ABSTRACT

Title of thesis: ASSESSMENT OF NICOTINE DEPENDENCE AND ITS DEMOGRAPHIC CORRELATES AMONG AFRICAN AMERICAN SMOKERS

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Despite scientific evidence that smoking is highly addictive, little information is available on the prevalence of nicotine dependence among African American smokers. The primary objective of this study was to examine the associations between demographic variables, socioeconomic status, self reported smoking history and the level of nicotine dependence among African American smokers. This study was a cross-sectional secondary analysis of data collected during a randomized clinical trial from African American participants (n=206). The results showed that age of smokers, number of years of regular smoking, low education level and negative perception of ability to quit smoking were associated with high nicotine dependence. The multivariate analysis showed that those with negative perception of their ability to quit smoking had greater odds of having high nicotine dependence. The findings suggested that tailored interventions should include components that increase self efficacy among African American smokers depending on the level of nicotine dependence.

ASSESSMENT OF NICOTINE DEPENDENCE AND ITS DEMOGRAPHIC CORRELATES AMONG AFRICAN AMERICAN SMOKERS

By

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CHAPTER I- INTRODUCTION

1.1. Background of the Problem

Cigarette smoking is responsible for nearly 1 in 5 deaths in the United States and is the most preventable cause of premature death (American Cancer Society [ACS], 2007). Smoking is a known cause of cancer, heart disease, stroke, complications of pregnancy, and chronic obstructive pulmonary disease (Centers for Disease Control and Prevention [CDC], 1990). Smoking has been linked to leukemia, cataracts, and pneumonia, and accounts for about one-third of all cancer deaths (Belluzzi, Wang, & Leslie, 2005). The overall rates of death from cancer are twice as high among smokers as nonsmokers, with heavy smokers having rates that are four times greater than those of nonsmokers (CDC, 1982). Foremost among the cancers caused by tobacco use is lung cancer; cigarette smoking has been linked to about 90 % of all lung cancer cases, which is the number-one cancer killer of both men and women (ACS, 2005). Smoking is also associated with cancers of the mouth, pharynx, larynx, esophagus, stomach, pancreas, cervix, kidney, ureter, and bladder (National Institute on Drug Abuse, 2006). It is estimated that approximately 440,000 persons die of a cigarette smoking-attributable illness per year, resulting in 5.6 million years of potential life lost, $75 billion in direct medical costs, and $82 billion in lost productivity (CDC, 2002a).

Among ethnicities represented in the United States (U.S.), tobacco use disproportionately impacts African Americans who incur an increased relative risk of mortality from diseases associated with tobacco use, including coronary heart disease, stroke, and respiratory cancers (United States Department of Health and Human Services

[USDHHS], 1998). An unexplained irony is that African Americans smoke fewer cigarettes per day (USDHHS, 2000; Garfinkel, 1984) and tend to begin smoking later in life (Escobedo, Anda, Smith, Remington, & Mast, 1990) than Caucasians do, however their smoking-related disease mortality is higher. It is difficult to pinpoint a single factor or a definite combination of factors that influence the disproportional impact on African Americans. One of the reasons is that tobacco use itself is influenced by several kinds of factors; individual factors (e.g. age of initiation of smoking, level of nicotine dependence); (2) social factors such as societal norms; (3) environmental factors, such as access to health-care, quality of health care; and (4) cultural factors, such as traditional uses of tobacco, and acculturation in African American communities (USDHHS, 1998). An understanding of the role of these factors in shaping smoking behavior could help clarify racial differences and facilitate the understanding of effective smoking cessation interventions, among African Americans.

Generally speaking, nicotine dependence is the "vulnerability of the body to the addiction of the chemical nicotine, when delivered by various tobacco products" (Mayo Clinic, 2006). In addition to the physical dependence associated with nicotine, there is a strong psychological component to the dependency of most users of tobacco products, especially cigarette smokers. Smoking causes psychological dependence because the smoker associates the act of smoking with a pleasurable moment which also functions as a form of negative reinforcement; that is, use of nicotine eases or alleviates stress, anxiety, boredom and other negative emotions in the short term. Consequently, physical dependence on nicotine coupled with the psychological effects of smoking makes the habit hard to break. Understanding the level of physical dependence is crucial in

determining the appropriate treatment therapy and the level of dependence (low, medium, high) can also be used as an important predictive factor of smoking cessation (Breslau & Johnson, 2000). Furthermore, the level of nicotine dependence can also be used to determine whether nicotine replacement medication should be used, in what circumstances, and at what dosage (GlaxoSmithKline Consumer Healthcare, 2003; Shiffman et al., 2002).

The common methods of determining nicotine dependence are self-reporting of smoking behaviors and measurement of biochemical markers of nicotine in the body. The general strategy to measure biochemical markers is to assess concentrations of nicotine, its metabolites, or other chemicals associated with tobacco smoke in biological fluids. Tobacco smoke is an important source of carbon monoxide (CO). Although nicotine itself might cause health problems, most of the tobacco-induced disorders appear to be due to the carcinogens and CO in tobacco smoke rather than nicotine itself (Hughes, 1993; Benowitz 1998). Consequently, CO measurement is important for assessment of smoking behavior (Groman, Kunze, Schmeiser-Rieder, & Schoberberger, 1998). Self-reported smoking is a simple pen-and-pencil measure that has the advantage of minimal cost. One of the most commonly used self report methods to measure nicotine dependence is the Fagerström Test for Nicotine Dependence (FTND, Appendix I) (Heatherton, Kozlowski, Frecker, & Fagerström, 1991). The Fagerström scales offer brevity, ease of administration, and adequate test–retest reliability (Pomerleau, Carton, Lutzke, Flessland, & Pomerleau, 1994).

Relatively few studies have been directed toward understanding nicotine dependence and factors associated with smoking behaviors among African Americans

(Orleans et al., 1989; Hoffman, Cooper, Lacey, & Mullner, 1989). Moreover, the use of self-reported measures of smoking behavior to investigate racial differences in nicotine dependence, has received much less research attention compared to simple descriptive studies of smoking prevalence (USDHHS, 1998).

1.2. Statement of the Problem

Despite scientific evidence that nicotine is highly addictive, little information is available on the prevalence of nicotine dependence (Breslau, Johnson, Hiripi, & Kessler, 2001). Much more is known about the prevalence of smoking than nicotine dependence, especially regarding racial/ethnic patterns (USDHHS, 1998). Many studies have been conducted on smoking prevalence but not many that actually focused on the prevalence of nicotine dependence among African Americans. Some studies suggested that African Americans have high levels of nicotine dependence (Ahijevych & Gillespie, 1997; Royce, Hymowitz, Corbett, Hartwell, & Orlandi, 1993) but this finding was not consistent across studies (Andreski & Breslau, 1993; Kandel & Chen, 2000). Relatively little research has been conducted to clarify nicotine dependence and factors that are associated with it, among African-American smokers; even fewer studies have been identified that used FTND, to measure nicotine dependence in African American adults.

The lack of definitive literature points to the need for further research to better understand the contribution of factors that are associated with nicotine dependence among African American smokers. Some of the factors that could be related to nicotine dependence include age, gender, socioeconomic status (SES), age of initiation of regular smoking, and number of years of regular smoking. Despite the important contributions of the few studies that have included African American smokers, the relationships across

demographics (age, gender), SES and self-reported smoking behaviors have not been reported in African American smokers. These indicators may determine nicotine dependence among African Americans and can therefore provide valuable information about the differences in levels of nicotine dependence among African Americans, which in turn can lead to more specific intervention strategies.

A number of studies have addressed age of initiation of smoking and nicotine dependence (Breslau, Fenn, & Peterson, 1993), and racial differences in age of initiation (Hu, Davies, & Kandel, 2006). The results from the studies have shown that white adolescents start smoking at an earlier age, are more likely to persist in smoking, and become more dependent on nicotine than minority youths (USDHHS, 1998; Griesler & Kandel, 1998; Landrine, Richardson, Klonoff, & Flay, 1994). However, a better understanding of smoking initiation and its relation to dependence across different racial/ethnic groups is crucial to the development of effective programs and interventions. This study aims to help in filling the gap in the literature by studying the age of initiation of regular smoking in African American smokers in association with the levels of nicotine dependence.

Studies suggest that compared with men, female smokers tend to be less dependent on nicotine (Benowitz & Hatsukami, 1998). King, Bendel and Delaronde (1998) demonstrated that female Caucasians smoke significantly more cigarettes than do female smokers of other races/ethnicities. Studies have been conducted to study the prevalence of smoking in African American males and females, however no single study has been identified that focused on nicotine dependence in African American males and females.

Socioeconomic status (SES) is strongly related to smoking behavior (Jarvis & Wardle, 1999). The strength of the relationship is depicted by the identification of disadvantaged groups by simple observation of their smoking prevalence (Graham, 1993). To a large extent, it is due to differential cessation rates between socioeconomic groups (Jarvis, 1997). There is a whole range of independent factors that predict smoking cessation. The odds of being a smoker are increased in those in lower occupational class groups (Jarvis & Wardle, 1999), and there is a substantial gradient by educational level (Breslau & Peterson, 1996). Education level is one of the most widely used indicators of socioeconomic status in health studies (Liberatos, Link, & Kelsey, 1988). Education level is used as a measure of SES because education level can be determined for all the individuals irrespective of their employment status. Nicotine dependence and education level a sa proxy for socioeconomic status have been examined extensively in terms of their independent relationship to smoking cessation; both are strong predictors of the propensity to quit and/or successful cessation (Jarvis & Wardle, 1999). However, the mechanism of the link between SES (education) and nicotine dependence has not been adequately explored, especially in African American smokers.

Similarly, research based on ability of smokers to quit smoking and number of quit attempts in the past, in association with dependence in African American smokers have not been precisely examined. Moreover, very few studies have (Groman & Bayer, 2000) examined the correlation of FTND and CO in a European population. Carbon monoxide measurement is the biomarker test which verifies self-reported dependence by smokers. It appears that no similar study has been conducted among African American smokers.

1.3. Significance of the Study

The primary objective of this study was to examine the associations between demographic variables (age, and gender) SES (education level), self-reported smoking and the level of nicotine dependence (low, moderate, high) among African American smokers using FTND. The secondary objective of the study was to examine the correlation between exhaled CO measurements, with the level of dependence, based on self-reported data. This study aimed to help enhance an understanding of nicotine dependence and factors that could be associated with dependence, among African American smokers. No identified study has investigated the association of demographics, SES, self reported smoking behavior, and exhaled CO to light, moderate and heavy nicotine dependence as measured by FTND, in an African American population. Thus, this study attempted to understand the dynamics of these variables in association with level of nicotine dependence among an African American population. The results of this study might provide directions for future research.

1. 4. Research Questions and Hypotheses

This study aimed to address the following questions among African American smokers:

Research Question: (1) Are demographic and SES variables (age, gender and education level) associated with the level of low, medium and heavy nicotine dependence in African American smokers?

Hypothesis- 1 (a) Male African American smokers have heavier nicotine dependence than female African American smokers.

1(b) Older smokers have heavier nicotine dependence than young smokers.

1(c) African American smokers with low education level have heavier nicotine dependence.

Research Question: (2) Does age of initiation of regular smoking predict the level of nicotine dependence in African American smokers?

Hypothesis- African Americans who initiate smoking at an early age are more heavily dependent on nicotine than those who initiate later.

Research Question: (3) Is number of years of regular smoking associated with the level of nicotine dependence in African American smokers?

Hypothesis- A longer period of regular smoking is associated with heavier dependence among African American smokers.

Research Question: (4) Is number of quit attempts in the past associated with the level of dependence on nicotine in African American smokers?

Hypothesis- African American smokers who have never tried to quit in the past have heavier nicotine dependence.

Research Question: (5) Is the perception of ability to quit smoking, with or without any assistance, associated with the level of nicotine dependence in African American smokers?

Hypothesis- African American smokers who have a negative perception of their ability to quit smoking report heavy nicotine dependence.

Research Question: (6) Is CO measurement correlated with nicotine dependence in African American smokers?

Hypothesis- Higher CO measurement is associated with heavy nicotine dependence among African American smokers.

CHAPTER II- BACKGROUND

2.1 Conceptual/analytical framework of the study

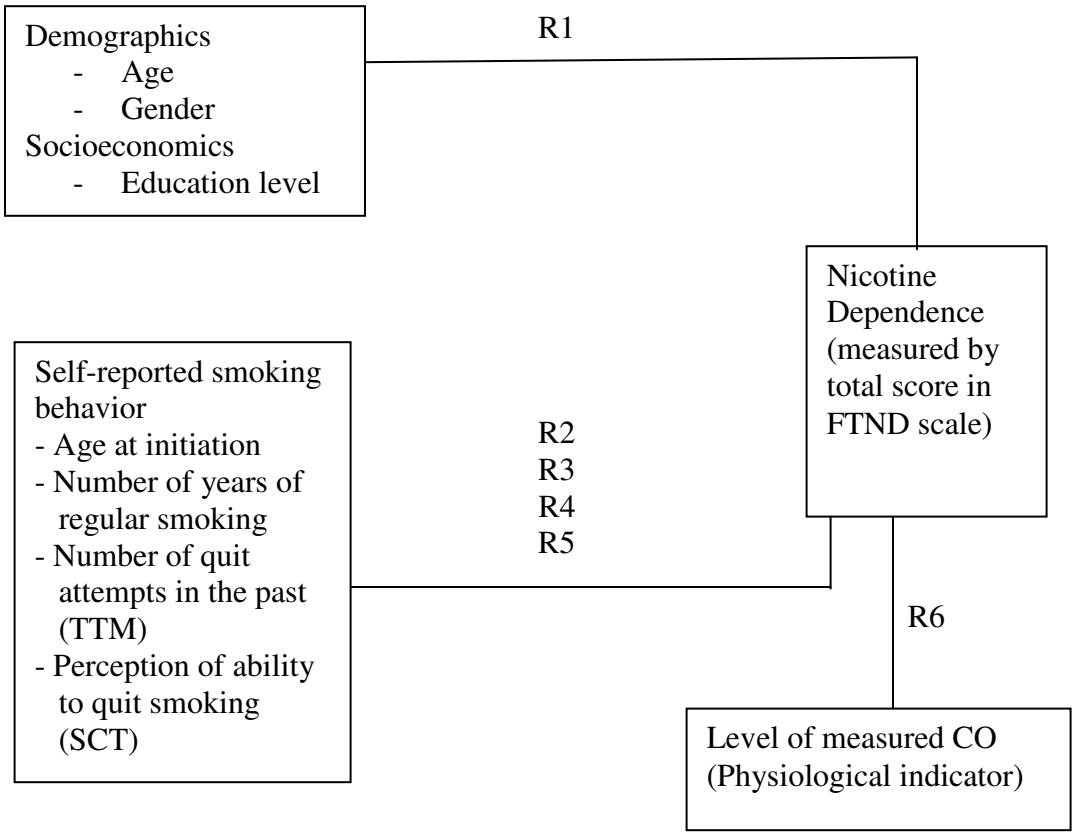


Figure 2.1. Conceptual framework of relationship between demographics, SES, smoking history, CO and nicotine dependence

Figure 2.1 represents a conceptual framework for the study. The study aimed to examine the association between demographic variables such as age and gender, SES measured by education level, self reported smoking behaviors and the level of nicotine dependence among African American smokers. The study also aimed to examine the

correlation between the exhaled CO, which is a physiological marker of smoking, and the level of nicotine dependence.

Since the study was originally designed for other purposes, the variables used in this study that are related to smoking behavior were not based on any specific health behavior theory or model. Therefore, the variables could not be studied using one single model or theory; however constructs of two models were used to understand smoking behavior based on theoretical frameworks. One of the questions asked in the smoking history such as "How many times have you tried to quit smoking before for at least 24 hours?" was clearly associated with the Stages of Change model (Prochaska & DiClemente, 1983). If an individual has never attempted to quit before, it suggests that the individual is still in Pre-Contemplation or Contemplation stage. Those who have attempted to quit smoking in the past can be presumed to have initiated Action stage but appeared unsuccessful. Another question asked in the smoking history, "Could you quit smoking if you wanted to?" could be studied as a proxy for self-efficacy, a construct of the Social Cognitive Theory (SCT; Bandura, 1977). The action of quitting smoking is related to the individual's perception of his or her ability to perform the action i.e. quitting smoking in this case. Therefore, two variables, that are associated with smoking behavior, were discussed based on these theoretical frameworks.

2.2. Health Behavior Theories

In a broad sense, health behavior refers to the actions of individuals, groups, and organizations as well as their determinants, correlations, and consequences, including social change, policy development and implementation, improved coping skills and enhanced quality of life (Parkerson et al., 1993). On an individual level, health behavior

is also defined as those personal attributes such as beliefs, expectations, motives, values, perceptions, and other cognitive elements; personality characteristics, including affective, and emotional states and traits; and overt behavior patterns, actions, and habits that relate to health maintenance, to health restoration, and to health improvement (Gochman, 1982; Gochman, 1997).

Over time, studies on smoking behavior have emerged from the implementation of behavior change theories and models into interventions in different population groups. Since they define what is to be measured, models and theories of health behavior change are essentially linked to the measurement of health behavior. These research-based models have precipitated a shift in how professionals understand and treat at-risk behaviors. Theoretical models fundamentally guide both current and future understanding of health behavior, as well as providing direction for research and intervention development. Each model or theory can be seen as a roadmap of the health behavior.

2.2.1. Transtheoretical Model

The Transtheoretical Model (TTM) has been proven very effective in explaining both the acquisition and cessation of many health related behaviors (Migneault, Pallonen, & Velicer, 1997). Ever since the conception of TTM (Prochaska & DiClemente, 1983), the model has been extensively used in interventions in the field of smoking. Before the formulation of the model, numerous psychotherapy outcome studies had demonstrated that people could successfully change their behaviors with the help of professional treatment. However, the studies modestly explained how people can change behaviors on their own.

Self-change had been documented to occur with alcohol abuse, smoking, obesity, and opiate use (Cohen et al., 1989; Orford, 1985; Roizen, Cahaland, & Shanks, 1978; Schachter, 1982; Tuchfeld, 1981). This encouraged researchers to propagate theories to "solve the puzzle of how people intentionally change their behavior with and without psychotherapy" (Prochaska, DiClemente, & Norcross, 1992). Thus, the Transtheoretical model emerged from analysis of theories in psychotherapy and behavior change.

The model uses stages of change to integrate processes and principles of change from theories of intervention (Glanz, Rimer, & Lewis, 2002). It incorporates five major stages of change, several processes of change, decisional balance based on pros and cons of the change and self-efficacy. The model interprets behavior change as a process that involves five stages; Precontemplation, Contemplation, Preparation, Action and Maintenance. Progression through these stages is viewed as cyclical rather than linear (Prochaska et al., 1992). The model also incorporates the construct of self-efficacy (Bandura; 1977, 1982), referring to temptations to perform the behavior or to refrain from the behavior.

Starting from studies regarding integration of the model to smoking behavior, the model has been expanded to other areas of health behavior. Others include "alcohol and substance abuse, anxiety and panic disorders, eating disorders and obesity, high-fat diets, HIV/AIDS prevention, mammography screening, medication compliance, unplanned pregnancy prevention, pregnancy and smoking, sedentary lifestyles, sun exposure, and physicians practicing preventive medicine" (Glanz et al., 2002). However, the model has been "investigated extensively in the area of tobacco smoking" (Schumann, Meyer, & Rumpf, 2005).

2.2.2. Social Cognitive Theory

Bandura (1995) defined perceived self-efficacy as the "beliefs in one's capabilities to organize and execute the courses of action required to manage prospective situations." Bandura (1977) proposed that self-efficacy is the most important prerequisite for behavior change because of its effect in an effort that is invested for accomplishment of a task and the level of attained performance. The theory has been found to be important to the treatment of addictive behaviors such as smoking. One area in health field where self-efficacy has been used extensively is in the field of smoking. Empirical evidence supports the premise that increasing self-efficacy during treatment enhances addictive behavior change and contributes to the maintenance of the change following treatment (Craighead, Flynn, & Rounds-Bryant, 1997). If the goal of nicotine dependence treatment is to maximize the likelihood of recovery in treatment and continuation of the process after treatment, then smokers could be more likely to achieve this goal when self-efficacy-enhancing interventions are incorporated into treatment of dependence.

Quitting the habit requires optimistic self-beliefs that can be instilled in smoking cessation programs (Baer & Lichtenstein, 1986). Efficacy beliefs to resist temptation to smoke predict reduction in the number of cigarettes smoked, the amount of tobacco per smoke, and the nicotine content (Godding & Glasgow, 1985). Mudde, Kok & Strecher (1989) found an increase in efficacy beliefs after treatment, and those who had acquired the highest levels of self-efficacy remained successful quitters as assessed in a one-year period. In the application of self-efficacy theory in the field of addiction, it is assumed that successful coping in a variety of high-risk situations increases perceived self-efficacy, which in turn reduces vulnerability to relapse (Marlatt & Gordon, 1985). Other

studies have demonstrated relationships between perceived self-regulatory efficacy and relapse occurrence or time of relapse, with correlations ranging from -.34 to -.69 (Colletti, Supnick, & Payne, 1985; DiClemente, Prochaska, & Gibertini, 1985).

2.3. Review of Relevant Literature

The review of the preliminary studies on self-report of smoking among African Americans identified few studies. Data from the 1987 National Health Interview Survey showed that African Americans were more likely than whites and Hispanics to report smoking their first cigarette of the day within 10 minutes of awakening (USDHHS, 1998). Similarly, telephone survey data on smoking, collected as part of the Community Intervention Trial for Smoking Cessation (COMMIT), indicated that African Americans were more likely than whites to smoke within 10 minutes of awakening (Royce et al., 1993) which is an indicator of nicotine dependence. The literature on predictors or correlates of smoking cessation among African Americans is limited (USDHHS, 1998).

Studies suggest that African Americans have higher level of cotinine per reported number of cigarettes smoked per day than whites (Wagenknecht et al., 1990; English, Eskenazi, & Christianson, 1994; Clark, Gautam, & Gerson, 1996). One possible explanation for the higher cotinine level among African Americans is that African Americans may absorb more nicotine from their cigarettes than whites (Benowitz, Perez-Stable, Herrera, & Jacob, 1995). Greater absorption could result from several factors, including group-specific patterns of smoking behavior (i.e., more and deeper puffs per cigarette or longer retention of tobacco smoke in the lungs) (Benowitz et al., 1995). Racial differences in nicotine metabolism could also influence the development of nicotine addiction. Several researchers have suggested that African Americans might

metabolize nicotine differently than whites (Wagenknecht et al., 1990; English et al., 1994; Benowitz et al., 1995). Results of studies of nonsmokers support this hypothesis (Wagenknecht, Manolio, Sidney, Burke, & Haley, 1993; Crawford et al., 1994; Knight, Eliopoulos, Klein, Greenwald, & Koren, 1996; Pirkle et al., 1996).

FTND is the most frequently used measure of self reported nicotine dependence. It has been used in a variety of settings in various samples of the population and has also been used in African American populations in some studies. The FTND was used in a sample of African Americans in a clinical trial of bupropion to assess nicotine dependence (Ahluwalia, Harris, Catley, Okuyemi, & Mayo, 2002). In another study the scale was used for tobacco dependence assessment in African American and European American teenage smokers (Moolchan & Schroeder, 2004). The FTND was also used to assess nicotine dependence to study treatment outcome of African American cocaine-dependent patients (Patkar et al., 2003). Moolchan, Berlin, Robinson and Cadet (2003) studied the characteristics of African American teenage smokers using FTND scores as one of their tools. The results showed that African Americans had lower FTND scores compared to non-African Americans but the scores were similar in both groups when the number of cigarettes smoked per day was adjusted.

Cigarette smoking plays a major role in the mortality of U.S. women. In the U.S. females lost an estimated 2.1 million years of life each year during the 1990s as a result of smoking-related deaths due to neoplastic, cardiovascular, respiratory, and pediatric diseases as well as from burns caused by cigarettes (CDC, 2002b). There are several reasons why women are affected in a different mode by smoking behavior. The most

important behavioral reason is because women appear to be more affected by the desire to smoke for weight control.

On the other hand, animal studies have shown gender-specific differences in nicotine concentrations in the brain, and these differences support the hypothesis that there are differences in nicotine distribution among females and males (Rosecrans, 1972; Rosecrans & Schechter, 1972; Hatchell & Collins, 1980). Beckett and associates (1971) suggested that the extent of nicotine metabolism is different among women and men, reporting that women nonsmokers excreted more nicotine and less cotinine in urine than did men nonsmokers.

Researchers have found that men and women differ not just in physiological aspect but also behavioral. Studies have suggested that men take puffs of larger volume and longer duration than women do and men generally inhale more smoke from each cigarette (Moody, 1980; Hofer, Nil, & Battig, 1991). It was observed that men had larger puff volume and longer puff duration than women did, however women tended to have greater increase in expired CO after smoking a cigarette (Battig et al., 1982). Nevertheless men had greater plasma nicotine level than woman (Hofer et al., 1991). Silverstein and coworkers (1980) suggested that, because women are more likely to report feeling sick after smoking their very first cigarette, they may be more sensitive than men to nicotine. In brief, the differences in gender in all of these aspects may affect plasma nicotine concentration, which in turn may affect nicotine dependence. Studies suggest that compared with men, female smokers tend to be less dependent on nicotine and more dependent on the environmental cues associated with smoking, such as the

sight and smell of tobacco, or the social aspects involved with the behavior (Hatsukami, Skoog, Allen, Bliss, 1995; Perkins, 1996).

The majority of studies have focused on age of initiation of smoking in relation to cessation. It is suggested that the inverse association between age at initiation and cessation, observed in relation to some illicit drugs (Kandel & Raveis, 1989) might apply also to cigarettes (Breslau & Peterson, 1996). Breslau and Peterson (1996) estimated the relationship between smoking cessation and age of initiation, and concluded that the likelihood of smoking cessation was greater in smokers who had begun cigarette smoking after age 13 than in those who had begun earlier. Early initiation of cigarette smoking has been associated with a greater potential for problems, including heavy daily consumption, longer duration of smoking, and nicotine dependence (Yamaguchi & Kandel, 1984; Breslau, Fenn, & Peterson, 1993; Breslau, Kilbey, & Andreski, 1994; Taioli, & Wynder, 1991; Escobedo et al., 1990).

There are data to suggest that early age of smoking initiation might be associated with a higher daily consumption of cigarettes and a longer duration of smoking in adulthood (Taioli & Wynder, 1991). "Evidence that first use of cigarettes before a specified age signals an increased probability of nicotine dependence would suggest that efforts to delay the onset of smoking might lead to reductions in smoking related morbidity" (Breslau, Fenn, & Peterson, 1993). Breslau, Fenn, and Peterson (1993) studied early smoking initiation and nicotine dependence in a cohort of 1200 young adults. Controlling for sex and race, persons who smoked their first cigarette at 14 to 16 years of age were 1.6 times more likely to become dependent than those who initiated

smoking at an older age. Smoking initiation before age 14 was not associated with increased probability of dependence.

The correlation of CO and FTND was studied in a sample of 241 patients in one study (Groman & Bayer, 2000). CO concentrations were measured with the Bedfont EC50 MICRO CO monitor. The Pearson's correlation between FTND and CO was found to be 0.354. The study concluded that assessment of smoking prevalence using self-administered questionnaires could be misleading to study the prevalence of addiction. It has been argued that smoking studies using self-administered questionnaires should at least also include the measurement of exhaled CO (Groman, 2000). This type of assessment using non-response bias by implementing the CO measurement was first used in 1997-1998 on medical students at the University of Vienna (Groman et al., 1998). The correlation between FTND and CO in that study was found to be 0.354.

2.4. Background on Tobacco Use

According to the CDC (2005a), there were 44.5 million adult smokers in 2004 in the U.S. According to the National Survey on Drug Use and Health, an estimated 70.3 million Americans of age 12 or older reported use of tobacco, 59.9 million (24.9% of the population) smoked cigarettes, 13.7 million (5.7 %) smoked cigars, 1.8 million (0.8%) smoked pipes, and 7.2 million (3.0%) used smokeless tobacco in 2004, confirming that tobacco is one of the most widely abused substances in the United States (Substance Abuse and Mental Health Services Administration [SAMHSA], 2005).

Epidemiologic data suggest that more than 70% of the smokers in the U. S. have made at least one prior quit attempt, and approximately 46% try to quit each year

(USDHHS, 2000). Unfortunately, most of these efforts are unsuccessful; among the 17 million adults who attempted cessation in 1991, only about 7% were still abstinent 1 year later (Hatziandreu et al., 1990; Fiore & Baker, 1995). Most smokers are aware of the health consequences of smoking and want to quit but have difficulty doing so (McGinnis, & Foege, 1993). While only 3-5 % of smokers who try to quit on their own are successful, long term success rates following behavioral modification therapy, remain low and only about 15-30 % smokers remain abstinent one year after therapy (Lando, Hatsukami, McBride, Pirie, & Hellerstedt, 1991).

Tobacco is a product processed from the fresh leaves of plants in genus *Nicotiana*. There are more than 4,000 chemicals found in the smoke of tobacco products. All tobacco products contain substantial amounts of nicotine and other alkaloids. Chemicals which alter behavioral and physiological activities are delivered to tobacco users when they smoke a cigarette or use other tobacco products. Whether these chemicals are absorbed in significant quantities and whether such absorption is related to the behavior of the user and are critical issues in understanding their role in addictive tobacco use. Of these chemicals, nicotine, first identified in the early 1800s, is the primary reinforcing component of tobacco that acts on the brain. It is an established fact that nicotine is the active pharmacologic agent that causes addictive smoking behavior.

The mental and physical state of the smoker, and the situation in which smoking occurs, can influence the way in which a particular cigarette will affect psychological perceptions (USDHHS, 1998). By inhaling tobacco smoke, an average smoker takes in 1 to 2 mg of nicotine per cigarette (Federal Trade Commission, 2000). There is considerable evidence that smokers adjust their smoking behavior to try to regulate or

maintain a particular level of nicotine in the body (Gritz, 1980; Russell, 1976). Nicotine is a powerful pharmacologic agent that acts in the brain and throughout the body. Actions include electrocortical activation, skeletal muscle relaxation, and cardiovascular and endocrine effects.

2.5. Pharmacokinetics of Nicotine

When tobacco is smoked, nicotine rapidly reaches peak levels in the bloodstream and enters the brain. Nicotine readily crosses the blood-brain barrier and accumulates in the brain shortly after it enters the body. Nicotine acts on specific binding sites or receptors throughout the nervous system. Nicotine exerts diverse pharmacologic effects in both the peripheral nervous system and central nervous system. Once in the brain, it interacts with specific receptors and alters brain energy metabolism in depending on the distribution of specific binding sites for the drug. Immediately after exposure to nicotine, there is a stimulation of the adrenal glands which results in discharge of adrenaline. The rush of adrenaline stimulates the body and causes a sudden release of glucose, as well as an increase in blood pressure, respiration, and heart rate (Benowitz, 1996a). Nicotine is absorbed readily from tobacco smoke in the lungs and from smokeless tobacco in the mouth or nose. With regular use, levels of nicotine accumulate in the body during the day and persist overnight. Thus, daily tobacco users are exposed to the effects of nicotine for 24 hours each day.

Nicotine that enters the blood is rapidly distributed to the brain. As a result, effects of nicotine on the central nervous system occur rapidly after a puff of cigarette smoke or after absorption of nicotine. Nicotine is extensively metabolized, primarily in

the liver, but also to a small extent in the lung. The primary metabolite of nicotine is cotinine. In cigarette smokers, cotinine has a half-life averaging 18 to 20 hr (Benowitz, Kuyt, Jacob, Jones, & Osman, 1983). Cotinine is present in the blood of smokers in much higher concentrations than nicotine. Cotinine blood levels average about 250 to 300 ng/mL in groups of cigarette smokers (Benowitz et al., 1983; Haley, Axelrad, & Tilton, 1983). Nicotine is excreted by glomerular filtration and tubular secretion within the kidney.

2.6. Nicotine Tolerance and Dependence

An issue of immense importance while dealing with nicotine is development of tolerance. Tolerance refers to decreasing responsiveness to a drug so that larger doses are required to produce the same magnitude of effect. When a smoker is subsequently exposed to repeated nicotine exposure, adaptation develops to many of the effects of nicotine. People who have not smoked before usually experience a number of uncommon effects after smoking a cigarette. Smokers indicate that initial exposure to tobacco smoke produces dizziness, nausea, vomiting, headaches, and dysphoria, effects that disappear with continued smoking which are rarely reported by chronic smokers (Russell, 1976; Gritz, 1980); however adaptation develops to many of these effects after repeated drug exposure.

In the past, drug dependence was equated with tolerance and withdrawal (Kalant, 1987) and tolerance or withdrawal was necessary for diagnosis of dependence under Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV; American Psychiatric Association [APA], 1987; Carroll, Rounsaville, & Bryant, 1994). Though tolerance is no longer necessary for such a diagnosis, it is still included in DSM-IV as

one of the criteria for drug dependence (APA, 1994) highlighting the continued importance of tolerance in clinical assessment of dependence. The concern in this study here is chronic tolerance rather than acute tolerance, because of the greater likelihood of chronic tolerance being associated with long-term dependence.

Development of tolerance requires agonistic binding with the nicotinic receptor which causes rapid reversible receptor desensitization within minutes. Intake of nicotine in dependent smokers may produce inactivation of receptors, which could lead to chronic tolerance. Chronic tolerance is developed when response to nicotine in the absence of preexisting nicotine in the blood is less following past exposure to nicotine than absence of past exposure. Nicotine tolerance is believed to reflect a decrease in the function, or sensitivity, of nicotine receptors (Marks, Grady, & Collins, 1993; McCallum et al., 1999). Chronic tolerance is thought to play a critical role in the onset and maintenance of tobacco dependence. The underlying principle why chronic tolerance is considered essential for dependence is that tolerance leads smokers to smoke more intensely and more frequently to maintain the same pleasure from nicotine. Greater intensity of smoking leads to onset of withdrawal symptoms during initial phases of abstinence, an index of dependence, which in turn promotes further smoking to relieve withdrawal. Therefore, chronic tolerance to any drug of abuse traditionally is critical to understanding drug dependence.

Nicotine dependence is the physical vulnerability of the body to the chemical nicotine, which is potently addicting when delivered from various tobacco-containing sources. Nicotine produces physical and mood-altering effects in the brain that are temporarily pleasing; these effects reinforce continued use of tobacco and nicotine

dependence. Nicotine causes physical dependence characterized by a withdrawal syndrome that is accompanied by nicotine abstinence. The sequence of nicotine abstinence includes a range of responses. For example, some symptoms are opposite form those produced when nicotine is given and which subside within a few days or weeks of nicotine abstinence; such responses are presumed to reflect a physiological rebound occurring in the absence of chronic drug exposure. Other responses are also opposite to those produced by nicotine administration but appear to primarily reflect the removal of nicotine exposure, and which may occur whether or not sufficient nicotine had been taken to produce physical dependence (USDHHS, 1988). In brief, the essential feature of nicotine dependence is a cluster of cognitive, behavioral and physiological symptoms indicating that the individual continues the use of nicotine despite significant related problems.

2.7. Determining Nicotine Dependence

The criteria for drug dependence, described in the 1988 Surgeon General's report on smoking and health (USDHHS 1988), include highly controlled or compulsive use of a drug, the use of a drug that produces psychoactive effects, and evidence that drug-taking behavior is reinforced by the effects of the drug. Addictive behaviors of dependence include stereotypic patterns of use, use despite harmful effects, relapse following abstinence and recurrent drug cravings. The World Health Organization describes drug dependence as "a behavioral pattern in which the use of a given psychoactive drug is given a sharply higher priority over other behaviors which once had a significantly higher value" (Edwards, Arif, & Hodgson, 1982).

Methods to determine nicotine dependence can be divided into various types: (1) general definition of substance dependence (APA, 2000), (2) Fagerström tests (Fagerström & Schneider, 1989; Heatherton, Kozlowski, Frecker, & Fagerström, 1991) and (3) consumption (Etzel, 1990; Heatherton, Kozlowski, Frecker, Rickert, & Robinson, 1989; USDHHS, 1988). The general definitions require fulfilling a minimum number of criteria. The most widely accepted definition is that of the APA's DSM criteria (APA, 2000). The latest DSM-IV criteria includes tolerance, withdrawal, unsuccessful attempts to stop, use in larger or longer amounts, giving up activities to use, spending a great deal of time acquiring, using or recovering from drug use, and use despite harm (APA, 2000).

The original Fagerström test, the Fagerström Tolerance Questionnaire (FTQ) (Fagerström & Schneider, 1989) consisted of consumption questions such as number of cigarettes per day (CPD) assuming that higher frequency of smoking was related to dependence, brand of cigarettes used (assuming more dependence was related to the brand with higher nicotine content), and depth of inhalation (assuming higher availability of nicotine was related to dependence). Two of the items were related to difficulty in restrictions such as refraining from smoking in forbidden places (frequent urges overcoming external restriction being related to physical dependence) and smoking when ill, reflecting signs of dependence. The other items emphasized on time of smoking and smoking earlier during the day, all of which, depict higher dependence. The FTND is a shortened version of the FTQ that excludes nicotine yield and inhalation items (Heatherton et al., 1989). Since time to first cigarette (TFC) is the most helpful item on the FTQ/FTND, it has been used as a dependence index itself (Kozlowski, Porter,

Orleans, Pope, & Heatherton, 1994). Finally, a Heavy Smoking Index (HSI) has been composed using both TFC and CPD (Heatherton et al., 1989).

The most commonly used consumption measure for assessing dependence has been CPD. The major advantage of CPD is that it is easy to measure. However, it weakly predicts withdrawal and compensation (USDHHS, 1988). The major liabilities of CPD are digit bias in its measurement (Klesges, Debon, & Ray, 1995; Patrick et al., 1994). Another consumption measure is cotinine which is a metabolite of nicotine (Etzel, 1990). Cotinine is a good measure of nicotine intake but is a weak predictor of difficulty in quitting. In some studies, it predicts response to dependence-based treatments (USDHHS, 1988). The major advantage of cotinine is that it is an objective measure. Its major liability is that it requires a biological specimen and is costly to obtain. Although TFC and HSI were previously discussed as variants of Fagerström criteria because their items are measures of how many and when cigarettes are used, they could also be considered consumption-based measures.

2.8. Treating Nicotine Dependence

Although smoking-related diseases are of major public health importance, nicotine dependence should be viewed as the primary problem and smoking-related diseases as consequences of nicotine dependence.

Most smokers are aware of the health consequences of smoking and want to quit but have difficulty doing so (McGinnis & Foege, 1993). It is evident that smoking is maintained by both pharmacologic and psychological determinants. The relative contributions of these determinants are inseparable and are likely to vary among individual smokers. While only 3-5% of smokers who try to quit on their own are

successful, long term success rates following behavioral modification therapy, remain low and only about 15-30 % smokers remain abstinent one year after therapy (Lando et al., 1991). Pharmacotherapy for drugs-of-abuse is generally used to minimize withdrawal, or to attenuate the reinforcing effects of nicotine. Currently available pharmacological aids for tobacco dependence include nicotine replacement therapy (NRT) such as nicotine gum, transdermal patch, inhaler, intranasal sprays and psychotropic drugs. The NRT agents deliver nicotine to prevent symptoms of physiologic withdrawal, which might result from abrupt cessation of nicotine use.

Several non-nicotine compounds have been tested for their efficacy in smoking cessation, but only two compounds have been approved by the FDA, bupropion and varenicline. Buproprion is a relatively weak inhibitor of the neuronal uptake of norepinephrine and dopamine, and does not inhibit monoamine oxidase or the re-uptake of serotonin. It is chemically unrelated to nicotine or other currently used agents and is effective in increasing the rate of smoking cessation (Hurt et al., 1997). Varenicline is a partial agonist, which has specificity for the alpha-4 beta-2 nicotinic acetylcholine receptor. It is safe and well-tolerated as a smoking cessation pharmacotherapy and in a heads up comparison was found to be more efficacious than placebo and bupropion sustained release (Jorenby et al., 2006; Gonzales et al., 2006). Since the vast majority of those who attempt to quit fail, treatments that assist smokers to achieve initial cessation and to maintain long-term abstinence is significant and urgent.

2.9. Assessment of Nicotine Dependence

Measurement of absorption of nicotine from tobacco products provides a means of quantification of consumption. Different measures vary in sensitivity, specificity, and

difficulty of analysis. Biochemical measures include assays of nicotine or its principle metabolite, cotinine (in plasma, saliva, or urine), thiocyanate (in plasma or saliva), and CO (in expired air) and carboxyhemoglobin concentrations. The average half life of cotinine in different body fluids in adults is approximately 20 hours, making it a useful indicator of the exposure to nicotine over the previous two to three days (Benowitz, 1996b).

CO measurement is an easy, useful and inexpensive method for obtaining objective data from smokers. A definite indication of smoking is found at 11 and more ppm CO; CO levels between 6 and 10 ppm may indicate light smoking, and definite non-smokers show up CO between 0 and 5 ppm. Individuals with CO values of 11–21 ppm are termed mild smokers, whereas those with CO values of more than 21 ppm are defined as heavy smokers (Groman, Bernhard, Blauensteiner, & Kunze, 1999). Biological markers provide more accurate information and are less susceptible to bias compared to self reporting of smoking status. Moreover, same level of exposure to nicotine could result in different level of availability of nicotine in the body depending on inhalation and absorption. Thus it is imperative to measure the level in the body to assess the usage of nicotine by an individual. Despite these advantages, biochemical measures are not the perfect measures to validate dependence. Cotinine level can be elevated in people who chew tobacco, people who are exposed to secondhand tobacco smoke or are involved in production and handling of tobacco (CDC, 2005a).

Self-report measures congregate information from various facets of smoking. This may reflect the possible influences for dependence on smoking behavior. The questions are non-invasive and offer confidentiality. On the other hand, self-reported method could

be unreliable since smokers tend to overestimate or underestimate their smoking habits, which may not be accurate. Self reporting can be unreliable if the subject is under social, environmental or medical pressure. Furthermore, the quantity of smoke products actually inhaled and absorbed varies by the manner of smoking. Because of these difficulties, increased emphasis has been placed on measuring exposure through the use of biological markers to provide more accurate estimates of smoking status.

However, a meta-analysis (Patrick et al., 1994) studied the accuracy of self reported smoking, with biochemical assessment as the concordance measure for evaluating its validity. For the purpose of the study bibliographic searches were conducted on all articles published between 1982 and 1991. Thirty studies containing comparisons between self-reported smoking and biochemical assessments were identified. The study concluded that self-reports of smoking were accurate in most of the cases with sensitivity of 87% and specificity of 89%.

2.10. Review of Fagerström Tolerance Questionnaire

A self-report measure for smoking that has received considerable acceptance by researchers in population studies is the FTQ (Fagerström, 1978). FTQ is an eight-item measure which was designed to assess facets of smoking behavior such as estimate and type of intake of nicotine, difficulty from restraining and other aspects of smoking.

2.10.1. Time to the first cigarette

Time to the first cigarette of the day has been studied extensively as a measure of nicotine dependence (Heatherton et al., 1989, Hughes et al., 2004; Kozlowski, et al., 1994). Some authors (Fagerström, 2003) have even suggested that time to first cigarette

may be the best single measure of nicotine dependence. The estimated half-life for nicotine in the blood is two hours. Due to the relatively short half-life of nicotine, dependent smokers have depleted plasma levels of nicotine upon arising. These smokers are likely to experience discomfort unless they quickly have their first cigarette. Existing evidence suggests that individuals who experience less light-headedness in response to the initial cigarette of the morning are generally heavier smokers with a longer smoking history (Pillitteri, Kozlowski, Sweeney, & Heatherton, 1997). Time to first cigarette has been found to be an excellent predictor of biochemical measures such as cotinine, nicotine and CO (Heatherton et al., 1989).

2.10.2. Number of cigarettes smoked

The most commonly used consumption measure of nicotine has been number of cigarettes smoked per day. The major advantage of this method is that it is easy to measure. The number of cigarettes smoked per day is a face valid measure of dependence on nicotine (Heatherton et al., 1991), and early studies assumed that dependence was a direct function of smoking rate (Brantmark, Ohlin & Westling, 1973). CPD has been shown to relate to exposure to tobacco constituents (Kozlowski & Herling, 1988; Hill, Haley, & Wynder, 1983).

The FTQ used three categories for cigarettes smoked per day 1-15, 16-25, and 26+; this distinction was inconvenient to use because there are usually 20 cigarettes in a pack and it is easy to self report smoking based on a pack for smokers. Moreover, Kozlowski, Heatherton and Ferrence (1989) found that, in spite of small differences in smoking rate between the groups, individuals who report smoking a package of 25 cigarettes per day have significantly higher CO levels than those who report smoking a

package of 20 cigarettes per day. The FTQ categorization may therefore obscure differences between those who report smoking 20 cigarettes per day and those who report smoking 25 cigarettes per day.

2.10.3. Nicotine yield

Literature indicates that as nicotine yield increases, the number of cigarettes smoked per day tends to decrease (Russell, 1979). All cigarettes can be subject to compensatory smoking i.e. more intensive smoking to compensate for reduced standard tar and nicotine yields (Rickert & Robinson, 1981; Fagerström, 1982). When cigarettes with higher nicotine yield are smoked, there are decreases in measures such as puffs per cigarette, puff duration and puff volume, number of cigarettes, and expired air CO; and increases in interpuff and intercigarette interval (Herning, Jones, Bachman, & Mines, 1981; Gust, & Pickens, 1982; McBride, Gijyatt, Kirkham, & Cumming, 1984). These changes in smoking are consistent with the interpretation that intensity of smoking is inversely related to nicotine dose, indicating that compensatory changes in smoking could be affected by nicotine itself. However, this may not be an easily quantifiable factor as some smokers may be unsure of nicotine yield, especially because manufacturers do not publicize yield rate on packages.

2.10.4. Inhalation

Although the process of smoking a cigarette may appear to be a simple behavior, it actually involves a complex series of events. Even the act of taking a single puff is complex. Typically, a smoker puffs a volume of smoke into the mouth, where it is held for a short period of time (Guillerm, & Radziszewski 1978; Medici, Unger, & Ruegger 1985). The puff itself can occur at any point during inhalation, although most commonly

it occurs toward the beginning of an inhalation (McBride et al., 1994; Guillerm, & Radziszewski, 1978). During inhalation, the puff is diluted with ambient air which may be inhaled through the nose, the mouth, or both (Rodenstein & Stanescu, 1985; McBride et al., 1984). The post-puff inhalation is generally longer and larger in volume than normal inspirations. After a variable period of breath holding, the smoker exhales, usually through the mouth (Rodenstein & Stdnescu, 1985). All of the above-mentioned behavioral factors can alter nicotine absorption.

The FTQ has three levels for inhalation, “not inhale”, “inhale sometimes” and “always inhale”. This item has been criticized on the grounds that it may not discriminate degrees of dependency. In general, smokers are able to report accurately whether they inhale or not (Herling, & Kozlowski, 1988), although it does not seem that smokers are accurate in estimating the depth of their inhalations (Stepney, 1982). The remaining FTQ questions are derived from theoretical concepts about the behavior of highly dependent smokers. These items have received the least empirical attention, and their concurrent validity is largely unknown.

Initially FTQ scores were found to be significantly correlated to increase in heart rate during smoking and changing in body temperature after smoking cessation (Fagerström, 1978). In a study (Pomerleau, Pomerleau, Majchrzak, Kloska, & Malakuti, 1990) FTQ scores were found to be correlated with continine levels in samples of subjects reporting for experimental sessions and subjects entering a smoking cessation clinic program. Several of the individual items proved to have statistically significant value.

Application of the FTQ proved to be unconvincing because of perceived psychometric deficiencies, including low levels of reliability and poor item selection (Heatherton et al., 1989; Lombardo, Hughes, & Fross, 1988; Pomerleau, Majchrezak, & Pomerleau, 1989; Pomerleau et al., 1990). Lichtenstein and Mermelstein (1986) found that the FTQ has low internal consistency with alpha coefficient 0.55 for one sample, and 0.51 for the other.

2.11. Introduction to FTND

To address some of the psychometric weaknesses of FTQ, Heatherton et al., (1991) proposed a 6-item revision and renamed the scale FTND. Primary modification of the scale included the elimination of two items, nicotine content of cigarettes and frequency of inhalation, and expanded the scoring format for two items, time to first cigarette and number of cigarettes smoked per day. Although the other items did not add appreciably to the prediction of biochemical levels, they may relate to the behavioral issue of smoking cessation (Heatherton et al., 1991). The behavioral measures such as having difficulty refraining from smoking in forbidden places or smoking when ill may provide insight for smokers.

2.11.1. Reliability and Validity of FTND

A valid measure of dependence on nicotine is essential for determining the extent of dependence for effective treatment. Using a non-clinical sample of smokers Heatherton et al. (1991), reported that FTND corrected some of the psychometric and conceptual problems of the FTQ. The result from the study showed improved internal consistency for FTND and coefficient alpha for the FTND was computed to be 0.61

compared to 0.48 of the FTQ. This was a substantial improvement considering that fewer items usually lead to lower reliability.

In another study, Pomerleau et al. (1994) found that internal consistency for the FTND was somewhat higher than that for the FTQ, replicating previous findings of Hetherton et al. (1991). Payne, Smith, Mccracken, McSherry and Antony (1994) examined the psychometric properties of FTND in a sample of smokers seeking treatment. FTND had higher internal consistency than FTQ and yielded factors that accounted for a greater percentage of item variance relative to the 2-factor solution for FTQ. FTND has demonstrated reasonable reliability and validity when used in cross-sectional or prospective studies. Results from a study that retrospectively assessed FTND scale scores showed to have acceptable reliability (Hudmon, Pomerleau, Brigham, Javitz & Swan, 2005).

Not only has the reliability and validity of the FTND been tested in regular smokers, but it has also been examined in varieties of sample population with concomitant medical conditions. The results of a study done by Buckley et al. (2005) revealed that the FTND had good test–retest reliability, convergent validity, and discriminant validity in a population of smokers with psychiatric conditions.

The FTND has also been tested in several other languages. Etter, Duc, and Perneger (1999) studied the French version of the FTND in a population of relatively light smokers and Dijkstra, Bakker, and Vries (1997) studied the Dutch version. Both the French language translation and the Dutch version had level of internal consistency with alpha values of 0.70 and 0.71 respectively. Likewise, Vink, Willemsen, Beem, and Boomsma (2005) studied the scale in a sample of Dutch smokers and ex-smokers. The

internal consistency of FTND in the study was found to be reasonably high with Cronbach's alpha of 0.65 for male smokers, 0.69 for female smokers, 0.66 for male ex-smokers and 0.71 for female smokers.

The major advantages of the Fagerström tests are that they are easy-to-obtain self-report measures and have been shown to have predictive validity in many tests (Fagerström & Schneider, 1989; Kozlowski et al., 1994; Pomerleau et al., 1989). Their major liability is their poor psychometric features and the fact that much of their validity may depend on their measures of consumption (Etter et al., 1999). Nevertheless, it is one of the most frequently used self-report scales to measure nicotine dependence.

CHAPTER III- METHODS

3.1. Study Overview

This study was a secondary analysis of data collected during a clinical trial, which was a multi center, randomized, parallel group, comparative trial to evaluate the efficacy of Nicotine Hydrogen Tartrate Gum (4 mg) and a Coated Nicotine Polacrilex Gum (4 mg) versus Uncoated Nicotine Polacrilex Gum (4 mg) on the speed to subjectively meaningful relief of acute craving in adult smokers. The primary objective of the trial was to measure each experimental gum versus Nicorette® with respect to the time required for participants to attain subjectively "meaningful" relief from acute craving, following a smoking cue intended to provoke craving. The secondary objective of the trial was to compare experimental gum versus 4mg Nicorette® with respect to time required to attain subjectively complete craving relief, reduction in subjectively-rated craving intensity and product acceptability and liking.

The completion of the clinical trial required two visits to the study site. The second visit (Visit 2) had to be within seven days of the first visit (Visit 1) based on the protocol of the trial. The first visit to the center was a screening visit during which all the screening procedures were completed. The second visit was the trial period which consisted of an orientation session, a treatment session and a post-treatment interview.

The study was a multi center study in which three investigational research centers participated, for a total enrollment of approximately 657 subjects. For the purpose of this study, data collected from only one of the centers (University of Maryland, College Park) was taken into consideration. The information collected only during the first visit was

utilized. The study variables included FTND scale scores (Appendix I, demographics, smoking history (Appendix II), and exhaled CO. A brief summary of the clinical trial procedures are as follows.

3.2 Clinical Trial Study Procedures

3.2.1 Screening period

Screening procedures during Visit 1 consisted of documenting demographics, medical histories, obtaining pregnancy tests, and assessing eligibility based on the trial protocol. At Visit 1, the following procedures were performed for each participant:

- Obtained signed and dated Informed Consent from each participant who expressed an interest in the study and who followed through all the prescreening procedures
- Obtained expired air CO level, using a calibrated Bedfont CO measurement device
- Assessed smoking dependence, using the FTND
- Assessed smoking history (self-reported):
  - How many attempts have you made to quit smoking that lasted at least 24 hours?
  - How long ago was the last one?
  - Have you ever used any of these medications to help you quit smoking?

Nicotine gum, Nicotine nasal spray, Nicotine Patch, Nicotine Inhaler, Nicotine Lozenge or Bupropion

- Obtained medical and medication history, including relevant preexisting conditions, and whether they were continuing
- Obtained demographics which included age, sex, and race.
- Performed pregnancy tests (if applicable)

• Verified conformance with inclusion /exclusion criteria (Discussed in 3.3.2.)

Subjects who fulfilled all necessary criteria for trial participation were assigned eight-digit unique subject identification (ID) numbers. The subject ID began with the four digit site code (1004), followed by four digit sequential subject codes, ascending from 1001. Appointments were made for eligible subjects to return for Visit 2 within 7 days of Visit 1. Participants were required to abstain from smoking or using any other tobacco or nicotine product overnight before their scheduled appointment. They were also asked to abstain from alcohol for 24 hours, and caffeine or food for 1 hour prior to Visit 2.

3.2.2 Trial period

Visit 2 was scheduled for 1.5 hours, beginning at approximately 7:30, 9:00 or 10:30 am. The hour and a half total time included an orientation session, followed by a treatment session.

3.2.2.1. Orientation Session

The following procedures were conducted during the orientation session:

• Expired air CO was measured. Subjects who admitted not being abstinent overnight, or who had a CO ≥ 10 ppm were discontinued from the study, based on protocol deviation.

• Inclusion / Exclusion criteria was reviewed

• Concomitant medications were recorded (non-exclusionary)

• Each subject was supplied with an assessment binder and instructions were reviewed by the study staff for completing them.

3.2.2.2. Treatment Session

During the treatment sessions, participants were seated in a comfortable chair in a well-lit, temperature-controlled, air-purified, sound-attenuated room. One piece of their assigned gum type (A, B or C, according to the randomization list) was brought into the room in a medicine cup by a staff member. Before leaving the room, the staff person turned on an audio CD with all the instructions to be followed by the participant for the completion of the treatment session. The participants followed all the instructions as per the audio CD and completed the treatment session (For details, see Appendix III). All of the activities in the room were watched on closed circuit video which was monitored by a study staff in another room.

3.2.2.3. Post-Treatment Interview

A study staff went to the room and performed the post-treatment interview with each participant as the last procedure of Visit 2. Adverse events experienced during the process of chewing the gum were recorded and subjects were asked to rate the taste, consistency, and flavor of the provided gum, on a scale with the following range: "Excellent, Very Good, Good, Fair, Poor, Very Poor, or Terrible". Subjects also defined what "meaningful relief" meant to them during this trial and they were remunerated for their participation. The study staff then reviewed the FTND scale with each participant and explained the total FTND score and the level of dependence as explained in section 3.5.1. These procedures were personalized for each participant during the session.

3.3. Study Methods

3.3.1. Participant recruitment

Participants at University of Maryland, College Park site were recruited via print advertisements in a local newspaper. Participants who responded to the advertisements were pre-screened on the phone where they were given information about the study. The phone screener asked respondents about their medical and smoking history, medical and psychiatric conditions, and concomitant medications. If this prescreening indicated that the caller was eligible for the screening phase, an appointment was made within thirty days of the telephone interview for the in-clinic screening visit.

3.3.2. Enrollment

The eligibility criteria were designed to select subjects for whom protocol treatment was considered appropriate. All relevant medical and non-medical conditions were taken into consideration when deciding whether this protocol was suitable for a particular subject. Subjects that met all of the inclusion criteria were eligible for enrollment into the trial.

3.3.2.1. Inclusion Criteria

- Male or female, at least 18 years of age
- Smoked daily for at least three years
- Smoked the first cigarette of the day within 30 minutes of waking
- Had the ability to chew gum
- Had a baseline CO level greater than 10 ppm at Visit 1
- Able to read and understand English

• Signed and dated the trial's informed consent document, indicating that the subject had been informed of all pertinent aspects of the trial.

• Willing and able to comply with scheduled visits, treatment plans, laboratory tests, and other trial procedures

• Willing to abstain from smoking and from any other nicotine or tobacco use overnight prior to the testing period

• Female subject of childbearing potential using a medically acceptable method of birth control for at least 1 month prior to Visit 1, i.e., oral contraceptives, intrauterine device, Norplant®, Depo-Provera®, or double-barrier and had a negative urine pregnancy test at Visit 1.

3.3.2 2. Exclusion Criteria

Subjects who presented with any of the following were not included in the trial:

• Trying to quit smoking and/or had had undergone other treatments for smoking cessation within 30 days of study entry, such as counseling, acupuncture, or herbals.

• Had quit smoking or had attempted to quit smoking within 30 days prior to enrollment

• Had used any form of tobacco other than cigarettes such as cigars, pipes, smokeless tobacco, or snuff within 30 days of study entry

• Had used any form of nicotine replacement therapy such as nicotine gum, nicotine patch, nicotine lozenge, nicotine inhaler, or nicotine nasal spray within 30 days of study entry

• Has a known or suspected hypersensitivity to nicotine gum

• Had a dental or other condition (e.g., temporomandibular joint) that precluded the use of nicotine gum

• Was female and was pregnant or lactating, or had plans to become pregnant within 1 month

• Had heart disease, an irregular heartbeat or a heart attack within the past 3 months

• Had uncontrolled high blood pressure

• Had stomach ulcer

• Had insulin dependent diabetics

• Was enrolled in another clinical study at the time of the study

• Had a problem with drug or alcohol abuse within the previous three months

• Had any severe acute or chronic medical or psychiatric condition that could increase the risk associated with trial participation or investigational product administration, or could interfere with the interpretation of trial results and, in the judgment of the investigator, made the subject inappropriate for entry into this trial.

• Had used excluded medications, which had the potential to modify craving and intensity levels within 30 days of Visit 1 including:

−All illicit "street" drugs, or prescription medications not prescribed for the subject

−Bupropion (Wellbutrin, Zyban), nortriptyline, or clonidine, taken for any condition

−Any investigational drug

• Participant was excluded if any of the following had been taken within 14 days of Visit 1:

− Medications commonly prescribed for anxiety, depression or seizures, including (but not limited to) tricyclic antidepressants, MAO inhibitors, Effexor, Prozac, Tegretol, etc.

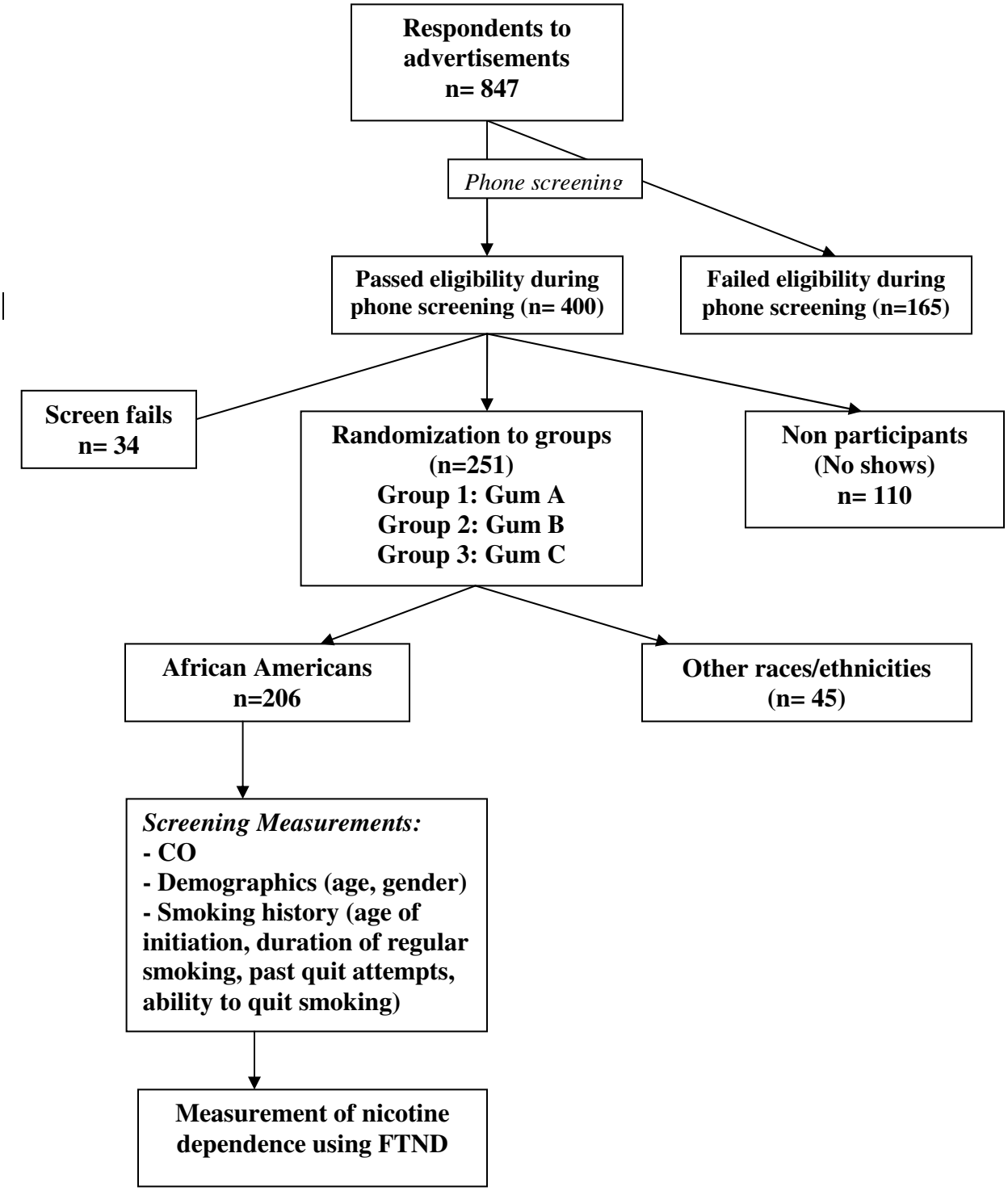
- Pain killers, including methadone, morphine, Tylenol-3 or other codeine-based medications; oxycontin or oxycodone, Endocet, Percocet, etc.
- Special dietary supplements (St. John's Wort, ginkgo biloba)

3.4. Research Design

From the advertisements and word-of mouth, a total of 847 respondents who lived close to the site, called about study participation. After the phone-screening, 400 participants were accepted in the study and 165 were rejected, based on the eligibility criteria. Those accepted were scheduled for their first visit to the center. A total of 110 respondents did not show up for their first visit. A total of 251 subjects were randomized (to one of 3 gum groups) in the study after they met all the eligibility criteria. There were a total of 34 participants who screen-failed, after being randomized in the study for various reasons including medical conditions, exclusionary medications, CO level less than 10, etc. (See Figure 3.1).

Over the course of approximately three months, 251 participants were recruited. Out of the 251 participants, 206 were African Americans. The demographics, smoking history, CO measurement and FTND scores of the African American participants collected during their screening visit as a part of their participation in the clinical trial, was used for the purpose of this study. Therefore, this study was designed as a cross-sectional study to assess levels of nicotine dependence in African American smokers and to study various factors that could be associated with dependence among African American smokers.

Figure 3.1 Overall Research Design of the Study



3.5 Variables

3.5.1. Dependent variable

The dependent variable in the study was the level of nicotine dependence which was derived from the total score of the FTND scale. The FTND scale consists of six questions. In the scale, for each question a score is given which is added to give the total FTND score ranging from 0 to 10. The first question, "How soon after you wake up do you smoke your first cigarette?" has four response options "Within 5 minutes", "6-30 minutes", "31- 60 minutes" and "After 60 minutes"; each option is given a score of 3, 2, 1, and 0 respectively. The second question, "Do you find it difficult to refrain from smoking in places where it is forbidden?" has "yes" and "no" response options, which is scored as 1 and 0 respectively. The third question "Which cigarette do you hate to give up the most?" has two options "the first one in the morning" which is scored as 1 and "any other", which is scored as 2. The forth question, number of cigarettes smoked per day has been categorized as "0-10", "11-20", "21-30", and "31 and more" and is scored as 0, 1, 2, and 3 respectively. The answer to the fifth question "Do you smoke more frequently during the first hours after waking than during the rest of the day?" and the last question "Do you smoke if you are so ill that you are in bed most of the day?" are scored as 1 for "yes" and 0 for "no".

The level of nicotine dependence is derived from the total score of the FTND. In the original scale, levels of dependence based on the total score have been categorized as:

Score	*Level of Dependence*
0-2	Very low dependence
3-4	Low dependence
5	Medium dependence
6-7	High dependence
8-10	Very high dependence

Based on the exploratory nature of the study and small sample size, it was expected that the FTND score was tri-chotomized. The total score of 0 to 4 was categorized as low dependence, 5 as medium dependence, and 6 to 10 as heavy dependence.

3.5.2. Independent Variables

Demographics, SES and smoking history of the smokers were the chief independent variables that were studied. Data collected only from African American smokers (n=206) were analyzed; African Americans of Hispanic ethnicity were excluded to provide a homogeneous sample. Data was drawn from information collected during the screening visit (Visit 1). Demographic variables included age and gender of the participants and SES included education level of the participants. Variables including age first started smoking regularly, number of years of regular smoking, number of quit attempts in the past, and perception of ability to quit smoking were derived from the smoking history. Some of the questions in the smoking history were categorical. The number of times a quit attempt was made for at least 24 hours was categorized as "never", "once", "2 to 5 times", "6 to 10 times" and "more than 10 times". Because of the

small sample size, the categories “6 to 10 times” and “more than 10 times” were combined into one category, “6 or more times”. The variable of perception of ability to quit smoking was categorized as “no”, “yes” and “don’t know”. The category “don’t know” was again combined into the “no” category for analysis because of small sample size.

3.6. Measures and Coding of the Variables

3.6.1. Demographics and SES

Demographic variables included age and gender. Gender included two categories, “male” and “female”. “Male” was coded as 1 and “female” was coded as 2. Similarly, SES variable included education level which was categorized as “less than college” and “college or more”.

3.6.2. Smoking History

Age first started smoking regularly was collected from the self-reported smoking history question, “How old were you when you started smoking regularly?” as number of years. Number of years of regular smoking was obtained by deducting initial age of regular smoking from age of the participant, at the time of the study.

Variable number of quit attempts in the past for at least 24 hours was collected from the smoking history question, “How many attempts have you made to quit smoking that lasted at least 24 hours?”

	Coding of the variable
Never	1
Once	2

2-5 times	3
6 or more -times	4

Perception of ability to quit smoking was collected from the smoking history question, "Could you quit smoking if you wanted to?"

	Coding of the variable
No	0
Yes	1

3.6.3. CO Measurement

To examine the correlation of physiological indicator of smoking and self reported dependence, CO concentrations measured by the Bedfont EC50 MICRO CO monitor (calibrated monthly), was used. During the trial CO was measured on two occasions, at screening visit and at the second visit. For the proposed study, only CO measured during the first visit was considered. The smokers were not informed of the test before the measurement, therefore during the measurement, participants were smoking as usual. Individuals with CO values of 10–21 ppm were termed mild smokers, whereas those with CO values of more than 21 ppm were defined as heavy smokers (Groman, Bernhard, Blauensteiner, & Kunze, 1999) as discussed in Chapter II.

3.7. Analyses

All of the statistical analyses were done using SPSS 14.0. Based on previous research, the hypotheses of the proposed study were unidirectional; therefore, all

statistical tests were one-tailed. The level of significance was fixed at 5 %. The analyses consisted of three steps.

3.7.1. Descriptive Statistics

First, the frequency of participants in terms of their demographic data i.e. age and gender, SES (educational level), and self reported smoking variables were calculated as percentage. Second, the rates of levels of dependence (low, medium and high) were calculated and for each independent variable.

3.7.2. Bivariate Correlation

Hypothesis 6: Higher CO measurement is associated with heavy nicotine dependence.

The Pearson correlation was used to examine the correlation between CO and total FTND score.

3.7.3. Unadjusted analysis

To test study hypotheses, a series of logistic regression models were run. The data was analyzed using 3 different univariate logistic models between dependent variables (low, medium and high dependence) and each independent variable to examine the relationships. Three unique logistic models were used for modeling levels of dependence, low dependence was compared with medium dependence; low dependence was compared with high dependence; medium dependence was compared with high dependence. The unadjusted odds ratios (ORs) and the 95% confidence intervals (CIs) were examined. The univariate logistic regression examined the dependent variable and each of the

independent variables in separate analyses to test the proposed hypotheses, as listed below.

3.7.3.1. Hypothesis Testing

The following analyses were performed to test each of the study hypotheses:

Hypothesis 1 (a): Male African American smokers have heavier nicotine dependence than female African American smokers.

1 (b): Older African American smokers have heavier nicotine dependence than young smokers.

1 (c): African American smokers with low education level have heavier nicotine dependence.

Three unique logistic regression tests were used to test the relationship between gender of the participants and the FTND score in all the three groups, low versus medium, low versus high and medium versus high. Binary logistic regression was used with the categorical dependent variable (FTND score) with three levels and independent variable (gender) with two levels. Similar tests were run with levels of dependence and education level which was a categorical variable with two levels. Likewise, binary logistic regression was used with age (continuous independent variable) and FTND score (categorical dependent variable with three levels) in all the three groups. The unadjusted OR and 95% CI were examined.

Hypothesis 2: People who initiate smoking at an early age are more heavily dependent on nicotine and those who initiate later are associated with lower level of nicotine dependence.

Three unique logistic regression tests were used to test the relationship between age at initiation (continuous independent variable) and FTND score in all the three groups viz. low versus medium, low versus high and medium versus high. Binary logistic regression was used with the categorical dependent variable (FTND score) and independent variable for each group. The unadjusted OR and 95% CI were examined.

Hypothesis 3: Longer period of regular smoking is associated with heavier dependence.

Three unique logistic regression tests were used to test the relationship between number of years of regular smoking (continuous independent variable) and FTND score in all the three groups viz. low versus medium, low versus high and medium versus high. Binary logistic regression was used with the categorical dependent variable (FTND score) and independent variable for each group. The unadjusted OR and 95% CI were examined.

Hypothesis 4: Smokers who have never tried to quit have heavier nicotine dependence.

Three unique logistic regression tests were used to test the relationship between number of attempts to quit smoking (categorical independent variable) and FTND score in all the three groups viz. low versus medium, low versus high and medium versus high. Binary logistic regression was used with the categorical dependent variable (FTND score) and independent variable for each group. The unadjusted OR and 95% CI were examined.

Hypothesis 5: Smokers who have a negative perception of their ability to quit smoking are associated with heavy nicotine dependence.

Three unique logistic regression tests were used to test the relationship between perception of ability to quit smoking (categorical independent variable) and FTND score in all the three groups viz. low versus medium, low versus high and medium versus high. Binary logistic regression was used with the categorical dependent variable (FTND score) and independent variable for each group. The unadjusted OR and 95% CI were examined.

3.7.4. Multivariate Adjusted Analysis

Multivariate logistic regression was conducted to examine the unique combination of factors to identify the most significant variables in explaining nicotine dependence. The original models included statistically significant independent variables ($p<0.05$) from the univariate logistic regression tests. All statistically significant independent variables from univariate logistic regression were included in the multivariate models using a full entry model. Adjusted OR and 95% CI were examined to assess the significance of the relationships.

3.8. Power Calculation

Power calculation for this study was done using G power 3.0.8 version (Faul, 2006). Since literature has not identified the effect size for this type of study, the power of the study was estimated based on a given sample of 206 at $\alpha=.05$ using the effect size conventions (0.02=small; 0.15=medium; 0.30=high).

	Effect size		
	Small (0.02)	Medium (0.15)	High (0.3)
Power	0.3	0.9	0.99

Since the sample size was given (n=206), the present study, assumed a power of 0.3 for a small effect size.

3.9. Ethical Conduct of the Trial

Since the study was conducted across multiple sites, it was the responsibility of the investigator of the respective study site to have prospective approval of the trial protocol, protocol amendments, informed consent forms, advertisements, and other relevant documents from the Institutional Review Board. For this study the approval was obtained from University of Maryland, local Institutional Review Board. The trial was performed in accordance with the protocol, International Conference on Harmonization Good Clinical Practice guidelines, and applicable local regulatory requirements and laws.

3.9.1. Protection of Human Subjects

It was the responsibility of the investigator, the principal investigator at each site to get approval of the experiment protocol, informed consent and other study documents from the Institutional Review Board. The study ensured that each participant or his/her representative was well-informed about the study. To serve this purpose, a study staff did a presentation of the consent form to make sure all the subjects understood the content of the consent form. The participants could have all their questions answered before they signed the informed consent at Visit 1.

The study site obtained and retained signed consent forms from each participant. The informed consent form included the following:

- Purpose of the research

- Inclusion exclusion criteria for eligibility
- Detailed procedure of the study methods
- Potential risks to all study participants and risks to subjects of childbearing potential
- Benefits from the study including financial compensation
- Issues of voluntary participation in the study
- Contact information of the principal investigator, and information about where to seek further information

Each page of the consent form was initialed and dated by the participant and a full signature was also mandatory on the final page. The consent was obtained in English. A copy of the signed consent form was given to each participant.

CHAPTER IV RESULTS

4.1. Sample Characteristics

Table 4.1 shows the characteristics of the sample population. The distribution of African American smokers (n=206) based on gender was male 51% and female 49%. The average age of the participants was 44 years (range 18 to 76 years) at the time of the study. Only 9.7% of the participants had completed college education or more.

Out of the 206 African American smokers, 71.8% (148) were mild smokers and 28.2% (58) were heavy smokers, based on their CO measurement. The average age at initiation of regular smoking, at least one cigarette per day was 17 years (range 8 to 44 years) and the average number of years of regular smoking was 27 years. Of the participants reporting to have attempted to quit smoking in the past, 27.7% (57) reported attempting to quit smoking once, 29.6% (61) 2-5 times, 10.7% (22) 6 times or more and 32% (66) reported never having tried to quit smoking. Similarly, 84% (173) of the participants had a negative perception of their ability to quit smoking even if they wanted to, 16% (33) had a positive perception. The mean score of exhaled CO measurement was 18 with a maximum of 39 and minimum of 10. The distribution of scores in the FTND scale approximated a normal distribution with scores ranging from 2 to 10 (mean= 5.79, SD=1.659; Figure 4.1).

Characteristics of participants based on their levels of nicotine dependence are displayed in Table 4.2. The distribution of gender among the participants was nearly equal in all the levels of dependence i.e. low, medium and high (male=45.7% female=54.3%; male=53.8% female=46.2%; male=52.1% female=47.9% respectively). The average age of participants at the time of the study was nearly equal in all 3 groups;

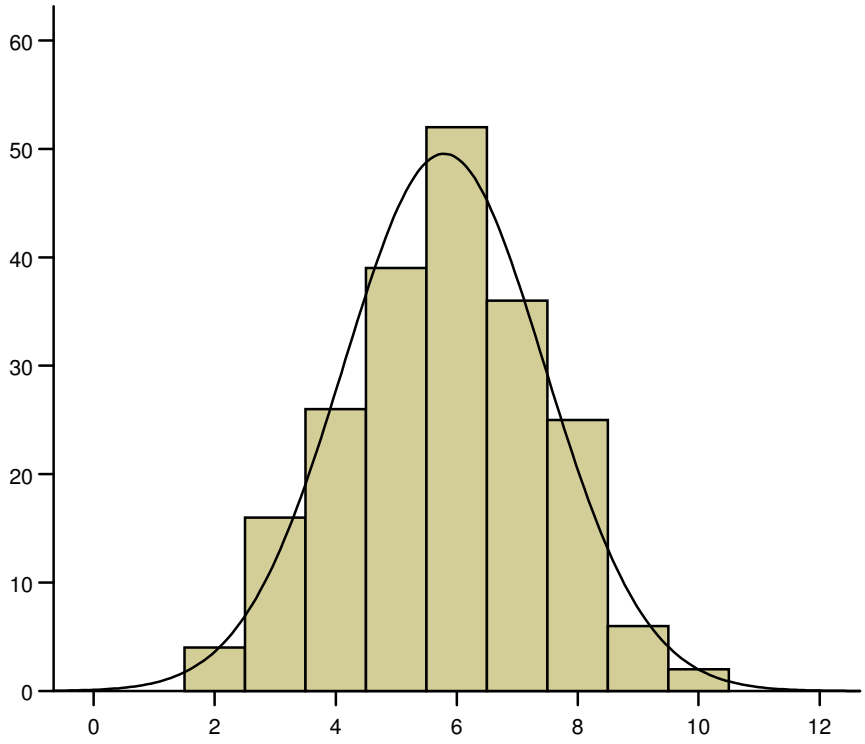
42, 43 and 45 years in low, medium and high dependence groups respectively. The distribution of educational level showed that smokers with education level less than college were likely to have high nicotine dependence than those with college education. Similarly, the average age at initiation of smoking in all the 3 groups was nearly the same; 17, 18 and 17 years in low, medium and high dependence groups respectively. The average number of years of regular smoking among participants was 24 years in participants with low dependence, 26 and 29 years in participants with medium and high dependence respectively.

The percentage of participants who had made attempts to quit smoking in the past 2-5 times were 34.8%, 38.5% and 24.8% in low, medium and high dependence categories respectively; 6 or more times were 8.6%, 12.8% and 10.7% in low, medium and high dependence categories respectively. Similarly, the percentage of participants who had tried to quit smoking once in the past was 26.1%, 20.5% and 30.6% in low, medium and high dependence categories respectively; the percentage of participants who had never tried to quit smoking in the past was 30.4%, 28.2% and 33.9% in low, medium and high dependence categories respectively. The percentage of smokers in the low, medium and high dependence categories who had negative perception of their ability to quit smoking was 69.6%, 84.6% and 89.2% respectively. Similarly, the percentage of smokers in the low, medium and high dependence categories who had positive perception of their ability to quit smoking was 30.4%, 15.4% and 10.7% respectively.

Table 4.1.
Characteristics of sample population based on Demographics, SES, and Smoking Behaviors

	African American Smokers (n=206)
Demographics	
Gender	
Male	51%
Female	49%
Mean Age (years)	44
Education Level	
College or more	9.7% (20)
Less than college	90.3% (186)
Self-reported Smoking Behavior	
Type of smoker	
Mild	71.8% (148)
Heavy	28.2% (58)
Average age at initiation (years)	17
Average years of regular smoking	27
No. of quit attempts	
Never	32% (66)
Once	27.7% (57)
2-5 times	29.6% (61)
6 or more times	10.7% (22)
Ability to quit if wanted to	
No	84% (173)
Yes	16% (33)
Mean FTND score	5.79
Average CO measurement (ppm)	18

Figure 4.1. Distribution of FTND score



FTND score of the participants

Mean =5.79
Std. Dev. =1.659
N =206

Table 4.2.
Prevalence of Level of Nicotine Dependence by Demographics, SES, and Smoking Behaviors among African American Smokers

	Level of Nicotine Dependence		
	Low (n=46)	**Medium (n=39)**	**High (n=121)**
Demographics			
Gender			
Male	21(45.7%)	21(53.8%)	63(52.1%)
Female	25(54.3%)	18(46.2%)	58(47.9%)
Mean Age (years)	42	43	45
Education Level			
Less than College	41 (89.1%)	31 (79.5%)	114 (94.2%)
College or more	5 (10.9%)	8 (20.5%)	7 (5.8%)
Self-reported Smoking Behavior			
Average age at initiation (years)	17	18	17
Average years of regular smoking	24	26	29
No. of quit attempts			
Never	14(30.4%)	11(28.2%)	41(33.9%)
Once	12(26.1%)	8(20.5%)	37(30.6%)
2-5 times	16(34.8%)	15(38.5%)	30(24.8%)
6 or more times	4 (8.6%)	5 (12.8%)	13 (10.7%)
Ability to quit if wanted to			
No	32(69.6%)	33(84.6%)	108(89.2%)
Yes	14(30.4%)	6(15.4%)	13(10.7%)
Mean FTND score	3.48	5.0	6.93
Average CO measurement (ppm)	17.43	17.3	18.5

Table 4.3.
Unadjusted Odds Ratio for Relationships between Levels of Nicotine Dependence and Predictors [a] (Demographics, SES, and Self-reported Smoking Behaviors) among African American Smokers

	Levels of Nicotine Dependence		
Predictors	Low vs Medium Odds Ratio (95% CI) [b]	Low vs High Odds Ratio (95% CI)	Medium vs High Odds Ratio (95% CI)
Demographics			
Gender			
Male	1.389(0.590-3.269)	1.293(0.654-2.555)	0.931(0.452-1.920)
Female	1.00	1.00	1.00
Age	1.016(0.975-1.059)	**1.040(1.004-1.078)***	1.021(0.984-1.060)
Education level			
Less than college	0.473(0.141-1.586)	1.986(.597- 6.6)	**4.203(1.414-12.491)****
College or more	1.00	1.00	1.00
Self-reported Smoking Behavior			
Age at initiation	1.009(.938-1.086)	0.983(0.925-1.044)	0.971(0.909-1.037)
No. of years of regular smoking	1.011(.974-1.049)	**1.038(1.005-1.072)***	1.025(0.990-1.060)
No. of quit attempts			
Never	0.629(0.136-2.914)	.901(0.252-3.223)	1.434(0.420-4.892)
Once	0.533(0.109-2.616)	.949(0.260-3.467)	1.779(0.493-6.421)
2-5 times	0.750(0.169-3.333)	0.577(0.161-2.06)	0.769(0.231-2.562)
6 or more times	1.0	1.0	1.0
Ability to quit if wanted to			
No	2.406(0.823-7.035)	**3.635(1.551-8.519)****	1.510(0.532-4.286)
Yes	1.0	1.0	1.0

*** P<.05; ** P≤.01**
[a] The last category was used as the reference.
[b] CI= Confidence Interval

Table 4.4.
Adjusted Odds Ratio for Relationships between Level of Nicotine Dependence and Predictors [a] (Demographics, SES and Self-reported Smoking Behaviors) among African American Smokers

	Levels of Nicotine Dependence		
Predictors	Low vs Medium Odds Ratio (95% CI)[b]	Low vs High Odds Ratio (95% CI)	Medium vs High Odds Ratio (95% CI)
Demographics			
Gender			
Male	N/S	N/S	N/S
Female	N/S	N/S	N/S
Age	N/S	1.018(0.950-1.091)	N/S
Education level			
Less than college	N/S	N/S	N/S
College or more			
Self-reported Smoking Behavior			
Age at initiation	N/S	N/S	N/S
No. of years of regular smoking	N/S	1.024(0.961-1.091)	N/S
No. of quit attempts	N/S	N/S	N/S
Never			
Once			
2-5 times			
6 or more times			
Ability to quit if wanted to			
No	N/S	**3.760(1.562-9.051) ****	N/S
Yes		1.0	

**** P<.01.**
[a] The last category was used as the reference.
[b] CI= Confidence Interval

4.2. Univariate Analysis

Table 4.3 shows the unadjusted odds ratio for relationships between demographic factors (age and gender), SES (education level), self-reported smoking behaviors and levels of nicotine dependence.

Hypothesis Testing

Hypothesis 1 (a): Male African American smokers have heavier nicotine dependence than female smokers.

1 (b): Older African American smokers have heavier nicotine dependence than young smokers.

1(c) African American smokers with low education level have heavier nicotine dependence.

Binary logistic regression was used to analyze the relationship between gender of the participants in the 3 levels of dependence. The results revealed that in all the three categories i.e. low versus medium dependence, low versus high dependence and medium versus high dependence, the gender of the participant was not a significant predictor of level of nicotine dependence.

In case of age of the participants at the time of the study, the results revealed that age of the participants was a significant predictor of nicotine dependence in the low versus high dependence category. Older participants were more likely to have high nicotine dependence rather than low dependence (OR= 1.040, 95% CI=1.004-1.078). There was not a significant relationship between age of the participants in the low versus medium or medium versus high dependence category.

The education level of the smokers was found to be a significant predictor in the medium versus high dependence category (OR= 4.203, 95% CI- 1.414-12.491). Smokers with low education level are associated with high dependence rather than medium dependence. No similar relation was found in the low versus medium and low versus high (Table 4.3.).

Hypothesis 2: African Americans who initiate smoking regularly at an early age are more heavily dependent on nicotine than those who initiate later.

Binary logistic regression was used to analyze the relationship between ages of initiation of smoking regularly among the participants in the 3 levels of dependence. The results revealed that in all the three categories i.e. low versus medium dependence, low versus high dependence and medium versus high dependence the initial age of smoking of the participants was not a significant predictor of level of nicotine dependence.

Hypothesis 3: A longer period of regular smoking is associated with heavier dependence among African American smokers.

Binary logistic regression was used to analyze the relationship between the numbers of years of regular smoking of the participants in the 3 levels of dependence. The results revealed that number of years of regular smoking is a significant predictor of nicotine dependence in the low versus high dependence category. Smokers who had smoked regularly for more years were likely to have high nicotine dependence rather than low dependence (OR= 1.038, 95% CI=1.005-1.072). There was not a significant

relationship between number of years of regular smoking of the participants in the low versus medium or medium versus high dependence category (Table 4.3.).

Hypothesis 4: African American smokers who have never tried to quit in the past have heavier nicotine dependence.

Binary logistic regression was used to analyze the relationship between attempts to quit smoking and the levels of dependence. The results revealed that in all the three categories i.e. low versus medium dependence, low versus high dependence and medium versus high dependence number of quit attempts in the past or never having tried to quit smoking was not a significant predictor of levels of nicotine dependence.

Hypothesis 5: African American smokers who have a negative perception of their ability to quit smoking report heavy nicotine dependence.

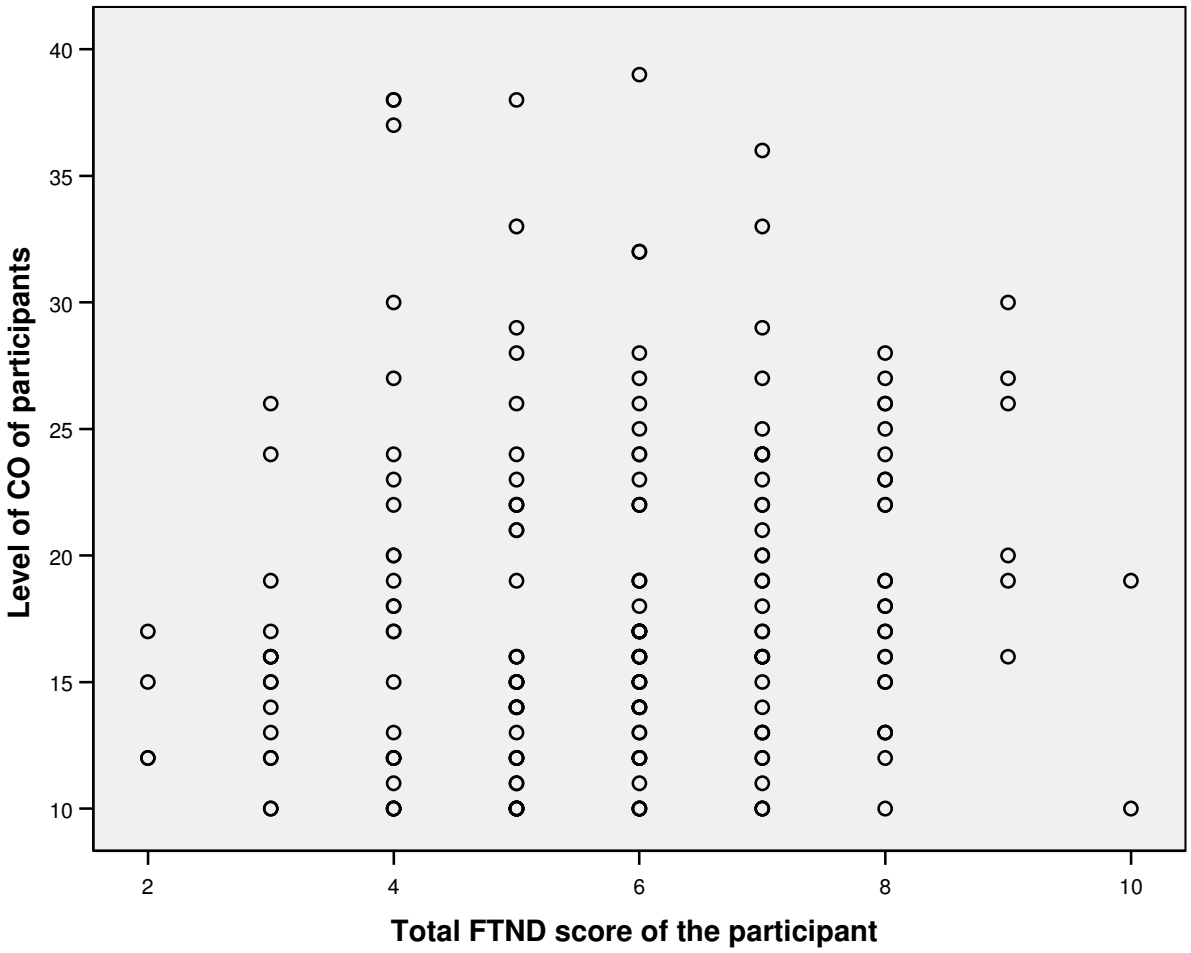
Binary logistic regression was used to analyze the relationship between the perception of ability to quit smoking of the participants and the levels of dependence. The results revealed that the perception of ability to quit smoking is a significant predictor of nicotine dependence in the low versus high dependence category. Smokers who had negative perception to quit smoking were likely to have high nicotine dependence rather than low dependence (OR= 3.635, 95% CI=1.551-8.519) compared to smokers who had a positive perception of ability to quit smoking.

4.3. Bivariate Analysis

Hypothesis- Higher CO measurement is associated with heavy nicotine dependence among African American smokers.

The Pearson correlation of the FTND and the measured CO was $r=0.137$ ($p<0.05$). African American smokers reporting high dependence reported statistically significant high exhaled CO levels. Figure 4.1 shows the plotting of exhaled CO measurement of the participants in the Y axis and the FTND scores in the X axis.

Figure 4.2 Correlations between FTND and CO (r=0.137)



4.4. Multivariate Analysis

A multivariate logistic regression analysis was conducted only in the category of low versus high nicotine dependence. The model included all statistically significant variables from the univariate logistic regression model. African American smokers who reported having negative perception of their ability to quit smoking had greater odds (OR= 3.76, CI: 1.56-9.05) of having high nicotine dependence rather than having low nicotine dependence (Table 4.4).

CHAPTER V- DISCUSSION

5.1. Summary of findings

The study aimed to examine the associations between demographic variables, SES, self-reported smoking behaviors and nicotine dependence among African American smokers. The study also attempted to examine the correlation between a physiological marker of smoking and self-reported levels of nicotine dependence. Results from this study fill in the gap in the literature of factors associated with nicotine dependence among African Americans and expand the existing knowledge of nicotine dependence among African American smokers. This is one of the very few studies that has exclusively attempted to examine nicotine dependence in African American smokers based on self-reported data. The findings of this study have significant implications for the design of interventions for prevention or treatment of nicotine dependence among African Americans.

5.1.1. Prevalence of characteristics based on demographics, SES and smoking behaviors

Descriptive analysis of the study revealed that in all the categories of dependence, the distribution of males and females was almost equal. Moreover, the distribution was highest in the high dependence category in both males and females. It was surprising that the average age of the participants at the time of the study, the average age of initiation of smoking and the number of years of regular smoking was almost the same in all 3 categories of levels of dependence among African American smokers. Most of these variables have been shown to have significant associations with nicotine dependence (Breslau et al., 2001). At first glance, the findings of this study, that these variables were

unrelated to nicotine dependence, might appear to conflict with previous findings; however, previous studies did not estimate the association of the factors with the levels of dependence (low, medium and high) as this study, but rather compared the variables among nicotine dependent and non-dependent smokers. In the ability to quit smoking category, the highest frequency of smokers who had a negative perception in their ability to quit smoking was consistent across all the levels of dependence. The findings of this study supports previous findings on racial differences in smokers' potential for quitting (Giovino, Henningfield, Tomar, Escobedo, & Slade, 1995).

5.1.2. FTND scores

The FTND score distribution demonstrated a Gaussian distribution with a mean of 5.79, which is relatively high compared to FTND means in other studies. There are two possible explanations for the high FTND scores. One of the possible reasons is that the data was collected from a sample of smokers, for whom eligibility to participate in the study did not require any interest in quitting smoking; during the screening process questions were asked to the participants to ensure that they were not undergoing any other nicotine-related modification program or were not making any efforts in trying to cut down on the level of smoking. This was required by the original trial from which data for this study was analyzed. Since the trial was not a smoking cessation study, the eligibility criteria that was included in the newspaper advertisements for the study clearly mentioned that participation in the study did not require the smokers to quit smoking. This sampling issue led to a skewed sample as reflected on the FTND score. The other reason is that one of the entry criteria for participant eligibility was that the

participants had to smoke their first cigarette within 30 minutes after waking up in the morning. This question was asked during the telephone screening as per the original study protocol. Only those smokers, who smoked their first cigarette in the morning within 30 minutes after waking up, were included in the study. On the other hand, the timing of first cigarette is one of the questions of the FTND scale, which measures nicotine dependence. According to the original FTND scale, individuals who smoke the first cigarette within the first 30 minutes get a score of 2 (See Appendix I). Therefore, the smokers who were accepted in the study already had a score of 2 on the FTND scale upon entering the study. This entry criterion inflated the base score of the participants in the FTND scale which could have affected the total FTND score.

5.1.3. Gender and nicotine dependence

As noted, the results of this study showed that gender was not a predictor of levels of nicotine dependence. This result was inconsistent with the results from previous studies (Benowitz, & Hatsukami, 1998), which showed that female smokers are more dependent on nicotine. This result was also not consistent with studies (Fagerström et al., 1996) that showed that male smokers have higher FTND scores which serves as a proxy for higher nicotine dependence compared to female smokers. One of the most accepted explanations for difference in the level of nicotine dependence in women is a faster metabolism of nicotine (18.8 ml/min/g in women versus 15.6 in men) (Benowitz, Lessov-Schlaggar, Swan, & Jacob, 2006). The current study failed to establish any association between gender and the level of nicotine dependence. One of the possible reasons for failing to find the association could be the choice of FTND as a scale to measure nicotine

dependence. Richardson et al. (2007) showed that FTND scale has limitations when it comes to measuring nicotine dependence based on gender. That is, the authors indicated that gender differences in nicotine dependence may undermine the ability of the FTND scale to present an adequate picture of dependence. Another possible reason for failing to demonstrate an association between gender and the levels of dependence could be the small sample size of this study with a small statistical power of 0.3.

5.1.4. Age and nicotine dependence

The results of the study showed that age of smokers was significantly associated with nicotine dependence i.e. older smokers were likely to report heavier dependence than younger smokers. This result supported our hypothesis; however, the same result was not found in the low versus medium and medium versus high groups. This result was consistent with findings of larger population studies (National Survey on Drug Use and Health, 2008; Breslau et al., 2001), although most of the previous studies were not exclusively conducted among African American smokers. Yet, the association of age and nicotine dependence has not been consistent across studies. Vink et al. (2005) did not find a correlation between FTND score and age of smokers. That study was conducted in Europe, in a different population and the present study was conducted in the U.S.; the location of the study could have been an influencing factor (Fagerström et al., 1996). Altogether, the result in this study is significant in the low versus high dependence category; the evidence is limited as the sample population is not sufficiently representative. Future research is required to verify the nicotine dependence level in different age groups across populations.

5.1.4. Education level and nicotine dependence

Previous studies have shown that low education level is related to nicotine dependence (Siahpush**,** McNeill**,** Borland**,** & Fong, 2006). This study reiterated the result that smokers with low education level are more likely to have high dependence. High level of nicotine dependence among smokers of low SES has been associated with financial and psychological stress and social disadvantage (Cohen, & Williamson, 1988). A possible explanation for this is that smokers with low SES experience a more stressful life and smoke more as a method of coping with stress, resulting in higher nicotine dependence. The outcomes suggest that population intervention may be less effective for smokers with low education level, and therefore targeted interventions are necessary for smokers with a lower education level.

5.1.5. Initial age of regular smoking and nicotine dependence

Despite all the evidence that suggested that initial age of regular smoking is linked to nicotine dependence, the present study failed to establish any association between the initial age of regular smoking and level of nicotine dependence. The most likely explanation for this result is possibly the small sample size with small statistical power. Previous studies on the effects of age of initiation of smoking, as opposed to initiation of *regular* smoking (smoking at least one cigarette per day), have largely focused on starting age and likelihood of cessation in different populations (Breslau et al., 1993; Hu et al., 2006; Breslau & Peterson, 1996). Only few studies have examined the associations between nicotine dependence and initial age of *regular* smoking. Studies done on the relationship between age of initial regular smoking and nicotine dependence

have shown that age of initiation of smoking is an essential factor in predicting dependence. Vink et al. (2005) showed that the lower age of initiation of regular smoking is associated with higher FTND score. That study was in line with other studies (Lando et al., 1999; John et al., 2003). Lando et al. (1999) in their findings showed that early age of initiation of smoking predicts more dependent smoking. Most of the above mentioned studies were population studies with large sample population; whereas this study represented clinical trial participants who had to meet several entry criteria to be in the study.

5.1.6. Duration of smoking and nicotine dependence

The results revealed that number of years of smoking was significantly associated with levels of nicotine dependence thus supporting the hypothesis that a long period of smoking could be a predictor of heavy nicotine dependence. However, similar results were not seen in the medium and low dependence groups. This result was consistent with other studies that suggested that higher number of years smoked is associated with a higher FTND score, and high dependence (Vink et al., 2005). One possible explanation of this phenomenon is that nicotine dependence is a result of gradual progression over years through various stages of tobacco use i.e. preparation, experimentation, regular use and ultimately dependence (Loughlin et al., 2003). Moreover, development of dependence requires lengthy and regular tobacco use (USDHHS, 1994). Although the finding of this current study was consistent with the existing literature, future research is needed to explain the relation between levels of dependence in association with years of

smoking; this differential might be essential when determining treatment interventions in population.

5.1.7. Past quit attempts and nicotine dependence

Surprisingly, the result from this study failed to establish any relationship between the levels of nicotine dependence and the number of quit attempts in the past. One of the reasons for the insignificant result in this study could be again, the small sample size, which is a major limitation of this study. Moreover, the question about attempts to quit was categorized into five categories and this reduced the number of smokers in each category. The frequency of smokers in the "6-10 times" and "more than 10 times" was very low and even merging the two categories did not make a significant difference in the results. It is an established fact that nicotine dependence could function as a barrier in making attempts to quit smoking (John et al., 2004). Discomforts experienced by nicotine dependent smokers could play a role in prompting smokers to avoid these symptoms, thereby impeding smoking cessation. There is contrasting evidence suggesting that nicotine dependent smokers make more quit attempts. A study conducted among dependent and non-dependent smokers had shown that nicotine dependent smokers make more quit attempts than nondependent smokers however, they are less successful in staying abstinent than nondependent smokers (John et al., 2004). Every year millions of people around the world quit smoking and although the smoking cessation rates have increased in the past years (CDC, 2005b), the majority of smokers eventually relapse.

5.1.8. Self-efficacy and nicotine dependence

A significant relationship was found between the perceptions of ability to quit smoking, studied as a proxy for self-efficacy, and the level of dependence among low versus high dependence smokers. Previous studies on self efficacy and smoking, for the most part, focused on confidence in ability to quit smoking (Baer & Lichtenstein, 1988). Therefore, it was of interest to study self-efficacy in terms of physical dependence of the smoker to nicotine and to examine if it affects perception of ability to quit smoking. Moreover, the extent to which self efficacy impacts cessation among African American nicotine dependent smokers has not been previously examined. The hypothesis in this study that smokers with negative perception of their ability to quit smoking will report heavy nicotine dependence was based on the assumption that dependent smokers tend to be less interested in quitting and less confident of their ability to quit.

The result of this study asserts the importance of assessment of level of dependence and self efficacy while developing intervention strategies for smoking cessation. Smokers can usually be placed into one of five stages of change according to their intention to quit smoking within specified time periods as described by Stages of Change model (Prochaska & DiClemente, 1983; Prochaska, DiClemente, & Norcross, 1992). Movement through the stages of Pre-contemplation, Contemplation, Preparation, Action and Maintenance involves a recycling process of progression and relapse (Prochaska, Velicer, DiClemente, Guadagnoli, & Rossi, 1990). In one study, stage of change was found to be predictive of quit smoking rates and was negatively associated with nicotine dependence and positively associated with self-efficacy (DiClemente et al., 1991).

Quitting the habit of smoking requires optimistic self-beliefs that can be fostered in the context of smoking cessation programs (Baer & Lichtenstein, 1988). The relationship between self efficacy and nicotine dependence can provide the rationale for the use of stages of change theoretical framework in program development. For instance, smokers with positive perception to quit and low nicotine dependence could be targeted by a program focusing on movement to the Action stage using nicotine replacement as an adjunct to counseling. Those with negative perceptions to quit and high nicotine dependence might be provided counseling on the benefits of quitting and assistance with increasing self-efficacy to quit (Vernon, Crane, Prochaska, Fairclough, & MacKenzie, 1999).

Finally, results from the multivariate analysis after adjusting for the effects of the significant risk factors, revealed that smokers with negative perception of their ability to quit smoking were more likely to report heavy nicotine dependence. As discussed previously, smoking cessation programs should incorporate the aspect of self-efficacy in order to achieve effective outcomes.

5.1.9. CO measurement and FTND scores

The bivariate analysis between the FTND score and CO measurement showed a modestly significant correlation in this study. Based on previous studies, a high correlation was not expected in this study as CO and FTND are less sensitive markers of nicotine intake. The FTND contains a number of items unrelated to nicotine intake (Heatherton et al., 1991) and CO has a short half-life and therefore is unstable. Moreover, the FTND scale and CO are a measure of different phenomena; FTND measures physical

dependence and CO measures exposure to harmful substances. Nevertheless, CO measurement is a biomarker of smoking that is simple and economical to be used in survey studies. It also provides objective data in the assessment of smoking behaviors. Therefore, assessment of nicotine dependence may not require the measurement of CO**.** In addition to the self-reported questionnaire, there is a need for other reliable measures to assess nicotine dependence.

5.2. Limitations of the study

The current study has a number of limitations. The data for this study was collected as a part of a clinical trial that was sponsored by Pfizer. All the procedures of the trial were completed as per the protocol designed by the sponsor. This study was conducted as a secondary analysis of the data collected during the trial. Therefore, there was no opportunity to incorporate all variables that could capture psychosocial aspects of smoking in the questionnaires. Although, the participants filled out questionnaires about demographics and smoking behaviors, some of the important aspects of smoking behaviors such as perceived severity, previous quit attempts and relapses, self efficacy etc. were not captured. Evidently, the questions were not based on any theoretical framework related to health behavior. However, some aspects of behavior change theories such as Stages of Change and Social Cognitive Theory, i.e. self efficacy were available. The inability to systematically explain smoking behavior related-factors that could be associated with nicotine dependence, based on a theoretical framework is a major limitation of this study.

As previously mentioned, only the data collected in the trial during the first or the screening visit was included in this study. The first visit was scheduled during the afternoon at 2 pm, at which time the exhaled CO was measured. Some of the participants might have come from work and had not had the opportunity to smoke during the afternoon. This might have affected their CO measurement, which is dependent on the duration of time between smoking and measuring CO. This could have skewed the measurement of CO for those who were coming to the study site from work and may not have accurately reflected their nicotine dependency.

Since this study was a secondary analysis and data was collected from only one of the study sites, the sample size of the study was small. This was reflected in the small statistical power of the study. The small size might have affected the statistical significance of some of the results. That is, as with all cross-sectional studies, although the prevalence of nicotine dependence in African American smokers can be determined, the description of the temporal relationships between the factors is compromised, thus the question of causality is not addressed.

Likewise, due to the self-report method of data collection, the findings of the study and the reliability of the data is subject to biases. The validity of self-reported smoking has been often questioned. There could have been issues related to self-report such as selective recall or lack of recall when participants were reporting their smoking behaviors. Moreover, smokers are most often believed to underestimate their smoking level (Haley & Hoffmann, 1985) which could affect their level of dependence. One of the possible explanations for this phenomenon is that, “not smoking” is a socially desirable

behavior. Consequently, smokers may be more likely to embellish the extent to which they would comply with the social norms of "not smoking."

The data for the current study were collected from University of Maryland, College Park. The site had used the DC Metro free newspaper to recruit participants for the study. A majority of the participants who expressed their interest to participate and who were randomized into the study were African American smokers from DC metropolitan area. Although education level was captured by this present study, other aspects of socioeconomic status such as employment status, income level etc. were not captured by this study. Given that education level was found to be associated with dependence, the ability to interpret findings for socioeconomic status was limited. Future studies should incorporate SES as a predictor of nicotine dependence in African American smokers. Other variables of SES such as income level, employment etc. have to be considered in future studies. Furthermore, since the participants were from a metropolitan area, it is unclear whether the findings of this study can be generalized to African American smokers in other regions of the country. Thus, the external validity of this study is limited.

5.3. Implications

Despite these limitations, the present study has contributed to the existing literature. The current literature reflects paucity of research into factors contributing to nicotine dependence conducted among African American smokers, although the prevalence of smoking has been studied in this population. Another significant contribution of this study is that, the FTND scale has not been exclusively studied in

African American smokers before; this study used the scale to measure dependence in this population which has not been found in the available literature. These findings have implications for research in prevention of smoking among African American smokers. First, it highlights the need to take early steps into prevention of smoking at an early stage. The association of older age and longer period of regular smoking with high dependence underscores the significance of early prevention of smoking and importance of delaying, if not preventing, smoking onset. That means interventions have to be designed in school settings or other places to involve adolescents in preventing early initiation of smoking.

Self-efficacy, positive perception of ones ability to quit smoking was identified as a strong factor that seemed to increase the likelihood of smokers having lower dependence. The findings suggested that interventions should include components that increase self efficacy depending on the level of dependence and be based on theoretical framework such as, stage of change. These theories guide the understanding and development of programs and provide guidance in the translation of skills and confidence into action. In order to achieve more effective prevention of nicotine dependence, interventions specifically tailored to African American smokers and that are culturally sensitive will be required to decrease the prevalence of nicotine dependence among African Americans.

Future studies should be conducted among a larger sample of African American smokers that would capture psychosocial variables of smoking. Adequate attention should be given to incorporation of SES variables. Studies should focus on prevalence of

nicotine dependence and not just prevalence of smoking so that the impact is on primary and secondary prevention.

APPENDICES

Appendix I

Fagerström Test for Nicotine Dependence (FTND)

1. How soon after you wake up do you smoke your first cigarette? Score
□ Within 5 minutes 3
□ 6–30 minutes 2
□ 31–60 minutes 1
□ After 60 minutes..... 0

2. Do you find it difficult to refrain from smoking in the places where it is forbidden (e.g., in church, at the library, in cinema)?
□ Yes.....1
□ No 0

3. Which cigarette would you hate most to give up?
□ The first one in the morning 1
□ Any other 0

4. How many cigarettes/day do you smoke?
□ 10 or less 0
□ 11–20..... 1
□ 21–30..... 2
□ 31 or more 3

5. Do you smoke more frequently during the first hours after waking than during the rest of the day?
□ Yes..... 1
□ No 0

6. Do you smoke if you are so ill that you are in bed most of the day?
□ Yes..... 1
□ No 0

Total Score:

Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerström, K. O. (1991). The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction,* 86, 1119–1127.

Appendix II

Smoking History Questionnaire

1. How old were you when you started smoking regularly? ……

2. How many times have you tried to quit smoking before (at least 24 hours)?

…….. Never
…….. Once
…….. 2 to 5 times
…….. 6 to 10 times
…….. More than 10 times

3. Could you quit smoking if you wanted to?

…….. No
…….. Yes
…….. Don't know

Appendix III

Treatment Session Procedures

When dispensing the gum, the responsible study staff directed the subjects on the appropriate chewing instructions provided with their gum. Two gum products had instructions to "chew it like ordinary gum for 30 minutes". The other gum product had the following instructions: "Chew the gum slowly until it tingles. Then park it between your cheek and gum. When the tingle is gone, begin chewing again, until the tingle returns".

The subject was then left alone in the room. To ensure compliance with the cue exposure and gum-chewing protocols, participants were monitored unobtrusively via closed-circuit video and audio equipment, and step-wise instructions were delivered via pre-recorded audiotape.

Adaptation - Participants were given 5 minutes of adaptation.
Baseline Craving Assessment (Pre-Cue) - Participants completed a baseline questionnaire for craving assessment as follows:

Use numbers from 0 to 100 to indicate how you are feeling, with 0 being "not at all", and 100 being "the strongest feeling possible", in response to the following five statements:

1. I have a desire for a cigarette right now

2. If it were possible, I would smoke now

3. All I want right now is a cigarette

4. I have an urge for a cigarette

5. I crave a cigarette right now

Cue Exposure Procedure - Two minutes following baseline craving assessments, subjects followed procedures for exposure to the cue, standardized to previous trial techniques (Sayette & Hufford, 1994; Niaura et al., 1998).

Subjects were instructed to lift an opaque bowl, under which a pack of cigarettes of their favorite brand (as determined in their smoking history taken at Visit 1), a lighter and an ashtray were placed. Participants were instructed by the pre-recorded audiotape to open the pack of cigarettes, remove a cigarette, light it without placing it in their mouths, and to hold the lit cigarette directly in front of them without smoking it. These procedures had been standardized to take approximately 30 seconds. Participants were instructed to hold and look at the lit cigarette for 60 seconds and then to extinguish it in the ashtray.

Craving Assessment (Post-Cue) - Immediately following extinguishing of the cigarette, subjects completed a post-cue (pretreatment) craving assessment, identical to the baseline assessment.

Gum Administration –Approximately 2 minutes after the start of the Cue Exposure, gum administration was initiated by the audio taped instructions to start chewing their gum according to the instructions previously provided for their type of gum.

Craving Assessments - Subjects completed assessments of craving and degree of craving relief as directed at 2, 4, 6, 9, 12, 15, 20, 25, and 30 minutes after initiating treatment in the provided binders, as follows:

Use numbers from 0 to 100 to indicate how you are feeling, with 0 being "not at all", and 100 being "the strongest feeling possible", in response to the following five statements:

I have a desire for a cigarette right now

If it were possible, I would smoke now

All I want right now is a cigarette

I have an urge for a cigarette

I crave a cigarette right now

Then, for assessment at the required time (2, 4, 6, 9, 12, 15, 20, 25, 30 minutes), participants were asked to indicate the level of craving relief as a result of chewing the gum as:

No relief

Little / some relief

Meaningful relief

Complete relief

Treatment Completion - After the 30-minute assessment, subjects were instructed to remove the gum from their mouth, and return it to the medicine cup. They then relaxed for 5 minutes and then complete the 35 minute assessment.

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