyses, with higher scores indicating higher levels of depressive symptoms. Participants filled out the BDI at every study visit. See Appendix C.

Environmental Reward

Reward Probability Index (RPI; Carvalho et al., 2011) is a 20-item scale that is comprised of two factors: Reward Probability and Environmental Suppressors. The RPI is based on Lewinsohn's model of depression and was used to measure environmental reward. The RPI measures access to environmental rewards and response contingent positive reinforcement. Sample items from this subscale include: "I have many interests that bring me pleasure", and "I have many opportunities to socialize with people". The Environmental Suppressors index measures exposure to aversive or punishing stimuli in the environment. Sample items from this subscale include: "My behaviors often have negative consequences", "I have had many unpleasant experiences", and "Changes have happened in my life that have made it hard to find enjoyment". Participants are asked to rate their responses on a Likert scale ranging from "Strongly Agree" to "Strongly Disagree". The total score was used as our dependent variable, consistent with previous literature (Carvalho et al., 2011; Collado, Castillo, Maero, Lejuez, & MacPherson, 2014). Higher scores indicated higher levels of positive reinforcement in the environment. The RPI has high convergent validity (r=.65-.81, and α=.692 for the total score, and α=.86 for the reward probability subscale and α=.80 for the environmental suppressors subscale in the current sample) with measures of activity, avoidance, reinforcement, and depression in a sample of undergraduate students (Carvalho et al., 2011). It has also been used to measure access to environmental rewards in undergraduates with depression (Carvalho et al., 2011), Latinos with elevated depressive symptoms (Collado, Castillo, Maero, Lejuez, &

MacPherson, 2014) and HIV positive substance users in treatment (Magidson et al., 2015). Participants filled out the RPI at every visit. See Appendix D.

Goal-Directed Activation

The Behavioral Activation for Depression Scale (BADS; Kanter, Mulick, Busch, Berlin, & Martell, 2006). The BADS is a 25-item scale that measures purported changes in client behavior that should occur over the course of BA (i.e. increase in goal-directed activation). The measure is comprised of four scales that measure four distinct factors: Activation, Avoidance/Rumination, Work/School Impairment, and Social Impairment. The total score, in addition to the factors, demonstrated good factor structure, internal consistency (α ranging from .79-.87), construct validity, and test-retest reliability in undergraduate samples (Kanter at al., 2006), and α=.87 in the current sample. The first factor, Activation, represents focused, goal-directed activation and completion of scheduled activities. Avoidance/Rumination represents avoidance of negative aversive states and engaging in rumination rather than active problem solving. Work/School Impairment represents the consequences of inactivity and passivity on work and school responsibilities. The Social Impairment factor represented social isolation. We used the total score in all our analyses, with higher scores indicating higher levels of goal-directed activation. Participants filled out the BADS at every study visit. See Appendix E.

Data Analysis

Primary Aims 1a and 1b:

To examine our serial mediation model, we used structural equation modeling (SEM) to test mediation. We used M*plus* version 6.12 (Muthen & Muthen, 2011) for our SEM analyses. Mplus allows for the estimation of missing data using full information maximum likelihood (FIML). FIML allows for the inclusion of all available data points to estimate population

parameters. We examined the standard errors and *p*-values of the direct and indirect effects using bootstrapping. The indirect effect was considered significant if the bootstrapped 95% confidence interval did not include zero. We examined several indices of fit to determine the fit of the model to the data, including the chi-square test of model fit, Root Mean Square Error of Approximation (RMSEA), Comparative Fit Index (CFI), and Tucker Lewis Index (TLI). Guidelines suggest that good fitting models evidence a CFI $\geq$0.85, TLI $\geq$0.95 and RMSEA $\leq$0.05 (Bollen, 1989). For the multiple mediation analyses, we estimated three pathways from our independent variable (IV-BATS or ST) to our dependent variable (DV-NRT adherence) through our mediators, M1 (session 4 environmental reward or goal-directed activation, in separate models) and M2 (session 8 depressive symptoms). We chose these time points because participants were given the patch and instructed to start using it at session 4 (and had 8 weeks' worth of patches, to last until 1 month follow-up). We chose session 8 to examine our mediating variables at the end of treatment. These time points also allow for the examination of whether changes in the mediators (environmental rewards/goal-directed activation) were more likely to precede changes in the second mediator (depressive symptoms), and are ultimately associated with overall NRT adherence. Because smoking history and session attendance has been shown to affect patch adherence (Alterman et al., 1999, Cooper et al., 2004), we controlled for past quit attempts and number of cigarettes per day, as well as number of treatment sessions attended ("dose" of therapy; Cooper et al., 2004). In addition, we controlled for baseline and mid-session levels of our outcome variables in order to assess change over time. The a1 path represented the effect of treatment on session 2 RPI/BADS, the a2 path represented the effect of treatment on session 8 BDI, the a3 path represented the effect of session 4 RPI/BADS on session 8 BDI, the b1 path represented the effect of session 4 RPI/BADS on NRT adherence, the b2 path represented the

effect of session 8 BDI on NRT adherence, and the c' represented the direct effect of treatment on NRT adherence (See Figure 1).

Chapter 3: Results

Preliminary Analyses

First, we examined all variables for univariate normality (see Table 2 for descriptive statistics) and log-transformed variables that were not normally distributed. We found that baseline BDI (kurtosis=3.83 (*SE*=.36)), session 4 BDI (kurtosis=3.77 *SE*=.49), and session 8 BDI (kurtosis=4.63, *SE*= .463) were all outside acceptable ranges for skewness and kurtosis (≥3 kurtosis, ≥1 for skewness). We transformed the skewed variables and used the transformed values throughout our analyses. We then examined descriptive statistics for overall NRT adherence. Adherence to the patch was low, with an average of 750 hours wearing the patch out of 1,344. This means that, on average, participants exhibited an average of 55% adherence. Furthermore, only 19% of participants exhibit 100% adherence, and 20% exhibited 80% or greater adherence ("good" adherence is often considered 80% or higher; DiMatteo et al., 2014). There were no differences in NRT adherence between treatment conditions.

Regarding treatment attendance, participants attended an average of 3.4 (*SD*=3.0) sessions, with attendance significantly better in the ST condition. For both conditions, in total, fifteen percent attended all 8 sessions, and 34.2% attended 6 sessions or more (80% adherence). In the BATS condition, 10 participants attended all 8 sessions. In the ST condition, 17 participants attended all 8 sessions. In order to examine differences in attrition between the ST and BATS groups, we conducted a *t*-test comparing rates of attendance between the conditions. Participants in the ST condition attended significantly more sessions (*M*=4.0, *SD*=3.0) than in BATS (*M*=2.9, *SD*=3.0; *t*(182)=2.47, *p*=.010). We also compared levels of attendance between

men and women and found that women were significantly more likely to attend 6 or more sessions than men ($t(182)=2.026$, $p=.04$).

Next, we looked at correlations between key study variables (see Table 3). NRT adherence did not significantly correlate with any demographic predictors, and because we did not find any significant associations and because the literature does not support strong demographic differences in NRT adherence, we did not control for any demographic variables in our models. However, participant age (*M* age=44.61, *SD*=11.51) was significantly associated with number of treatment sessions attended ($r=.35$, $p<.001$). Higher NRT adherence was significantly associated with low BDI at session 4 ($r=-.31$, $p=.004$), high RPI at session 4 ($r=.26$, $p=.016$), higher number of previous quit attempts ($r=.24$, $p=.016$), and higher number of treatment sessions attended ($r=.59$, $p<.001$). Sessions attended, previous quit attempts, cigarettes smoked per day, and baseline and mid-treatment values of potential mediators were controlled for in all subsequent analyses.

Mediation Models[2]

Environmental Rewards:[3]

Our first primary hypothesis was that increases in environmental reward (RPI) at session 4 would produce decreases in depressive symptoms at session 8, and these paths would mediate the relationship between treatment condition and NRT adherence. In order to examine this hypothesis, we tested a serial mediation structural equation model in which we regressed NRT adherence onto depressive symptoms, which was regressed onto environmental reward (RPI),

[2] We ran all our mediation analyses using just participants that had attended at least one session, which yielded similar results.

[3] We ran analyses examining separate RPI subscales (reward probability and environmental suppressors). Neither model fit the data well (environmental suppressors: $\chi 2$ (df=11)=17.825, $p=.086$; RMSEA=0.102 (90% CI: 0.000-0.185); CFI=.710; TLI=.210; reward probability: $\chi 2$ (df=11)=20.692, $p=.037$; RMSEA=0.121 (90% CI: 0.030-0.201); CFI=.789; TLI=.424).

which, in turn, was regressed onto treatment condition (see Figure 5). We also included related covariates (quit attempts, cigarettes per day, sessions attended), as well as baseline and mid-treatment values of proposed mediators (in order to assess change over time). This serial mediation model provided an adequate fit to the data: $\chi 2$ (df=11)=12.43, p=.332; RMSEA=0.047 (90% CI: 0.00- 0.15); CFI=.95; TLI=.85). The indirect path from treatment to NRT adherence through session 4 RPI and session 8 BDI was not significant (coefficient =-.004, *SE*=.01, p=.764, CI [-.03 -.02]). Furthermore, none of our proposed pathways were significant, including: the a1 path (*S.E.*=.05, p=.224, CI [-.42 to .12), the a3 path (*SE*=1.47, p=.745, CI [-3.28 to 2.35]), the b2 path (*SE*=.08, p=.106, CI [-.30 to .03]), or the c' path (*SE*=.15, p=.357, CI [-.42 to .15]). Further, the paths outside our main serial mediation model were not significant: from treatment to depressive symptoms (*S.E.*=.37, p=.736, CI [-.85 to .60]), nor from RPI to adherence (*SE*=.47, p=.280, CI [-.41 to 1.42). See Figure 5 for coefficients and visual representations of this serial mediation model, and Figure 7 for a visual representation of all our pathways and coefficients.

Behavioral Activation Scale for Depression

Our second primary hypothesis was that increases in goal-directed activation (BADS) at session 4 would produce decreases in depressive symptoms at session 8, and these paths would mediate the relationship between treatment and NRT adherence (see Figure 6). For this test, we tested a serial mediation structural equation model in which we regressed NRT adherence onto depressive symptoms, which was regressed onto goal-directed activation (BADS), which, in turn, was regressed onto treatment condition. We also included related covariates (quit attempts, cigarettes per day, sessions attended), and baseline values of proposed mediators (in order to assess change over time). This model evidenced adequate model fit: $\chi 2$ (df=14)=12.898, p=.535; RMSEA=0.000 (90% CI: 0.000-.096); CFI=1.00; TLI=1.00. The indirect path from treatment to

NRT adherence through session 4 BADS and session 8 BDI was not significant (coefficient =-.002, *SE*=.01, *p*=.863, CI [-.02 to .02]). Further, none of our proposed paths from treatment to BADS, nor from BADS to depressive symptoms were significant: the a1 path (*S.E.*=.05, *p*=.234, CI [-.20 to .04]), or the a3 path (*SE*=.85, *p*=.864, CI [-1.82 to 1.53]). However, the path from depressive symptoms to NRT adherence was significant (*SE*=.08, *p*=.017, CI [-.35 to -.03]). Regarding paths outside of our main serial mediation model, the a2 path, or the path from treatment to depressive symptoms was not significant (*S.E.*=.31, *p*=.929, CI [-.63 to .58]), however, interestingly, the path from BADS to adherence was significant (*SE*=.42, *p*=.006, CI [.33 to 1.96]). The c' was not significant (*SE*=.13, *p*=.720, CI [-.30 to .21]). See Figure 6 for a depiction of the results of this serial mediation model, including the coefficients for each path, and Figure 8 for a visual representation of all our pathways and coefficients.

To summarize, neither of our serial mediation models were significant. However, there was a significant main effect of goal-directed activation at session 4 on NRT adherence, as well as a main effect of depressive symptoms at session 8 on NRT adherence in the model examining goal-directed activation as mediator one.

Chapter 4: Discussion

The purpose of this study was to examine nicotine patch adherence among individuals enrolled in a Randomized Controlled Trial of Behavioral Activation vs. Standard Treatment for smoking cessation (BATS). Overall, patch adherence was low, with no differences in adherence between conditions, although attendance was significantly better in the ST.

The primary aim of this study was to examine a serial mediation model in which treatment condition predicted changes in the primary targets of BATS (environmental reward or

goal-directed activation), which predicted changes in depression, which in turn predicted higher medication adherence. This was the first study, to our knowledge, that not only investigated the relationship between these variables, but also investigated these relationships in models that explored various pathways to examine NRT adherence from a behavioral framework. Despite our models being theoretically driven, our findings did not yield significant results for any of the proposed mediators.

When examining the relationship between treatment condition, environmental rewards (RPI), depressive symptoms, and NRT adherence, none of our proposed paths were significant. When examining the relationship between treatment, goal-directed activation, depressive symptoms, and NRT adherence, though the serial mediation model as a whole was not significant, there were significant paths between goal-directed activation and NRT adherence, and depressive symptoms and NRT adherence, such that higher goal-directed activation at session 4 and lower depressive symptoms at session 8 significantly predicted higher NRT adherence, while controlling for sessions attended, smoking history variables, and these variables at earlier time points. Notably, treatment condition did not predict any of our dependent variables.

Regarding the main effects of low depressive symptoms and high goal-directed activation on NRT adherence, these findings were in line with our hypotheses. It appears that decreases in depressive symptoms from mid-treatment to end-of-treatment and increases in goal-directed activation from baseline to mid-treatment each independently predicted high NRT adherence. Though the relationship between depressive symptoms and NRT adherence has not been investigated in smokers attempting to quit, the finding that depressive symptoms predict poor adherence is consistent with literature in the broader field of medication adherence

(Ciechanowski et al., 2000; Lin et al., 2004; Gonzalez at al., 2007; Bane at al., 2006; Safren et al., 1999; Ammassari et al., 2004; Katon, 2003; DiMatteo et al., 2000). Indeed, individuals with depression are three times more likely to be noncompliant with treatment recommendations for a variety of conditions compared to their non-depressed counterparts (DiMatteo et al., 2000). Furthermore, our finding is consistent with the medication adherence literature supporting that a decrease in depressive symptoms is associated with increased medication adherence. A 2012 RCT examining an intervention aimed at increasing adherence to diabetes medication and antidepressant medication, which incorporated additional psychosocial treatment for depression, showed that patients who received this intervention exhibited greater adherence to both medications as well as improved depressive symptoms and diabetes outcomes (Bogner et al., 2012). A review article on depressive symptoms, and cardiovascular disease also suggests that depression treatment results in increased quality of life and longevity among patients with cardiovascular disease, though it is unknown whether this finding could be attributed to improved medication adherence (Musselman et al., 1998). Clearly, more research is needed to elucidate the relationship between successful depression treatment and improvements in medication adherence. Findings from our study show that improved depressive symptoms resulting from (either) treatment significantly predicted better adherence to the nicotine patch.

This was the first study, to our knowledge, that found a significant relationship between goal-directed activation and NRT adherence, though there is research to suggest that goal-directed activation may associated with medication adherence in other medical conditions. For example, Ryan and Wagner (2003) examined predictors of adherence to highly active antiretroviral medication among individuals living with HIV/AIDS, and found that routinization of pill regimen and factors associated with participants' ability to maintain these routines (i.e.,

taking medication at the same time of day), were associated with better adherence (Ryan & Wagner, 2003). Though this concept is slightly different from goal-directed activation, there is a strong overlap between setting schedules and sticking to them and the concept of accomplishing goals set in BA. Thus, it appears that increases in goal-directed activation did not affect NRT adherence through our hypothesized path, but nonetheless affected NRT adherence.

It is curious that we did not find a relationship between goal-directed activation and depression in this model, given that BA is hypothesized to improve depression through increases in goal-directed activation. This was the first study, to our knowledge, to directly test these proposed mechanisms of action: environmental rewards and goal directed activation. Clearly, more research needs to be done in the area of testing mechanisms of action in BA (MacPherson et al., 2010).

Further, it is interesting that there was a significant relationship between goal-directed activation and NRT adherence, but not environmental reward and adherence in this model (though there was a significant bivariate correlation among NRT adherence and environmental reward at session 4). It could be that the assessment timeframe is not long enough to capture changes in pleasure/reward that could result from increased goal-directed activation. That is, goal-directed activation is likely to change faster than the experience of positive environmental reward (which comes downstream) and thus had a significant impact on NRT adherence in the model we tested, whereas environmental reward did not.

It is interesting that we did not find differences between treatment groups on any of our mediating or dependent variables. It could be that individuals who received ST as opposed to BATS were not significantly different because the BA did not contribute substantially more than ST in terms of changing environmental rewards or goal-directed activation, despite these factors

being specific treatment targets of BA. The ST protocol was based off of the standard of care that has been used for smoking cessation (Brown et al., 2001; MacPherson et al., 2010). This treatment also incorporates elements that have been effective for treating depression (e.g. social support, behavioral strategies). Additionally, though ST does not explicitly target reinforcement in the environment or goal-directed activation, it is possible that those who followed the protocol subsequently increased environmental rewards due to incorporating avoid/alter/substitute activities for smoking. For example, standard treatment suggests that one should avoid situations in which it may be tempting to smoke and one should engage in more smoke-free activities. So, it is possible that if an individual spent time with his/her family instead of smoking, this accomplishes the same goal as, for example, if a participant in the BATS condition had a value of spending more time with his/her family. Though the mechanisms and explanations may be different, in many ways ST and BATS look very similar. Furthermore, the finding that there were no differences in treatment on depression in either of our models is consistent with several prior studies showing that even smokers who received additional treatment for depression, compared to smoking cessation treatment alone, did not differ on depression scores post-treatment (Burgess et al., 2002; Brown et al., 2001). This means that although BA has been shown to treat depressive symptoms, BA may not translate to a superior treatment (compared to standard treatment) regarding predicting NRT adherence.

Another explanation for the lack of differences between treatments could be that BATS did not offer helpful material above and beyond ST regarding predictors of adherence. It could be that participants were overloaded with material and could not focus on solely on quitting smoking with all the content BATS offered. Indeed, Behavioral Activation was developed as a parsimonious treatment for depression (Lejuez et al., 2001; 2011), and adapted for smoking

cessation to be a simple treatment for smoking, compared to Cognitive-Behavioral Therapy (CBT). However, the elements involved in BATS are cumbersome for patients (i.e. homework completion, discussion of values, activity monitoring), perhaps too much so for the current sample of participants, low-income smokers with elevated depressive symptoms. It is possible that the Standard Treatment condition offered sufficient intervention while not overburdening the participants, and perhaps this is why we observed better treatment attendance in this condition. In fact, Hopko and colleagues (2011) discussed the treatment failure of BA for treating depressed individuals, and outlined possible reasons for such failure including lack of understanding or resonating with the treatment rationale, failure to identify values, and homework compliance. In this case, with the application of BA to smoking cessation, it is quite possible that participants did not understand the link between values identification and smoking cessation, and thus were not motivated to adhere to the treatment.

There were some significant bivariate correlations that warrant attention. For example, higher NRT adherence was associated with high session 4 environmental reward (RPI) and low session 4 depressive symptoms (BDI). Low baseline RPI was associated with high session 4 goal-directed activation (BADS), and high session 4 BDI. Further, low baseline BDI was associated with high session 4 RPI, and, lastly, BDI and RPI were correlated at every time point. As with an improvement in depressive symptoms, it seems that higher positive reward from the environment was associated with greater NRT adherence in this sample. This is consistent with literature in the HIV/AIDS field that has shown an association between lower perceived punishment in the environment and medication adherence among substance users with HIV/AIDS (Magidson et al., 2015). This was the first study to our knowledge that examined this relationship among adult smokers attempting to quit.

Regarding who is adherent to NRT, aside from those with increased goal-directed activation and decreased depressive symptoms, results showed that higher number of sessions attended is correlated with increased NRT adherence. This is in line with research showing that participants who attend more sessions exhibit better NRT adherence (Cooper et al., 2004). However, from this association we do not know if individuals are more adherent to the patch because they attended more sessions, or if there may be a third variable that may explain the people that exhibited greater NRT adherence and session attendance. For instance, conscientiousness and agreeableness have been shown to predict high compliance rates to NRT among adolescents (Scherphof et al., 2014). Future research should examine the role of personality factors on NRT adherence among treatment seeking adult smokers.

In addition to session attendance, we also found that the number of past quit attempts was positively associated with increased adherence to the patch, which is consistent with the extant research (Lam et al., 2004). This could be because smokers who have made more attempts to quit in the past are more motivated to stop smoking, and thus exhibit better NRT adherence. Smoking history is thus important to consider when attempting to predict who may adhere to the patch. Furthermore, regarding predictors of treatment adherence overall, though we did not find any demographic variables related to NRT adherence, results showed that older age was associated with increased session attendance, as was being female. This is consistent with literature showing that older individuals have better smoking outcomes including adherence to the patch (Lam et al., 2004; Burns and Levinson, 2008). In our study, we did not find that being male is associated with greater patch adherence, though there is some literature to suggest this may be the case (Lam et al., 2004; Burns and Levinson, 2008). Demographic predictors of session attendance could be important because healthcare providers may be able to identify those

individuals more or less likely to succeed in a smoking cessation program. Future research should also examine demographic characteristics of patch users in order to identify who is likely to adhere to the nicotine patch.

Findings from this study have important implications for intervention. First, it is clear that the smoking field needs novel interventions for NRT adherence, considering the low rate of adherence found in this study and the literature more broadly. Results from our study showed that lower depressive scores at the end of treatment and increased goal-directed activation at mid-treatment predicted higher NRT adherence. This means that providers could recommend treatment for depressive symptoms and lack of goal-directed activation if they want patients to wear the patch in accordance with recommended guidelines. Practically, this could mean that providers could briefly assess the activities a patient is engaging in, and suggest increasing activities that yield positive benefits, including social support and behavioral strategies to avoid smoking. This could help with NRT adherence and ultimately smoking cessation, though more research needs to be done in this area.

Furthermore, it is clear that more attention needs to be paid to patch adherence in smoking cessation trials. It appears that simply giving participants the patch and explaining the instructions is insufficient to promote continued adherence. The smoking field can draw from the larger field of medication adherence in this regard. For example, Life-Steps (Safren et al., 2001) is a treatment designed specifically to address barriers and problem solve nonadherence to highly active antiretroviral medication among individuals living with HIV/AIDS. Additionally, Motivational Interviewing (MI) has been shown to improve health outcomes (e.g. decrease viral load) among individuals living with HIV/AIDS (Ogedegbe, Schoenthaler, Richardson, Lewis, Belue, Espinosa, & Charlson, 2007). Alhough in the current study, both the BATS and ST

condition provided problem-solving around issues regarding the patch if participants voiced them, perhaps smoking cessation treatment should incorporate patch use directly within treatment protocols, perhaps incorporating MI or Life-Steps approaches.

Our study has several strengths. First, we used a racially and ethnically diverse sample, which extends well to the general population of smokers, and also targets a specific group of individuals vulnerable to cigarette smoking. Second, though our hypotheses were not supported, this was the first study to examine the theorized mechanisms of change using Behavioral Activation more broadly. Third, the rich hourly data that we used to define NRT adherence is an important strength of the study, even though the retrospective reporting of this could be considered a limitation.

Limitations and Future Directions

There are several limitations to the current study. First, the small sample size and low rates of treatment attendance may yield limited power and thus make it difficult to detect serial mediation effects. Rates of dropout were high (10%), and session attendance was low (3 sessions on average, and 26% attended 0 sessions). However, the high drop-out rate that we observed in this study is consistent with studies utilizing a population of low-income smokers (Borrelli et al., 2002, MacPherson et al., 2010). Specifically, the drop-out rates for the study that set the stage for the current study were high, with fewer than half completing all 8 sessions (MacPherson et al., 2010). Due to the high drop-out rates in our current study and the low percentage of participants who received the intervention, we are unable to draw firm conclusions regarding the efficacy of the intervention. Future studies should attempt to address this low retention rate, perhaps by holding the sessions in the community, or in primary care settings, rather than a laboratory on a

large college campus. Indeed, participants have cited distance and transportation as barriers to attending smoking cessation clinical trials (Borrelli et al., 2002).

Another important concern regarding the high drop-out rates we observed is the amount of missing data. Because mediation requires larger sample sizes (Fritz & McKinnon, 2007), a major limitation of our study is a lack of power, limiting our ability to draw firm conclusions regarding our findings. Though we utilized inclusive implementations of FIML to estimate missing data, which is recommended if the missing data exceeds 10% (Little, Jorgensen, Lang, & Moore, 2013), it is possible that our analyses still suffered from lack of power. Future studies should consider a more parsimonious model in order to maximize the data.

Another concern is the retrospective nature of reporting NRT adherence. Although this method has been using in previous studies (Fish et al., 2009; Lam et al., 2005; Wiggers et al., 2006) there may be inaccuracies in reporting hourly patch use due to the time delay (one week to one month). Furthermore, we do not have a measure with which to validate the use of the TLFB to measure NRT adherence in this study. Though a strength of the current study is the hourly measurement of adherence, there may be recall effects. Additionally, we do not have a measure of when, during the 24 hours, the participants removed the patch. Future studies should address this limitation by incorporating real-time measures such as Ecological Momentary Assessment (EMA). Indeed, Ma and colleagues (2016) have addressed this gap in measuring NRT adherence using real-time. This is a promising direction, and future studies should examine psychological and environmental predictors of NRT adherence utilizing these methods.

The measurement of NRT adherence raises another limitation of our study. Because our measurement of NRT adherence reflected cumulative patch use (beginning at session 4 when the patch was distributed through the 1 month follow-up), our measurement of adherence overlapped

somewhat with the session 8 time point in our serial mediation model. Thus, our model was not fully testing mediation using the ideal ordering of variables, however, we chose to proceed despite this limitation because we wanted to obtain a clear picture of adherence over 8 weeks.

Another limitation is that some of the findings from this study may not extend to a larger population of individuals who want to quit smoking, and perhaps purchase the nicotine patch over-the counter, because all the participants in this study were enrolled in treatment. However, because low depressive symptoms and increased goal-directed activation predicted adherence across treatments, we can conclude that behavior change in general (an important element in both treatments) may be useful for those individuals trying to quit smoking, although we cannot generalize this conclusion to individuals outside of a treatment protocol.

Another factor that limits generalization is that we excluded individuals who met criteria for Axis 1 psychopathology according to the DSM-IV. Though we cannot extend our findings to smokers with current psychopathology, despite high comorbidity (Grant et al., 2004), smokers with elevated depressive symptoms represent a significant amount of smokers (MacPherson et al., 2010; Leventhal et al., 2008) and the fact that our findings can generalize to this vulnerable group is a strength of the study.

Another important limitation is that we do not have homework completion data for either the BATS treatment or ST. It is possible that the reason we did not see differences in our dependent variables according to treatment is because participants were not fully engaged in the BATS treatment. Indeed, participants must be fully engaged in the treatment including monitoring activities, generating new, value-driven activities, and completing those activities to yield improvements in environmental reinforcement, goal-directed activation, and ultimately depressive symptoms (Lejuez et al., 2001; 2011, Daughters et al., 2008). Unfortunately, the

current study did not allow us to examine homework completion in order to investigate whether participants were fully engaged in BATS treatment. Future research should incorporate the collection of homework completion data in a systematic way.

An important future direction following the current study is to examine adherence trajectories over time, as well as their correlates. The NRT literature would benefit from examining the relationship between depressive symptoms and adherence prospectively in order to see if, as mood fluctuates, adherence fluctuates as well. Furthermore, there is research to suggest that adherence in the first few days and weeks of quitting is associated with better cessation outcomes (Ashare et al., 2013; Shiffman et al., 2008). There is also literature showing that there are different trajectories overtime, where some individuals adhere to recommendations throughout the duration of treatment, some decrease compliance moderately, and some decrease compliance significantly (Scherphof et a., 2014). Thus, there is a need to examine patterns of adherence over time and how these patterns predict cessation in this sample. In addition to prospective studies, future research might extend this model to see if depression affects smoking cessation through adherence to NRT. Further, there is a strong literature to suggest a relation between diagnosed depression and low medication adherence among individuals with a variety of illnesses including HIV/AIDS and diabetes (Safren et al., 2012). It may be that the model we tested would be supported if instead of elevated depressive symptoms, we were able to examine depression diagnoses as an independent variable.

Overall, results showed that the rates of adherence were quite low. This is in line with the current literature on NRT adherence rates (Roddy et al., 2006; Lam et al., 2005; Shiffman et al., 2008). Several reasons for not adhering to the patch have been identified, including forgetfulness and side-effects (Burns et al., 2008; Fish et al., 2009). One important limitation of the current

study is that we did not examine reasons for non-adherence. It could be the case that depressive symptoms and goal-directed activation uniquely predict reasons for nonadherence, and thus are an important direction for future research. It may be that individuals did not adhere because they started smoking again (unfortunately this was not directly measured), but it also may be the case that there were other reasons for nonadherence that we did not capture in this study that warrant attention.

This raises another important limitation: we were unable to examine smoking behavior while using the patch because we did not have a direct measure of this. As a consequence, we do not know if these individuals were smoking while wearing the patch, though we do know that this is common (Shaw et al., 1998; Beard et al., 2011). Future studies should incorporate measures of smoking while on the patch.

Though we do not know the reasons for nonadherence to the patch in the sample, the fact remains that adherence to NRT is low. Thus, an important future direction might be to use a more permanent form of nicotine replacement therapy. The smoking field would benefit from drawing from other disciplines that utilize more permanent forms of medication, such as Depo-Provera for birth control and Anatbuse for alcoholism which do not require daily (or hourly) adherence. Moreover, there has been progress in the tobacco field toward developing nicotine vaccines. These nicotine-specific antibodies are designed to block the additive effect of nicotine. For example, NicVax, a vaccine that was injected at intervals in the arms of individuals trying to quit, was developed in 2005. The vaccine worked by preventing the pleasurable feeling of nicotine and stopping the positive feedback associated with the feeling of smoking. Results from the phase II trial showed that 26% of smokers who responded to the vaccine were able to quit and stay abstinent for at least 30 days. However, results from phase II clinical trials did not show

the vaccine to be more effective than placebo (Hartmann-Boyce, Cahill, Hatsukami, & Cornuz, 2012). There have been three other nicotine vaccines developed as well; however, they either were not effective in the long-term or not generalizable. Several other nicotine vaccines are in early development and have not been tested in humans. Clearly, more research is needed to develop and test a more permanent treatment for nicotine dependence.

Another important factor to consider for future research is the setting in which the study took place. It is possible that session attendance would have improved had the study been in the community or in a primary care setting rather than on a university campus. Indeed, research suggests that integrating smoking cessation and patch adherence interventions into primary care settings is feasible and successful (Fiore et al., 2004; Smith, McCarthy, Japuntich, Christiansen, Piper, Jorenby, & Jackson, 2009; Papadakis, McDonald, Mullen, Reid, Skulsky, & Pipe, 2010). Findings from our study suggest that healthcare providers could, at minimum, suggest smoking cessation programs for individuals who are motivated to quit.

To conclude, the current study sought to extend previous research on the effect of Behavioral Activation Treatment for Smoking compared to Standard Treatment on NRT adherence, through mediators that BATS are hypothesized to target: environmental reward, goal-directed activation, and depressive symptoms. Though our mediation models were not supported, this study did shed light on the processes that contribute to low NRT adherence, namely increases in goal-directed activation and decreases in depressive symptoms. Consistent with a behavioral framework, goal-directed activation is imperative when considering noncompliance with NRT. Future research is needed to address the limitations of, and to extend, the current study in order to gain a complete picture of the processes that contribute to low NRT adherence

among adult smokers with elevated depressive symptoms enrolled in smoking cessation clinical trials.

Figure 1. **Conceptual multiple mediation model**

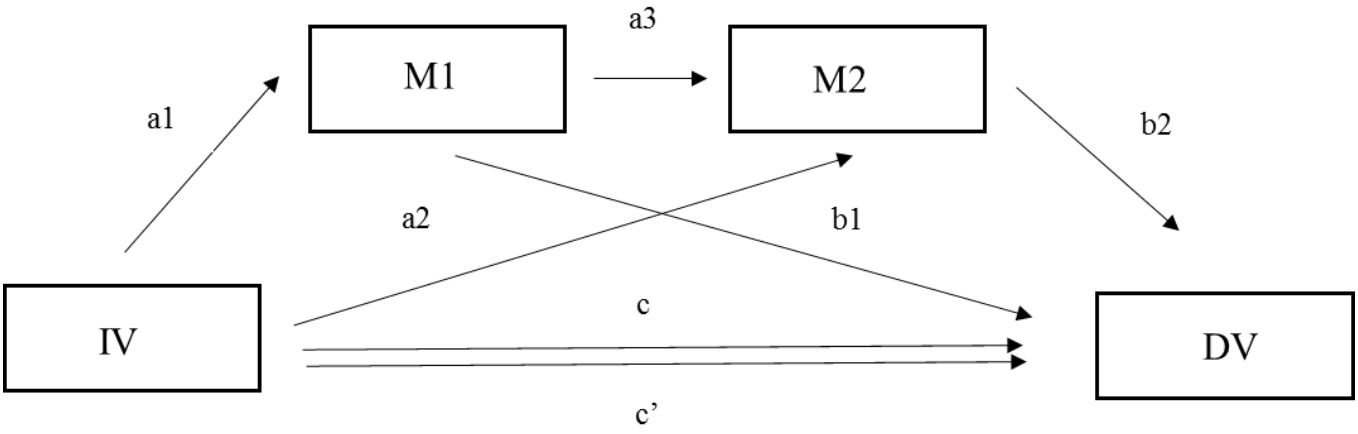


Figure 2. Consort Diagram

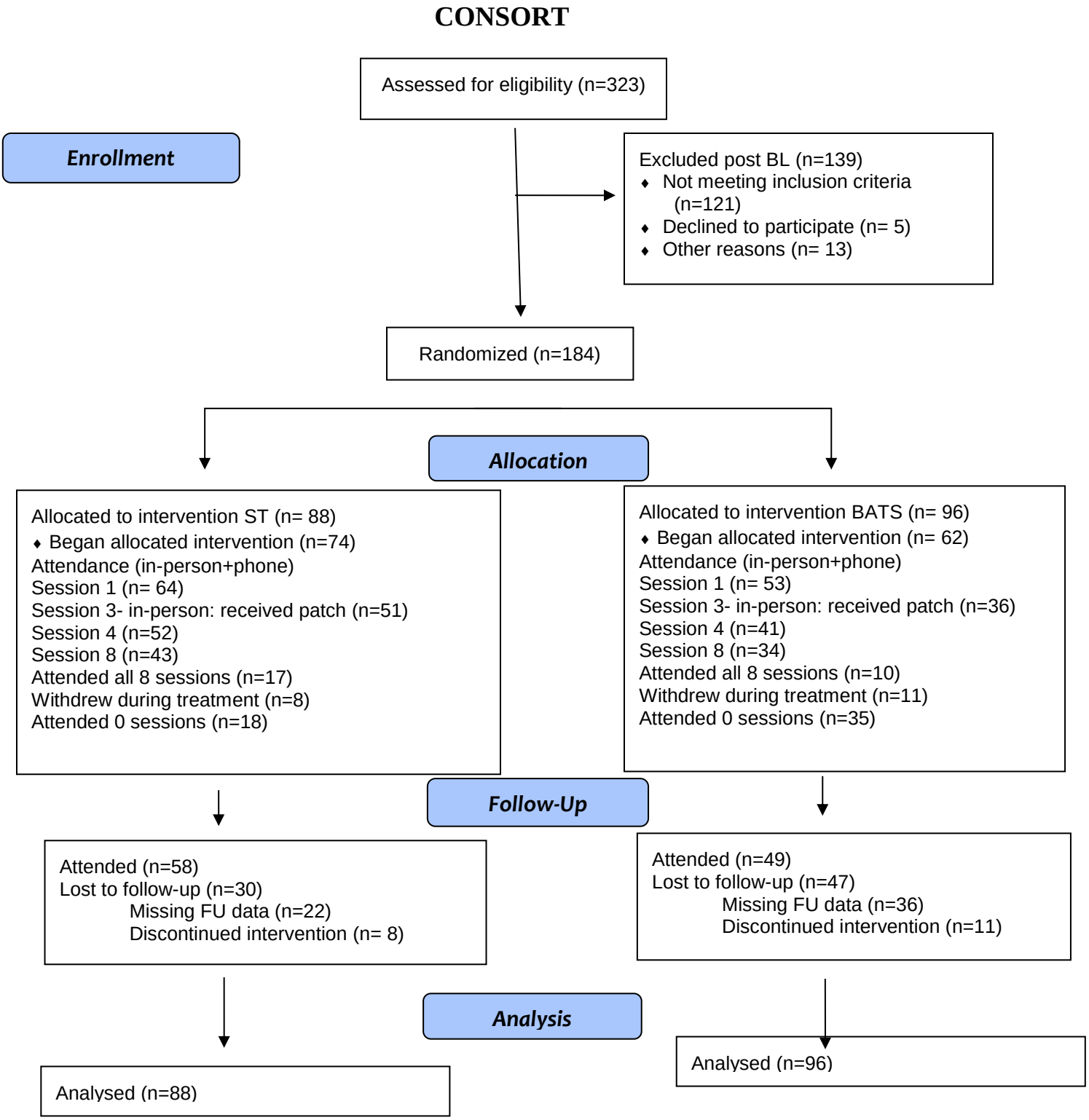


Figure 3. Study Timeline

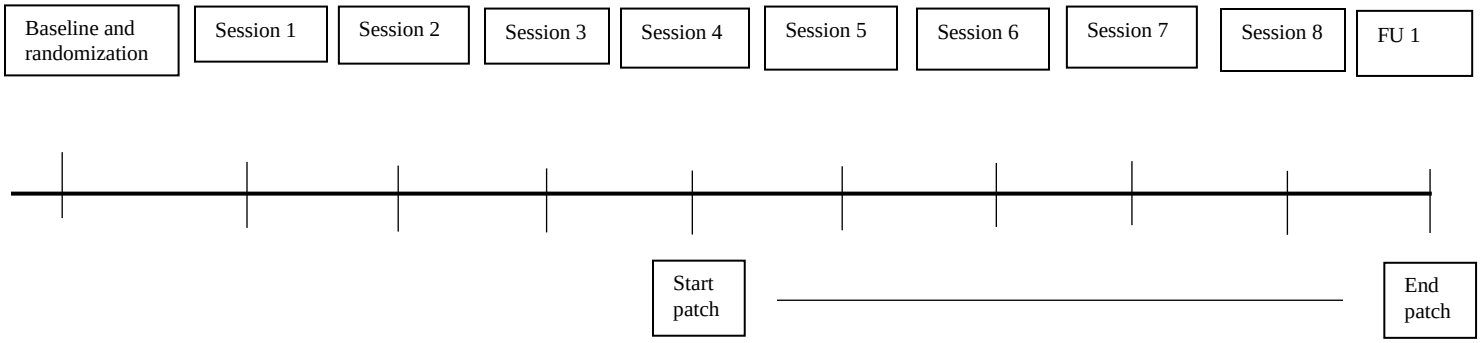


Figure 4. Timeline of study measures

	BL	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6		Session 7	Session 8	1 month Follow-up
Demographics	**X**										
Cigarette Smoking	**X**										
SCID	**X**										
BDI	**X**	**X**	**X**	**X**	**X**	**X**	**X**		**X**	**X**	**X**
BADS	**X**	**X**	**X**	**X**	**X**	**X**	**X**		**X**	**X**	**X**
RPI	**X**	**X**	**X**	**X**	**X**	**X**	**X**		**X**	**X**	**X**
TLFB						**X**	**X**		**X**	**X**	**X**

Table 1. Demographics and smoking history variables for total sample and baseline differences by treatment condition (BATS vs. ST)

	Overall (*n*=184)	BATS (*n*=96)	ST (*n*=88)	Statistic	p-value
Age (Mean, (SD))	44.61(11.51)	44.02(12.47)	45.25(10.38)	$t(181)=.72$	.471
Gender				$\chi^2(1)=1.26$	.261
Male	55.4%	59.4%	51.1%		
Female	44.6%	40.6%	48.9%		
Marital Status				$\chi^2(3)=1.67$	.638
Married	10.3%	11.5%	9.1%		
Separated	8.2%	7.3%	9.1%		
Living together	13.0%	15.6%	10.2%		
Single (including divorced, (widowed)	68.5%	65.6%	71.6%		
Race/Ethnicity				$\chi^2(1)=.172$	.679
Black	66.8%	70.8%	62.5%		
Hispanic	2.2%	3.1%	1.5%		
White	14.1%	14.6%	18.2%		
American Indian	6.0%	7.3%	6.1%		
Other	10.9%	4.2%	11.7%		
Annual income < $40,000	70.1%	67.8%	75.3%		
Employment				$\chi^2(5)=2.27$	.810
Unemployed	43.5%	43.8%			
Employed part time	20.1%	18.8%			
Employed full-time	23.4%	26.0%			
Student/stay at home parent	7.6%	7.3%			
Cigarettes per day (Mean, (*SD*))	14.29(*7.69*)	15.14(*8.53*)	13.36(*6.59*)	$t(173)=-1.541$	.125
Quit attempts (Mean, (*SD*))	2.97(*2.37*)	3.16(*3.32*)	2.27(*2.42*)	$t(181)=-1.132$	.259

Table 2. Descriptive Statistics for key study variables and comparisons between treatment conditions

	Whole sample (Mean, (*SD*)	BATS (Mean, (*SD*)	ST (Mean, (*SD*)	Min, Max (whole sample	Statistic	p-value
NRT Adherence- hours	750.74(*474.90*)	695.28(*497.96*)	801.94(*451.36*)	0,1344	*t*(98)=1.12	.26
BDI baseline	9.15(*8.05*)	10.00(*8.67*)	8.17 (*7.22*)	0,43.7	*t*(179)=-1.539	.126
BDI session 4	6.93(*6.74*)	6.38(*7.60*)	7.34(*5.99*)	0,38	*t*(90)=.702	.404
BDI session 8	5.42(*6.14*)	5.41(*5.82*)	5.43(*6.44*)	0,34	*t*(105)=.017	.986
RPI Total baseline	59.99(*8.48*)	59.74(*8.86*)	60.27(*8.06*)	34,80	*t*(177)=.422	.674
RPI Total session 4	60.02(*9.18*)	58.77(*9.59*)	61.02(*8.79*)	38,80	*t*(88)=1.15	.251
BADS Baseline	104.04(*22.25*)	103.47(*24.82*)	104.65(*19.32*)	33,145	*t*(178)=.35	.723
BADS Session 4	105.32(*23.16*)	106.40(*25.31*)	103.95(*20.34*)	18,144	*t*(91)=-.505	.615

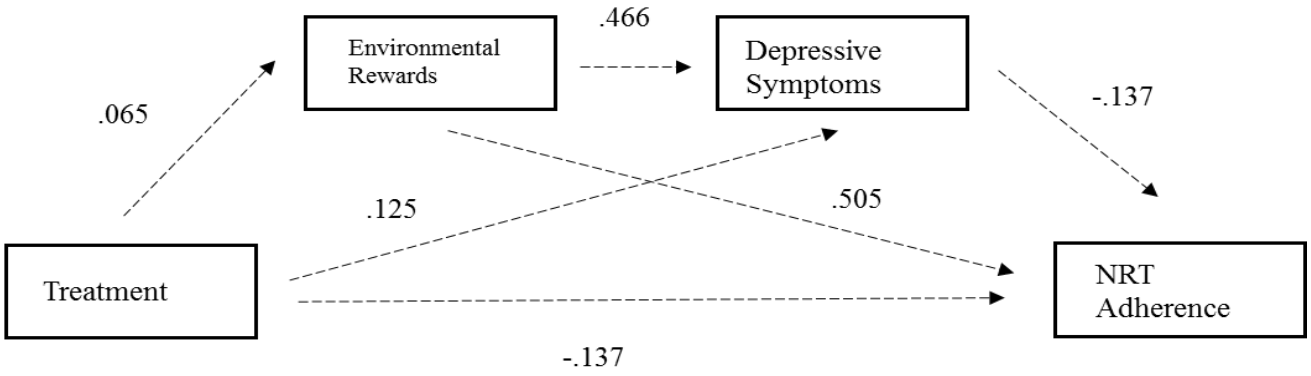
BDI= Beck Depression Inventory; RPI= Reward Probability Index; BADS=Behavioral Activation for Depression Scale

Table 3. Bivariate correlations among NRT adherence, environmental reward, goal-directed activation, depressive symptoms, cigarettes per day, lifetime quit attempts, and age.

	1	2	3	4	5	6	7	8	9	10	11	12
1. Hourly NRT Adherence	--	-.030	.263*	-.017	-.108	.084	-.309**	-.181	-.030	.240*	.149	.585**
2. Baseline RPI		--	.430**	.056	-.250*	-.585**	-.284**	-.188	.046	.032	-.018	-.073
3. Session 4 RPI			--	.191	.089	-.222*	-.493**	-.267*	.108	.023	-.155	.230*
4. Baseline BADS				--	.274**	-.058	-.194	-.022	-.026	.077	.005	.087
5. Session 4 BADS					--	.063	.118	.125	.081	-.198	-.048	-.145
6. Baseline BDI						--	.400**	.426**	-.113	-.005	-.087	.003
7. Session 4 BDI							--	.569**	-.054	-.147	-.098	-.263*
8. Session 8 BDI								--	.007	-.031	-.071	-.245*
9. CPD									--	-.033	.103	-.076
10. #Quit attempts										--	.069	.160*
11. Age											--	.342**
12. Sessions attended												--

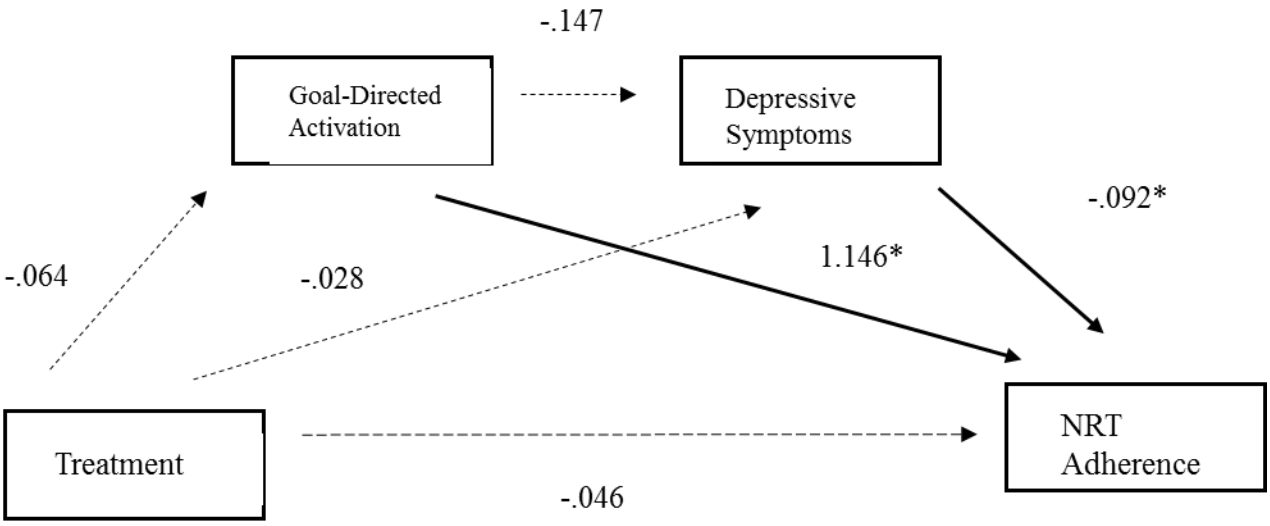
**p≤001; * p≤.05; NRT Adherence= Nicotine Replacement Therapy Adherence (higher score=better adherence; BDI= Beck Depression Inventory (higher scores = greater depressive symptoms), BADS Behavioral Activation for Depression Scale (higher scores = greater activation), RPI Reward Probability Index (higher scores = greater reinforcement); CPD= cigarettes per day; #Quit attempts= lifetime quit attempts

Figure 5. The association between treatment and NRT adherence with each pathway in the multiple mediation model examining environmental rewards as a mediator.



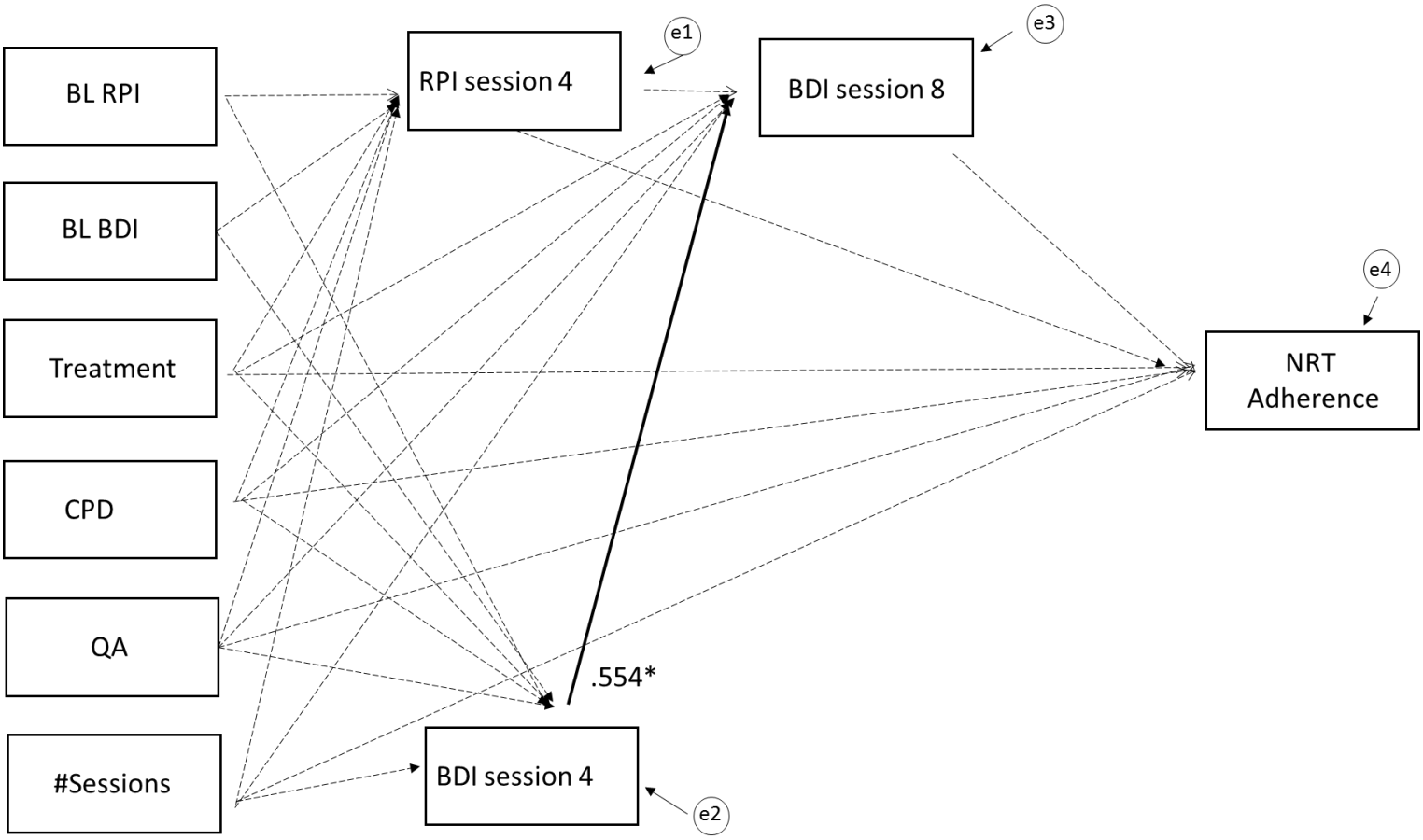
The pathways represented by arrows correspond to Figure 1. The arrows with a dashed line represents the non-significant path. The path estimation from the mediation analysis shown with each arrow is the unstandardized coefficient.

Figure 6. The association between treatment and NRT adherence with each pathway in the multiple mediation model examining goal-directed activation as a mediator.



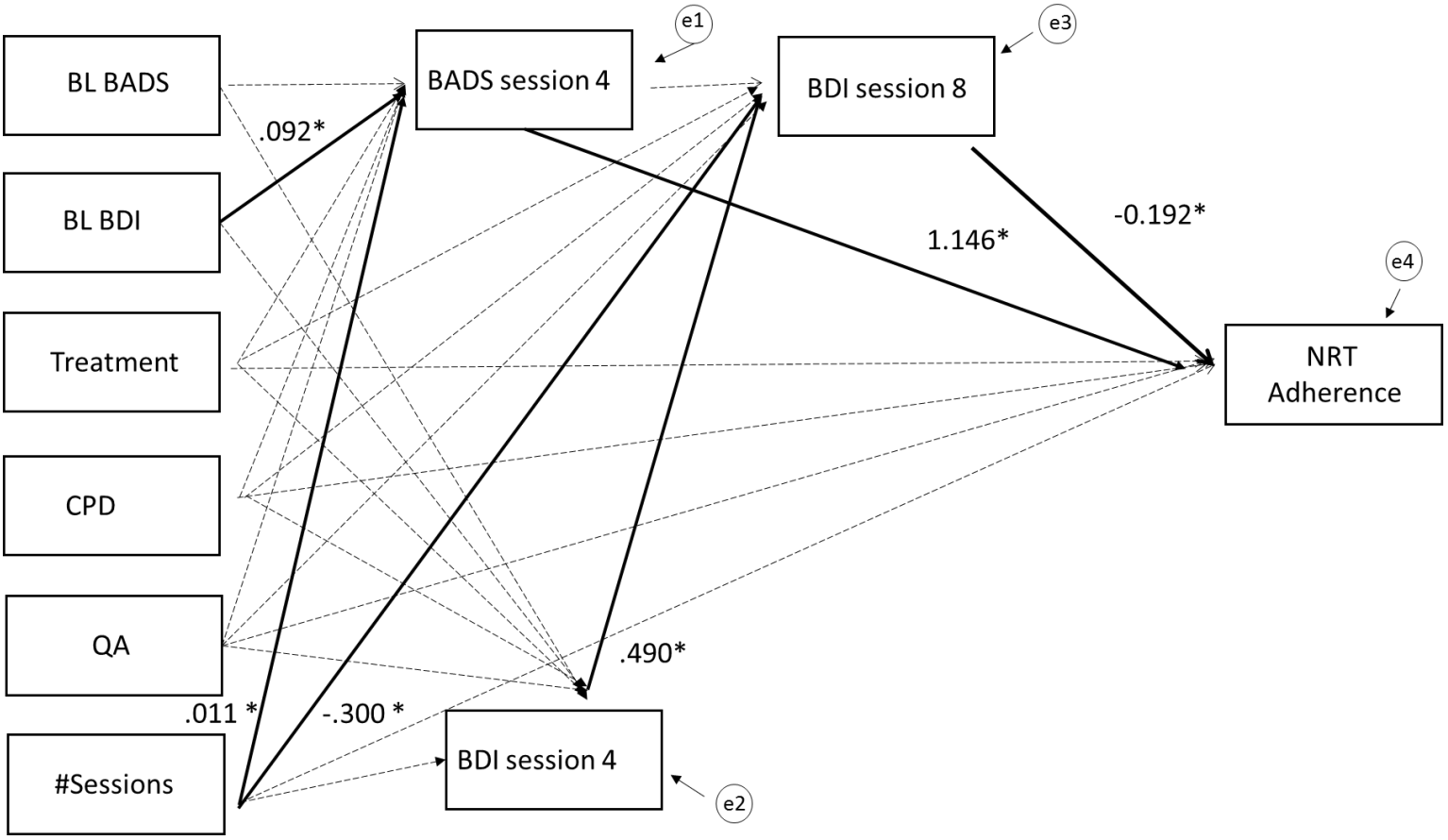
The association between treatment and NRT adherence with each pathway in the multiple mediation model. The pathways represented by arrows correspond to Figure 1. An arrow with a solid line represents the significant path between variables, and the arrow with a dashed line represents the non-significant path. The path estimation from the mediation analysis shown with each arrow is the unstandardized coefficient. *$p<0.05$

Figure 7. Mediation model with environmental reward as MI, including all paths and covariates



An arrow with a solid line represents the significant path between variables, and an arrow with a dashed line represents the non-significant path. The path estimation from the mediation analysis shown with each arrow is the unstandardized coefficient. *p<0.05 Treatment=BATS or ST, NRT Adherence= Nicotine Replacement Therapy Adherence (higher score=better adherence; Beck Depression Inventory (higher scores = greater depressive symptoms), RPI Reward Probability Index (higher scores = greater environmental rewards); CPD= cigarettes per day; QA= Quit Attempts)

Figure 8. Mediation model with goal-directed activation as MI, including all paths and covariates



An arrow with a solid line represents the significant path between variables, and an arrow with a dashed line represents the non-significant path. The path estimation from the mediation analysis shown with each arrow is the unstandardized coefficient. *p<0.05 Treatment=BATS or ST, NRT Adherence= Nicotine Replacement Therapy Adherence (higher score=better adherence; Beck Depression Inventory (higher scores = greater depressive symptoms), BADS Behavioral Activation for Depression Scale (higher scores = greater activation); CPD= cigarettes per day; QA= Quit Attempts)

Appendix A. Time-Line Follow Back

Participant #630

Sun	Mon	Tue	Wed
		[D#307] 1 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#308] 2 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____
[D#312] 6 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#313] 7 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#314] 8 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#315] 9 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____
[D#319] 13 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#320] 14 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#321] 15 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#322] 16 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____
[D#326] 20 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#327] 21 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#328] 22 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#329] 23 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____
[D#333] 27 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#334] 28 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#335] 29 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____	[D#336] 30 # Cigs: _____ # Drinks: _____ # Drugs: _____ QA: Y N Patch: _____

Circle if not used whole month: Cigs Drinks Drugs Patch Quit Attempt: Y N

Appendix B. Smoking History Questionnaire

SMOKING HISTORY QUESTIONNAIRE

For each question below, please write the number of the answer on the blank line(s) to the right of each item.

1. Are you a (*check one*):

   current smoker _____ ex-smoker _____ never smoker _____

If you never smoked cigarettes, move on to the next questionnaire. If you are a current or ex smoker, please continue.

2. How old were you when you first smoked a cigarette? _____

3. How old were you when you started regular daily cigarette smoking? _____

4. For how many years, did/have you smoked regularly? _____

5. Since you started regular daily smoking (and until you stopped if you are a previous smoker), what is the average number of cigarettes you smoked per day? _____

6. When smoking the heaviest, how many cigarettes did you smoke per day? _____

7. Think about your smoking during the last week, how many cigarettes did you smoke in an average day? _____

8. How many times in your life have you made a serious attempt to quit smoking? _____
   (If more than 9 times, put 9)

9. As best as you can remember, how long ago did you make your first attempt to quit smoking? _____

10. How many different times in your life have you made an attempt to quit smoking where you have stayed off cigarettes

for 12 or more hours? (Do not include time sleeping) _____

11. Since you first started smoking, what was the longest period of time that you were able to stay off cigarettes NOT COUNTING when you were in a place where you couldn't smoke (e.g., jail, treatment center)? (If less than 1 day, do not include time sleeping)

Appendix C. Beck Depression Inventory-II

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

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

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

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

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

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

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

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

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

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

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

11) Agitation
0. I am no more restless or wound up than usual.
1. I feel more restless or wound up than usual.
2. I am so restless or agitated that it's hard to stay still.
3. I am so restless or agitated that I have to keep moving or doing something.

12) Loss of Interest
0. I have not lost interest in other people or activities.
1. I am less interested in other people or things than before.
2. I have lost most of my interest in other people or things.
3. It's hard to get interested in anything.

13) Indecisiveness
0. I make decisions about as well as ever.
1. I find it more difficult to make decisions than usual.
2. I have much greater difficulty in making decisions than I used to.
3. I have trouble making any decisions.

14) Worthlessness
0. I do not feel I am worthless.
1. I don't consider myself as worthwhile and useful as I used to.
2. I feel more worthless as compared to other people.
3. I feel utterly worthless.

15) Loss of Energy
0. I have as much energy as ever.
1. I have less energy than I used to have.
2. I don't have enough energy to do very much.
3. I don't have enough energy to do anything.

16) Changes in Sleeping Pattern
0. I have not experienced any change in my sleeping pattern.
1a. I sleep somewhat more than usual.
1b. I sleep somewhat less than usual.
2a. I sleep a lot more than usual.
2b. I sleep a lot less than usual.
3a. I sleep most of the day.
3b. I wake up 1-2 hours early and can't get back to sleep.

17) Irritability
0. I am no more irritable than usual.
1. I am more irritable than usual.
2. I am much more irritable than usual.
3. I am irritable all the time.

18) Changes in Appetite
0. I have not experienced any changes in my appetite.
1a. My appetite is somewhat less than usual.
1b. My appetite is somewhat greater than usual.
2a. My appetite is much less than before.
2b. My appetite is much greater than usual.
3a. I have no appetite at all.
3b. I crave food all the time.

19) Concentration Difficulty
0. I can concentrate as well as ever.
1. I can't concentrate as well as usual.
2. It's hard to keep my mind on anything for very long.
3. I find I can't concentrate on anything.

20) Tiredness or Fatigue
0. I am no more tired or fatigued than usual.
1. I get more tired or fatigued more easily than usual.
2. I am too tired or fatigued to do a lot of the things I used to do.
3. I am too tired or fatigued to do most of the things I used to do.

21) Loss of Interest in Sex
0. I have not noticed any recent change in my interest in sex.
1. I am less interested in sex than I used to be.
2. I am much less interested in sex now.
3. I have lost interest in sex completely.

Appendix D. Reward Probability Index

Thinking about the past several months, please answer the following questions using this scale:
1 = Strongly Disagree
2 = Disagree
3 = Agree
4 = Strongly Agree

_____ 1. I have many interests that bring me pleasure.
_____ 2. I make the most of opportunities that are available to me.
_____ 3. My behaviors often have negative consequences.
_____ 4. I make friends easily.
_____ 5. There are many activities that I find satisfying.
_____ 6. I consider myself to be a person with many skills.
_____ 7. Things happen that make me feel helpless or inadequate.
_____ 8. I feel a strong sense of achievement.
_____ 9. Changes have happened in my life that have made it hard to find enjoyment.
_____ 10. It is easy to find good ways to spend my time.
_____ 11. I have the abilities to obtain pleasure in my life.
_____ 12. I have few financial resources, which limits what I can do.
_____ 13. I have had many unpleasant experiences.
_____ 14. It seems like bad things always happen to me.
_____ 15. I have good social skills.
_____ 16. I often get hurt by others.
_____ 17. People have been mean or aggressive toward me.
_____ 18. I have been very capable in jobs I have had.
_____ 19. I wish I could find a place to live that brought more satisfaction to my life.
_____ 20. I have many opportunities to socialize with people.

Factor #1 (Reward Probability)
Items: 1, 2, 4, 5, 6, 8, 10, 11, 15, 18, 20
Factor #2 (Environmental Suppressors)
Items: 3, 7, 9, 12, 13, 14, 16, 17, 19

Appendix E. Behavioral Activation for Depression Scale

Please read each statement carefully and then circle the number which best describes how much the statement was true for you DURING THE PAST WEEK, INCLUDING TODAY.

	Not at All 0	A little True 1	A lot True 2	Completely True 3
1. I stayed in bed for too long even though I had things to do.	○	○	○	○
2. There were certain things I needed to do that I didn't do.	○	○	○	○
3. I am content with the amount and types of things I did.	○	○	○	○
4. I engaged in a wide and diverse array of activities.	○	○	○	○
5. I made good decisions about what type of activities and/or situations I put myself in.	○	○	○	○
6. I was active, but did not accomplish any of my goals for the day.	○	○	○	○
7. I was an active person and accomplished the goals I set out to do.	○	○	○	○
8. Most of what I did was to escape from or avoid something unpleasant.	○	○	○	○
9. I did things to avoid feeling sadness or other painful emotions.	○	○	○	○
10. I tried not to think about certain things.	○	○	○	○
11. I did things even though they were hard because they fit in with my long-term goals for myself.	○	○	○	○
12. I did something that was hard to do but it was worth it.	○	○	○	○
13. I spent a long time thinking over and over about my problems.	○	○	○	○

BADS				
	Not at All 0	A little True 1	A lot True 2	Completely True 3
14. I kept trying to think of ways to solve a problem but never tried any of the solutions.	○	○	○	○
15. I frequently spent time thinking about my past, people who have hurt me, mistakes I've made, and other bad things in my history.	○	○	○	○
16. I did not see any of my friends.	○	○	○	○
17. I was withdrawn and quiet, even around people I know well.	○	○	○	○
18. I was not social, even though I had opportunities to be.	○	○	○	○
19. I pushed people away with my negativity.	○	○	○	○
20. I did things to cut myself off from other people.	○	○	○	○
21. I took time off of work/school/chores/responsibilities simply because I was too tired or didn't feel like going in.	○	○	○	○
22. My work/schoolwork/chores/responsibilities suffered because I was not as active as I needed to be.	○	○	○	○
23. I structured my day's activities.	○	○	○	○
24. I only engaged in activities that would distract me from feeling bad.	○	○	○	○
25. I began to feel badly when others around me expressed negative feelings or experiences.	○	○	○	○

References

Alterman, A. I., Gariti, P., Cook, T. G., & Cnaan, A. (1999). Nicodermal patch adherence and its correlates. Drug and Alcohol Dependence, 53, 159–165.

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

Anda, R. F., Williamson, D. F., Escobedo, L. G., Mast, E. E., Giovino, G. A., & Remington, P. L. (1990). Depression and the dynamics of smoking. A national perspective. *Jama*, *264*(12), 1541-1545.

Ashare, R.L., Wileyto, E.P., Perkins, K.A., Schnoll, R.A., 2013. The first 7 days of a quit attempt predicts relapse: validation of a measure for screening medications for nicotine dependence. *Journal of Addictive Medicine, 7,* 249–254.

Balmford, J., Borland, R., Hammond, D., & Cummings, K. M. (2011). Adherence to and reasons for premature discontinuation from stop-smoking medications: data from the ITC Four-Country Survey. *Nicotine & Tobacco Research*, *13*(2), 94-102.

Bandura, A., & Walters, R. H. (1963). Social learning and personality development.

Bandura, A. (1969). Principles of behavior modification.

Bane, C., Hughes, C. M., & McElnay, J. C. (2006). The impact of depressive symptoms and psychosocial factors on medication adherence in cardiovascular disease. *Patient Education and Counseling*, *60*(2), 187-193.

Barrett, P. (2007). Structural equation modelling: Adjudging model fit. *Personality and*

Individual Differences, *42*(5), 815-824.

Beard, E., McNeill, A., Aveyard, P., Fidler, J., Michie, S., & West, R. (2011). Use of nicotine replacement therapy for smoking reduction and during enforced temporary abstinence: a national survey of English smokers. *Addiction*, *106*(1), 197-204.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). Beck depression inventory-II. *San Antonio, TX*, 78204-2498.

Berlin, I., & Covey, L. S. (2006). Pre- cessation depressive mood predicts failure to quit smoking:

the role of coping and personality traits. *Addiction*, *101*(12), 1814-1821.

Bernstein, S. L., Rosner, J., & Toll, B. (2016). Concordance Between Timeline Follow-Back and Single Question Assessment of Self-Reported Smoking in a Clinical Trial. *Substance abuse*, *37*(3), 398-401.

Bogner, H. R., Morales, K. H., de Vries, H. F., & Cappola, A. R. (2012). Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. *The Annals of Family Medicine*, *10*(1), 15-22.

Bollen, K. A. (1989). *Structural equations with latent variables*. NY: Wiley.

Borrelli, B., Hogan, J. W., Bock, B., Pinto, B., Roberts, M., & Marcus, B. (2002). Predictors of quitting and dropout among women in a clinic-based smoking cessation program. *Psychology of Addictive Behaviors*, *16*(1), 22.

Breslau, C. D., Giese, A. A., Turnbull, J. J., Dickinson, M., & Johnson-Nagel, N. (2006). Predictors of tobacco use among persons with mental illnesses in a statewide population. *Psychiatric Services*, *57*(7), 1035-1038.

Brown, R. A., Lichtenstein, E., McIntyre, K. O., & Harrington-Kostur, J. (1984). Effects of

nicotine fading and relapse prevention on smoking cessation. *Journal of Consulting and Clinical Psychology, 52*(2), 307-308.

Brown, R. A., Burgess, E. S., Sales, S. D., Whiteley, J. A., Evans, D. M., & Miller, I. W. (1998). Reliability and validity of a smoking timeline follow-back interview. *Psychology of Addictive Behaviors*, *12*(2), 101-112.

Brown, R. A., Kahler, C. W., Niaura, R., Abrams, D. B., Sales, S. D., Ramsey, S. E., ... & Miller, I. W. (2001). Cognitive-behavioral treatment for depression in smoking cessation. *Journal of consulting and clinical psychology*, *69*(3), 471-480.

Brown, C., Madden, P. A. F., Palenchar, D. R., & Cooper-Patrick, L. (2000). The association between depressive symptoms and cigarette smoking in an urban primary care sample. *International Journal of Psychiatry in Medicine,* 30, 15–26.

Brown, R. A., Niaura, R., Lloyd-Richardson, E. E., Strong, D. R., Kahler, C. W., et al. (2007). Bupropion and cognitive-behavioral treatment for depression in smoking cessation. *Nicotine & Tobacco Research, 9*(7), 721.

Burgess, E. S., Brown, R. A., Kahler, C. W., Niaura, R., Abrams, D. B., Goldstein, M. G., & Miller, I. W. (2002). Patterns of change in depressive symptoms during smoking cessation: who's at risk for relapse? *Journal of consulting and clinical psychology*, *70*(2), 356-361.

Burns, E. K., & Levinson, A. H. (2008). Discontinuation of nicotine replacement therapy among smoking-cessation attempters. *American Journal of Preventive Medicine*, *34*(3), 212-215.

Carvalho, J. P., Gawrysiak, M. J., Hellmuth, J. C., McNulty, J. K., Magidson, J. F., Lejuez, C. W., & Hopko, D. R. (2011). The Reward Probability Index: Design and validation of a scale measuring access to environmental reward. *Behavior Therapy*, *42*(2), 249-262.

Carvalho, J. P., & Hopko, D. R. (2011). Behavioral theory of depression: Reinforcement as a mediating variable between avoidance and depression. *Journal of Behavior Therapy and Experimental Psychiatry*, *42*(2), 154-162.

Catley, D., Harris, K. J., Okuyemi, K. S., Mayo, M. S., Pankey, E., & Ahluwalia, J. S. (2005). The Influence of Depressive Symptoms on Smoking Cessation Among African Americans an a Randomized Trial of Bupropion. *Nicotine & Tobacco Research*, *7*(6), 859-870.

Centers for Disease Control and Prevention (CDC). (2016). "Current Cigarette smoking among Adults in the United States." Accessed July 7, 2016.

Charles, H., Good, C. B., Hanusa, B. H., Chang, C. C. H., & Whittle, J. (2003). Racial differences in adherence to cardiac medications. *Journal of the National Medical Association*, *95*(1), 17-27.

Chesney, M. A. (2000). Factors affecting adherence to antiretroviral therapy. *Clinical Infectious Diseases*, *30*(Supplement 2), 171-176.

Ciechanowski, P. S., Katon, W. J., & Russo, J. E. (2000). Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Archives of Internal Medicine*, *160*(21), 3278-3285.

Cinciripini, P. M., Wetter, D. W., Fouladi, R. T., Blalock, J. A., Carter, B. L., Cinciripini, L. G., & Baile, W. F. (2003). The effects of depressed mood on smoking cessation: Mediation by postcessation self-efficacy. *Journal of Consulting and Clinical Psychology*, *71*, 292–301.

Collado, A., Castillo, S. D., Maero, F., Lejuez, C. W., & MacPherson, L. (2014). Pilot of the

brief behavioral activation treatment for depression in latinos with limited english proficiency: preliminary evaluation of efficacy and acceptability. *Behavior Therapy*, *45*(1), 102-115.

Cooper, T. V., DeBon, M. W., Stockton, M., Klesges, R. C., Steenbergh, T. A., Sherrill-Mittleman, D., ... & Johnson, K. C. (2004). Correlates of adherence with transdermal nicotine. *Addictive Behaviors*, *29*(8), 1565-1578.

Cuijpers, P., Van Straten, A., & Warmerdam, L. (2007). Behavioral activation treatments of depression: A meta-analysis. *Clinical Psychology Review*, *27*(3), 318-326.

Cummings, K. M., Hyland, A., Ockene, J. K., Hymowitz, N., & Manley, M. (1997). Use of the nicotine skin patch by smokers in 20 communities in the United States, 1992–1993. *Tobacco Control*, 6(Suppl. 2), 63–70.

Daughters, S. B., Braun, A. R., Sargeant, M. N., Reynolds, E. K., Hopko, D. R., Blanco, C., & Lejuez, C. W. (2008). Effectiveness of a brief behavioral treatment for inner-city illicit drug users with elevated depressive symptoms: The Life Enhancement Treatment for Substance Use (LETS ACT!). *Journal of Clinical Psychiatry*, *69*(1), 122-129.

de Dios, M. A., Anderson, B. J., Caviness, C. M., & Stein, M. D. (2014). Early quit days among methadone-maintained smokers in a smoking cessation trial. *Nicotine & Tobacco Research*, *16*(11), 1463-1469.

DiMatteo M. R., Giordani P. J., Lepper H. S., Croghan T. W. (2002). Patient adherence and medical treatment outcomes: a meta-analysis. *Med Care, 40,* 794–811.

DiMatteo, M. R., Lepper, H. S., & Croghan, T. W. (2000). Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of internal medicine*, *160*(14), 2101-2107.

Fagerstrom K. O. (1984). Effects of nicotine chewing gum and follow-up appointments in physician-based smoking cessation. *Journal of Preventative Medicine,* 13, 517–527.

Ferster, C. B. (1973). A functional analysis of depression. *American Psychologist, 28,* 857-870.

Fiore, M. C., Smith, S. S., Jorenby, D. E., & Baker, T. B. (1994). The effectiveness of the nicotine patch for smoking cessation: a meta-analysis. *Jama, 271*(24), 1940-1947.

Fiore, M. C., McCarthy, D. E., Jackson, T. C., Zehner, M. E., Jorenby, D. E., Mielke, M., ... & Baker, T. B. (2004). Integrating smoking cessation treatment into primary care: an effectiveness study. *Preventive Medicine*, *38*(4), 412-420.

Fiore, M. C., Ja, C.R., Baker, T.B., et al. (2008). Treating tobacco use and dependence: update U.S. Public Health Service Clinical Practice Guideline executive summary. *Respir Care, 53*(9), 1217-1222.

First, M. B., & Gibbon, M. (2004). The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II). In: Hilsenroth, M. J. & Segal, D. L. (Eds.), *Comprehensive handbook of psychological assessment, Vol. 2: Personality assessment.* Hoboken, NJ: John Wiley & Son.

Fish, L. J., Peterson, B. L., Brouwer, R. J. N., Lyna, P., Oncken, C. A., Swamy, G. K., ... & Pollak, K. I. (2009). Adherence to nicotine replacement therapy among pregnant smokers. *Nicotine & Tobacco Research*, *11(5)*, 514-518.

Fritz, M. S., & MacKinnon, D. P. (2007). Required sample size to detect the mediated effect. *Psychological science*, *18*(3), 233-239.

Fu, S. S., Kodl, M. M., Joseph, A. M., Hatsukami, D. K., Johnson, E. O., Breslau, N., ... &

Bierut, L. (2008). Racial/ethnic disparities in the use of nicotine replacement therapy and quit ratios in lifetime smokers ages 25 to 44 years. *Cancer Epidemiology Biomarkers & Prevention*, *17*(7), 1640-1647.

Goldstein M. G., Niaura R., Follick M. J., Abrams D. B. (1989). Effects of behavioral skills training and schedule of nicotine gum administration on smoking cessation. *The American Journal of Psychiatry*, *146,* 56–60.

Gonzalez, J. S., Safren, S. A., Cagliero, E., Wexler, D. J., Delahanty, L., Wittenberg, E., ... & Grant, R. W. (2007). Depression, self-care, and medication adherence in type 2 diabetes relationships across the full range of symptom severity. *Diabetes care*, *30*(9), 2222-2227.

Grant, B. F., Hasin, D. S., Chou, S. P., Stinson, F. S., & Dawson, D. A. (2004). Nicotine dependence and psychiatric disorders in the United States: results from the national epidemiologic survey on alcohol and related conditions. *Arch Gen Psychiatry*, *61*(11), 1107-1115.

Hartmann-Boyce, J., Cahill, K., Hatsukami, D., & Cornuz, J. (2012). Nicotine vaccines for smoking cessation. *Cochrane Database Syst Rev*, *8*.

Hays J. T., Leischow S. J., Lawrence D., Lee T. C. (2010). Adherence to treatment for tobacco dependence: association with smoking abstinence and predictors of adherence. *Nicotine and Tobacco Research,* 12, 574–581.

Higgins, S. T., Heil, S. H., & Lussier, J. P. (2004). Clinical implications of reinforcement as a determinant of substance use disorders. *Annu. Rev. Psychol.*, *55*, 431-461.

Hopko, D. R., McNeil, D. W., Lejuez, C. W., Ashcraft, M. H., Eifert, G. H., & Riel, J. (2003). The effects of anxious responding on mental arithmetic and lexical decision task performance. *Journal of Anxiety Disorders*, *17*(6), 647-665.

Hopko, D. R., Lejuez, C. W., Lepage, J. P., Hopko, S. D., & McNeil, D. W. (2003). A Brief Behavioral Activation Treatment for Depression A Randomized Pilot Trial within an Inpatient Psychiatric Hospital. *Behavior Modification*, *27*(4), 458-469.

Hopko, D. R., Bell, J. L., Armento, M. E. A., Hunt, M. K., & Lejuez, C. W. (2005). Behavior Therapy for Depressed Cancer Patients in Primary Care. *Psychotherapy: Theory, Research, Practice, Training*, *42*(2), 236.

Hopko, D. R., Magidson, J. F., & Lejuez, C. W. (2011). Treatment failure in behavior therapy: Focus on behavioral activation for depression. *Journal of Clinical Psychology*, *67*(11), 1106-1116.

Ingersoll, K. S., Cropsey, K. L., & Heckman, C. J. (2009). A test of motivational plus nicotine replacement interventions for HIV positive smokers. *AIDS and Behavior*, *13*(3), 545-554.

Kanter, J. W., Mulick, P. S., Busch, A. M., Berlin, K. S., & Martell, C. R. (2007). The Behavioral Activation for Depression Scale (BADS): psychometric properties and factor structure. *Journal of Psychopathology and Behavioral Assessment*, *29*(3), 191-202.

Katon, W. J. (2003). Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. *Biological psychiatry*, *54*(3), 216-226.

Kenford, S. L., Fiore, M. C., Jorenby, D. E., Smith, S. S., Wetter, D., & Baker, T. B. (1994). Predicting smoking cessation: who will quit with and without the nicotine patch. *Jama*, *271*(8), 589-594.

Killen, J. D., Fortmann, S. P., Davis, L., Strausberg, L., & Varady, A. (1999). Do heavy smokers benefit from higher dose nicotine patch therapy? *Experimental and Clinical psychopharmacology*, *7*(3), 226.

Lam, T. H., Abdullah, A. S. M., Chan, S. S., & Hedley, A. J. (2005). Adherence to nicotine

replacement therapy versus quitting smoking among Chinese smokers: a preliminary investigation. *Psychopharmacology*, *177*(4), 400-408.

Lasser, K., Boyd, J. W., Woolhandler, S., Himmelstein, D. U., McCormick, D., & Bor, D. H. (2000). Smoking and mental illness: A population-based prevalence study. *Jama*, *284*(20), 2606-2610.

Leeman, R. F., Quiles, Z. N., Molinelli, L. A., Terwal, D. M., Nordstrom, B. L., Garvey, A. J., & Kinnunen, T. (2006). Attrition in a multi-component smoking cessation study for females. *Tobacco Induced Diseases*, *3*(2), 59-71.

Leventhal, A. M., Japuntich, S. J., Piper, M. E., Jorenby, D. E., Schlam, T. R., & Baker, T. B. (2012). Isolating the role of psychological dysfunction in smoking cessation: Relations of personality and psychopathology to attaining cessation milestones. *Psychology of Addictive Behaviors*, *26*(4), 838.

Lewinsohn, P. M. (1974). A behavioral approach to depression. In R. M. Friedman and M. M. Katz (Eds.). *The Psychology of Depression: Contemporary Theory and Research.* New York: Wiley.

Lewinsohn, P. M., & Shaffer, M. (1971). Use of home observations as an integral part of the treatment of depression: Preliminary report and case studies. *Journal of Consulting and Clinical Psychology*, *37*(1), 87.

Leventhal, A. M., Ramsey, S. E., Brown, R. A., LaChance, H. R., & Kahler, C. W. (2008). Dimensions of depressive symptoms and smoking cessation. *Nicotine & Tobacco Research*, *10*(3), 507-517.

Libet, J. M., & Lewinsohn, P. M. (1973). Concept of social skill with special reference to the

behavior of depressed persons. *Journal of Consulting and Clinical psychology*, *40*(2), 304.

Lin, E. H., Katon, W., Von Korff, M., Rutter, C., Simon, G. E., Oliver, M., ... & Young, B. (2004). Relationship of depression and diabetes self-care, medication adherence, and preventive care. *Diabetes care*, *27*(9), 2154-2160.

Lejuez, C. W., Hopko, D. R., Acierno, R., Daughters, S. B., & Pagoto, S. L. (2011). Ten year revision of the brief behavioral activation treatment for depression: revised treatment manual. *Behavior Modification*, *35*(2), 111-161.

Little, T. D., Jorgensen, T. D., Lang, K. M., & Moore, E. W. G. (2013). On the joys of missing data. *Journal of pediatric psychology*, *39*(2), 151-162.

Lewinsohn, P. M., & Graf, M. (1973). Pleasant activities and depression. *Journal of Consulting and Clinical psychology*, *41*(2), 261.

Ma, P., Kendzor, D. E., Poonawalla, I. B., Balis, D. S., & Businelle, M. S. (2016). Daily nicotine patch wear time predicts smoking abstinence in socioeconomically disadvantaged adults: An analysis of ecological momentary assessment data. *Drug and Alcohol Dependence*, *169*, 64-67.

MacPherson, Collado, Lejuez, Bown, Tull (2016). "Behavioral activation treatment for smoking (BATS) in smokers with depressive symptomatology", *Advances in Dual Diagnosis, 9 (2)*, 85 – 96.

MacPherson, L., Tull, M. T., Matusiewicz, A. K., Rodman, S., Strong, D. R., Kahler, C. W., ... & Lejuez, C. W. (2010). Randomized controlled trial of behavioral activation smoking cessation treatment for smokers with elevated depressive symptoms. *Journal of Consulting and Clinical Psychology*, *78*(1), 55-61.

Magidson, J. F., Listhaus, A., Seitz-Brown, C. J., Safren, S. A., Lejuez, C. W., & Daughters, S. B. (2015). Can behavioral theory inform the understanding of depression and medication nonadherence among HIV-positive substance users? *Journal of Behavioral Medicine*, *38*(2), 337-347.

Maier, W., & Philipp, M. (1985). Improving the assessment of severity of depressive states: A reduction of the Hamilton Depression Rating Scale. *Pharmacopsychiatry, 18,* 114-115

Martin-Sölch, C., Magyar, S., Kunig, G., Missimer, J., Schultz, W., & Leenders, K. L. (2001). Changes in brain activation associated with reward processing in smokers and nonsmokers. A positron emission tomography study. *Exp Brain Res, 139*(3), 278-286.

Martin-Sölch, C., Missimer, J., Leenders, K. L., & Schultz, W. (2003). Neural activity related to the processing of increasing monetary reward in smokers and nonsmokers. *Eur J Neurosci*, *18*(3), 680-688.

Matthews, A. K., Conrad, M., Kuhns, L., Vargas, M., & King, A. C. (2013). Project Exhale: preliminary evaluation of a tailored smoking cessation treatment for HIV-positive African American smokers. *AIDS patient care and STDs*, *27*(1), 22-32.

Maxwell, S. E., & Cole, D. A. (2007). Bias in cross-sectional analyses of longitudinal mediation. *Psychological Methods, 12,* 23-44.

Molyneux, A., Lewis, S., Leivers, U., Anderton, A., Antoniak, M., Brackenridge, A., ... & Britton, J. (2003). Clinical trial comparing nicotine replacement therapy (NRT) plus brief counselling, brief counselling alone, and minimal intervention on smoking cessation in hospital inpatients. *Thorax*, *58*(6), 484-488.

Mooney, M. E., Leventhal, A. M., & Hatsukami, D. K. (2006). Attitudes and knowledge about nicotine and nicotine replacement therapy. *Nicotine & Tobacco Research*, *8*(3), 435-446.

Moore, D., Aveyard, P., Connock, M., Wang, D., Fry-Smith, A., & Barton, P. (2009). Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis. *Bmj*, *338*, b1024.

Muthén LK, Muthén BO. Mplus User's Guide, Seventh Edition. Los Angeles, CA: Muthén & Muthén; 1998-2012.

Musselman, D. L., Evans, D. L., & Nemeroff, C. B. (1998). The relationship of depression to cardiovascular disease: epidemiology, biology, and treatment. *Archives of general psychiatry*, *55*(7), 580-592.

National Cancer Institute (U.S.). (2008). *Clearing the air: Quit smoking today*. Bethesda, Md.: U.S. Dept. of Health and Human Services, National Institutes of Health, National Cancer Institute.

National Cancer Institute, 2016. NCI Dictionary of Cancer Terms. Retrieved from http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=439409

Nezu, A. M., Ronan, G. F., & Meadows, E. A. 8c McClure, KS. (2000). Practitioner's guide to empirically-based measures of depression.

Niaura, R., Britt, D. M., Shadel, W. G., Goldstein, M., Abrams, D., & Brown, R. (2001). Symptoms of depression and survival experience among three samples of smokers trying to quit. *Psychology of Addictive Behaviors, 15,* 13–17.

Office for National Statistics. Smoking-related behaviour and attitudes. 2008. www.statistics.gov.uk/downloads/theme_health/ Smoking2005.pdf.

Ogedegbe, G., Schoenthaler, A., Richardson, T., Lewis, L., Belue, R., Espinosa, E., ... &

Charlson, M. E. (2007). An RCT of the effect of motivational interviewing on medication adherence in hypertensive African Americans: rationale and design. *Contemporary Clinical Trials*, *28*(2), 169-181.

Papadakis, S., McDonald, P., Mullen, K. A., Reid, R., Skulsky, K., & Pipe, A. (2010). Strategies to increase the delivery of smoking cessation treatments in primary care settings: a systematic review and meta-analysis. *Preventive Medicine*, *51*(3), 199-213.

Partnership for Drug Free Kids, (2015, January 15). Sales of Nicotine Patches and Gum Slow as More Smokers Turn to E-Cigarettes to Quit. Retrieved from http://drugfree.org/learn/drug-and-alcohol-news/sales-nicotine-patches-gums-slow-smokers-turn-e-cigarettes-quit/

Perkins, K. A., Lerman, C., Grottenthaler, A., Ciccocioppo, M. M., Milanak, M., Conklin, C. A., et al. (2008). Dopamine and opioid gene variants are associated with increased smoking reward and reinforcement owing to negative mood. *Behavioral Pharmacology*, *19*(5-6), 641-649.

Powell, J., Dawkins, L., & Davis, R. E. (2002). Smoking, reward responsiveness, and response inhibition: tests of an incentive motivational model. *Biological Psychiatry*, *51*(2), 151-163.

Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods, Instruments, & Computers*, *36*(4), 717-731.

Raupach, T., Brown, J., Herbec, A., Brose, L., & West, R. (2014). A systematic review of studies assessing the association between adherence to smoking cessation medication and treatment success. *Addiction*, *109*(1), 35-43.

Roddy, E., Romilly, N., Challenger, A., Lewis, S., & Britton, J. (2006). Use of nicotine replacement therapy in socioeconomically deprived young smokers: a community-based pilot randomised controlled trial. *Tobacco Control*, *15*(5), 373-376.

Ryan, G. W., & Wagner, G. J. (2003). Pill taking 'routinization': a critical factor to understanding episodic medication adherence. *AIDS care*, *15*(6), 795-806.

Safren, S. A., Otto, M. W., & Worth, J. L. (1999). Life-steps: Applying cognitive behavioral therapy to HIV medication adherence. *Cognitive and Behavioral Practice*, *6*(4), 332-341.

Safren SA, W Otto M, Worth JL, Salomon E, Johnson W, Mayer K, Boswell S. (2001). Two strategies to increase adherence to HIV antiretroviral medication: life-steps and medication monitoring. *Behaviour Research and Therapy*, 39(10):1151–1162.

Schayck, O. (2014). Nicotine vaccination—does it have a future? *Addiction*, *109*(8), 1223-1225.

Scherphof, C. S., van den Eijnden, R. J., Lugtig, P., Engels, R. C., & Vollebergh, W. A. (2014). Adolescents' use of nicotine replacement therapy for smoking cessation: predictors of compliance trajectories. *Psychopharmacology*, *231*(8), 1743-1752.

Schmitz J. M., Stotts A. L., Mooney M. E., Delaune K. A., Moeller G. F. (2007). Bupropion and cognitive–behavioral therapy for smoking cessation in women. *Nicotine and Tobacco Research, 9,* 699–709.

Shaw, J. P., Ferry, D. G., Pethica, D., Brenner, D., & Tucker, I. G. (1998). Usage patterns of transdermal nicotine when purchased as a non-prescription medicine from pharmacies. *Tobacco Control*, *7*(2), 161-167.

Shiffman, S., Sweeney, C. T., Ferguson, S. G., Sembower, M. A., & Gitchell, J. G. (2008). Relationship between adherence to daily nicotine patch use and treatment efficacy: secondary analysis of a 10 week randomized, double-blind, placebo-controlled clinical

trial simulating over-the-counter use in adult smokers. *Clinical therapeutics*, *30*(10), 1852-1858.

Shrout, P. E., & Bolger, N. (2002). Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychological methods*, *7*(4), 422-445.

Silagy, C., Lancaster, T., Stead, L., Mant, D., & Fowler, G. (2004). Nicotine replacement therapy for smoking cessation. *The Cochrane Library*.

Skinner, B. (1953). Some contributions of an experimental analysis of behavior to psychology as a whole. *American Psychologist*, *8*(2), 69-78.

Smith, S. S., McCarthy, D. E., Japuntich, S. J., Christiansen, B., Piper, M. E., Jorenby, D. E., ... & Jackson, T. C. (2009). Comparative effectiveness of 5 smoking cessation pharmacotherapies in primary care clinics. *Archives of internal medicine*, *169*(22), 2148-2155.

Smith, T. D., & McMillan, B. F. (2001). A Primer of Model Fit Indices in Structural Equation Modeling.

Sobell, L. C., & Sobell, M. B. (1996). *Timeline followback: A calendar method for assessing alcohol and drug use*. Toronto: Addiction Research Foundation.

Sobell, L. C., Sobell, L. C., & Sobell, M. B. (1978). Validity of self-reports in three populations of alcoholics. *Journal of Consulting and Clinical Psychology*, *46*(5), 901.

SRNT, W. (2002). Biochemical verification of tobacco use and cessation. *Nicotine Tob Res*, *4*(2), 149-159.

Stead, L. F., Perera, R., Bullen, C., Mant, D., Hartmann- Boyce, J., Cahill, K., & Lancaster, T. (2012). Nicotine replacement therapy for smoking cessation. *The Cochrane Library*.

Stein, M. D., & Anderson, B. J. (2003). Nicotine and drug interaction expectancies among

methadone maintained cigarette smokers. *Journal of substance abuse treatment*, *24*(4), 357-361.

Stein, M. D., Anderson, B. J., & Niaura, R. (2006). Nicotine replacement therapy: Patterns of use after a quit attempt among methadone- maintained smokers. *Journal of General Internal Medicine*, *21*(7), 753-757.

Swartz, S. H., Ellsworth, A. J., Curry, S. J., & Boyko, E. J. (1995). Community patterns of transdermal nicotine use and provider counseling.*Journal of general internal medicine*, *10*(12), 656-662.

US Department of Health and Human Services. (2014). The health consequences of smoking—50 years of progress: a report of the Surgeon General. *Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health*, *17*.

Wiggers, L. C., Smets, E. M., Oort, F. J., de Haes, H. C., Storm-Versloot, M. N., Vermeulen, H., ... & Peters, R. J. (2006). Adherence to nicotine replacement patch therapy in cardiovascular patients. *International Journal of Behavioral Medicine*, *13*(1), 79-88.