Outcome Milestones in Smoking Cessation: An Organizational Framework

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In this study, the utility and validity of three behavioral milestones, initial abstinence, lapse, and relapse, were investigated as an organizational framework for assessing and reporting outcomes in smoking cessation research. Tests of the framework were twofold: First, to establish that each milestone represented a significant barrier to successful smoking cessation, the proportion of participants failing to meet abstinence criteria at each milestone was investigated. Second, differences in variables that predicted outcomes between the milestones were examined. Changes in the importance of factors that predicted outcomes between the milestones were to suggest differences in the processes contributing to changes in trajectory towards end-state failure or success. The utility and validity of the milestones as an organizational framework was partially supported insofar as all of the milestones represented significant barriers to successful smoking cessation. However, few predictors of any outcome were identified. As a consequence, few instances of differential prediction between outcomes were found. This study, therefore, did not provide support for the utility of the milestones framework because preliminary findings did not provide an appropriate context in which it could be tested as a tool for identifying differential predictors of initial abstinence, lapse, and relapse.

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1. INTRODUCTION

Quitting smoking is difficult. An estimated 70% of smokers in the United States (33.2 million) want to quit, but the chances of any single, unaided quit attempt resulting in a successful quit range between 0.5% and 3% (see Jarvis, 2003). Indeed, more than 40% of the 50 million current smokers in the United States make at least one quit attempt each year (CDC, 2002).

Many behavioral and pharmacological interventions have been developed to promote smoking cessation (Fiore et al., 2000; USDHHS, 2000). Available cessation aids double rates of abstinence relative to controls (e.g. Fiore et al., 2000), yet no available therapy produces long-term abstinence rates greater than 50% (Fiore et al., 2000; Shiffman, 1993). Therefore, even with behavioral and pharmacological interventions, the most common outcome of a quit attempt is failure.

Developing and implementing successful smoking cessation interventions is difficult. Large bodies of literature have confirmed the importance of multiple factors to smoking cessation outcomes, including biological, psychological, behavioral, and cultural factors, as well as interactions among these factors (see Heishman, 1999 for a review). Current interventions have been designed to attenuate the risk of failure associated with many of these variables.

Less studied are changes in the importance of risk and protective factors for smoking abstinence at different points in the cessation process. Current research suggests that smoking cessation is best conceptualized as an ongoing, dynamic process -- not a fixed state (Piasecki & Baker, 2001). One possibility, therefore, is that factors affecting smoking abstinence do so differentially at different stages in the course of a quit attempt (Shiffman, 1989). Few studies have investigated this hypothesis.

1.1. The Stage-by-Stage Process of Smoking Cessation

Different factors may play greater or lesser roles in promoting smoking abstinence as each stage of the cessation process unfolds. Different challenges may be faced when smokers are initially establishing abstinence, subsequently trying to avoid a lapse, and if they do lapse, trying to avoid a relapse.

Acknowledgement of personal risk is a factor that may affect the transition from smoking to abstinence (Weinstein et al., 1998). Smoking is a pleasurable activity, and cessation, almost always coupled with craving and withdrawal symptoms, can be extremely unpleasant. Individuals unaware of the risks associated with smoking will most likely be unwilling to quit. Individuals concerned about the effects of smoking on their health, however, may be more likely to initiate abstinence.

If an individual manages to successfully achieve initial abstinence, prolonged abstinence must be maintained for the quit attempt to become a success. Although awareness of personal risk may be important for achieving initial abstinence, coping with threats to abstinence may be more important for prolonging abstinence. Consider a newly quit (ex)smoker in a highly stressful situation such as being stuck in traffic and late for work. The risk of smoking following effective coping (for example, having previously rid the car of all cigarettes) is much less than if he or she had not coped effectively and had kept a pack of "emergency" cigarettes in the car. The variables that best predict transitions from smoking to abstinence may be different from those that predict outcomes at later stages in the cessation process.

Most quit attempts include at least one smoking episode (Swan & Denk, 1987; Brandon et al., 1990). Even individuals aware of the risks of smoking who make effective efforts to cope are at a high risk for further smoking. Smoking during a quit attempt, or lapse, can be succeeded either by (1) recovery of abstinence; (2) progressively more smoking; or (3) intermittent

smoking. Differences in how an individual interprets and experiences a smoking episode during a quit attempt may affect whether abstinence is regained or whether smoking is resumed (Marlatt & Gordon, 1985; Marlatt 1982; Marlatt & Gordon, 1980; Piasecki et al., 2003). For example, if an individual believes that smoking during a quit attempt reflects an inability to quit, motivation to regain abstinence and coping with the desire to smoke will likely decrease, increasing the likelihood of future smoking. On the other hand, if the smoking episode is interpreted as an isolated event within an otherwise successful quit attempt, confidence and motivation to regain abstinence will likely remain high, as will the likelihood of further abstinence (Marlatt & Gordon, 1985). Similarly, the physiological effects of smoking after a prolonged period of smoking abstinence might precipitate changes in craving or withdrawal that affect the outcome of a quit attempt. Increased withdrawal symptoms, for example, could be due to mechanisms such as priming (Shaham et al., 2003), and decreased symptoms could be due to suppression of withdrawal by the direct pharmacologic actions of nicotine (Piasecki et al., 2003). What determines whether an individual will resume smoking after an isolated smoking episode may be contingent on processes that are initiated only after a lapse has occurred. Thus, factors which are not only distinct, but necessarily independent of those that promoted the transition from smoking to abstinence may predict outcomes following a lapse.

In sum, different challenges to abstinence likely arise throughout the process of smoking cessation; therefore, the importance of factors that promote or threaten abstinence likely varies as well. While researchers may have an understanding of what factors contribute to successful smoking cessation overall, little is known about how the degree of influence of such factors may change over the course of a quit attempt. One way to begin studying the processes contributing to end-state outcomes (outcomes measured at the end of a treatment trial) is to assess outcomes

at important intermediate points, or milestones, throughout the cessation process. Changes in the ability of factors to predict outcomes between assessment points can suggest processes that may contribute to changes in trajectory towards end-state failure or success. Moreover, identifying *where* changes in risk and protective factors occur could suggest points at which individuals are likely to encounter the most serious threats to abstinence. Ultimately, these points of change could be used to inform treatment administration so that interventions address the immediate needs of the prospective quitter as his or her needs change.

1.2. Assessment of Outcome Milestones

Current methods for assessing outcomes in smoking research are not amenable to a systematic study of the processes contributing to end-state outcomes. End-state outcomes are typically tallied at a predefined time-point without attending to the processes by which outcomes were achieved. While this method may be appropriate for measuring the ultimate impact of smoking, such as the effects of smoking on health, by emphasizing abstinence at an end-point alone, the route by which abstinence was achieved becomes obscured (Ossip-Klein et al., 1986). For example, analyses often do not distinguish between smokers who never achieve abstinence and those who achieve abstinence but then relapse (Ockene et al., 2000). Similarly, distinctions are seldom made between individuals who lapse (i.e., have a limited episode of smoking) and those who relapse (i.e., resume smoking at a level similar to that before the quit attempt), and report both indistinguishably as failed quit attempts (Piasecki & Baker, 2003; Ockene et al., 2000). At the end of a trial, researchers can only conclude that a successful or unsuccessful outcome has occurred – no information is gained about why an individual may or may not have succeeded.

1.3. Outcome Milestones in the Process of Smoking Cessation: An Organizational Framework

I propose that what is needed to facilitate a systematic study of the processes contributing to end-state outcomes is an organizational framework of the process of smoking cessation. Ideally, such a framework would consist of objective, behavioral markers at which intermediate outcomes can be assessed. An organizational framework, distinct from a theoretical model, would not posit specific mechanisms for progression towards smoking cessation outcomes. Rather, it would provide a common language and logic for integrating and interpreting data from multiple sources (Piasecki et al., 2002). Although organizational frameworks are never free of all theoretical suppositions (e.g. the DSM can be argued to implicitly endorse a medical conceptualization of mental disorder; Follett et al., 1992), organizational frameworks intentionally de-emphasize strong theory in order to engage investigators with diverse perspectives (Piasecki et al., 2002).

The goal of this organizational framework would be to provide researchers with a template for measuring and reporting smoking cessation process outcomes in a consistent and meaningful way. Consistency in the reporting of study outcomes could facilitate integration of work on smoking cessation from diverse theoretical perspectives, thus improving how the processes that contribute to successful quit attempts are understood.

Authors have previously suggested stage-based models of smoking cessation. For example, in the Transtheoretical Model of Behavior Change (TTM), the process of smoking cessation is described by five 'stages of change': Precontemplation, Contemplation, Preparation, Action, and Maintenance (Prochaska & DiClemente, 1983). Progression to each new stage serves as a milestone marker for intermediate outcome assessment. According to the TTM, individuals in the Precontemplation stage have no plans to make a quit attempt within the next six months. In the Contemplation stage, individuals plan to quit smoking within the next six

months, and in the Preparation stage, action towards change (smoking cessation) is intended within the next 30 days and some behavioral steps are taken in this direction. In the Action stage, overt modifications in smoking behavior were made within the past six months, and individuals are trying to maintain abstinence. Finally, in the Maintenance stage, individuals work to prevent relapse and are at a decreased risk for smoking as compared to at the Action stage. While the TTM makes useful distinctions between processes leading to initial smoking abstinence, the processes activated after abstinence has been achieved are not well differentiated other than by the passage of calendar days (as opposed to by qualitative changes in process). For example, transition from the Action to the Maintenance stage is determined simply by the achievement of an arbitrary period of abstinence.

In contrast, Marlatt and Gordon's (1985) Relapse Prevention model does focus on changes in process, but it is limited to processes occurring only after initial abstinence has been achieved. In this model, the behaviors of lapse and relapse are milestone markers for outcome assessment because different mechanisms are hypothesized to contribute to lapse and relapse. Moreover, the overall outcome is posited to depend upon the outcome of each of these two separate events. In the model, a lapse (a brief period of smoking during a quit attempt) occurs when an individual suffers from decreased self-efficacy following a failure to implement an effective coping response when the risk for smoking is high. This perceived failure to cope effectively is then followed by positive expectancies for the effects of smoking, thereby increasing the likelihood of a lapse. Thus, a lapse is thought to be largely driven by situational antecedents that activate particular intra-psychic events. In contrast, relapse (a resumption of regular smoking) is posited to occur if the individual attributes responsibility for the lapse to internal and stable characteristics of the self (Abstinence Violation Effect; AVE). In the model,

the AVE, combined with the intoxicating effects of substance use, increases the likelihood that a full-blown relapse will occur. The processes that are believed to lead to a relapse are viewed as different from those that lead to a lapse; they are extended in time and are more internal than those contributing to lapse. Moreover, the key process (AVE) is not active until after the lapse has occurred. The RP model provides a more detailed account of the cessation process after initial abstinence than the TTM. However, the RP model is incomplete insofar as it does not account for the processes contributing to the achievement of initial abstinence.

I propose that three behavioral milestones, or points of intermediate outcome assessment, comprise an organizational framework of the process of smoking cessation, with milestones 'Achievement of initial smoking abstinence,' 'lapse' and 'relapse' operationalized as follows: Initial smoking abstinence is 24 hours of no smoking (not even a single puff). Once abstinence is achieved, a lapse is any smoking (including a single puff). Once a lapse occurs, relapse is operationalized as three consecutive days of smoking at least five cigarettes per day, but is meant to conceptually reflect a resumption of regular smoking.

Each milestone is widely recognized as an integral part of the cessation process (Ossip-Klein et al., 1986; Brandon et al., 1990; Shiffman et al., 1986; Brownell et al., 1986; Garvey et al., 1992; Ockene et al., 2000); each is behavioral and can be measured objectively; the milestones can typically be measured within the span of time encompassed in a typical treatment trial[1], and each milestone is progressive, in that passing a milestone makes one eligible for the next. Indeed, if an individual does not stop smoking (achieve initial abstinence), he or she cannot logically

[1] Data suggest that the majority of initial abstinences, lapses, and relapses will typically occur within this time frame. For example, data show that most relapse occurs soon after quitting: 65% of subjects relapse within 30 days, and nearly 85% of initial lapses occur within 30 days (Garvey et al., 1992; Shiffman et al., under review);

lapse (Miller, 1996). Further, a lapse must occur before relapse (the sum of many lapses in close succession) is possible. More explicit definitions of the milestones will follow (see section 1.5).

1.4. Empirical Support for the Milestones Framework

Literature investigating a variety of drugs of abuse suggests that differences exist between predictors of outcomes at each milestone. These differences indicate that outcomes at the milestones may result from different processes. Below, data illustrating the differences between predictors of outcome at each milestone are reviewed.

1.4.1. Simultaneous Assessment of Predictors of Outcome at Multiple Milestones

1.4.1.1. Initial Abstinence

Few studies have included initial abstinence as an outcome; however, preliminary evidence suggests that predictors of initial abstinence may differ from those of subsequent milestones. In one large-scale study (n=400) of smokers in a worksite cessation program, the effects of multiple variables on initial and long-term abstinence were investigated (Curry et al., 1989). Motivation predicted initial but not long-term abstinence. Conversely, social support and stress predicted relapse, but not initial cessation. In short, variables that predicted outcomes at the different milestones were predominantly different. In a second study investigating predictors of initial abstinence (48h) and relapse (defined as smoking an average of 1(+) cigarettes per day since the previous assessment; Gulliver et al., 1995), failure to achieve initial abstinence was predicted by younger age and lower *baseline* self-efficacy, while lower *proximal* self-efficacy scores and lower *proximal* smoking-specific partner support scores predicted relapse. Again, predictors of failure to achieve initial abstinence and relapse were distinct.

Using an experimental paradigm, Brown et al (2002) reported differential response to a psychological stressor (serial addition task) and a physical stressor (inhalation of carbon monoxide-enriched air) between groups who had made prior quit attempts and achieved initial

abstinence, or groups that resumed smoking within 24h. Participants who did not achieve initial abstinence displayed lower levels of behavioral persistence, had higher levels of depressive symptoms, had a greater self-reported tendency to react to task stress with negative affect, and reported greater increases in dysphoria and urge to smoke in response to 12hr of nicotine deprivation. Predictors of later relapse included degree of dependence, number of years smoking, and number of serious quit attempts. Again, no overlap was found between predictors of outcomes at the two milestones.

1.4.1.2. Lapse and Relapse

Research spurred by Marlatt and Gordon's (1985) Relapse Prevention model has led to many studies of predictors of lapse and relapse. Primarily, investigators have used characteristics of the lapse itself to predict the occurrence of relapse. One such literature addresses differences in attributions after smoking leading to an isolated lapse or relapse. In this instance, the variable predicting relapse – attribution for the lapse – is not even defined prior to the lapse, and thus is unique to relapse. Numerous studies have reported that internal, stable, and global attributions about smoking during a quit attempt are associated with relapse, while external, dynamic, and specific attributions are more predictive of lapse. These findings have been replicated in studies of cigarette smoking, marijuana smoking, diet, and alcohol use (Goldstein et al., 1984; Curry, Marlatt and Gordon, 1987; O'Connell and Martin, 1987; Walton et al., 1994; Stephens et al., 1994; Ogden & Wardle, 1990; Shiffman et al., 1997); although, contradictory findings have been reported (Gutierres & Reich, 1988; Bradley, Gossop et al, 1992; Birke et al., 1990; Borland, 1990).

Researchers have also simultaneously investigated baseline predictors of lapse and relapse. Although little overlap exists in the predictors tested between studies, a consistent

finding is that the factors that predict lapse and relapse within individual studies differ. Investigations of abstinence from smoking, alcohol, and heroin have reported that predictors of lapse include decreased cognitive functioning (on a digit-symbol task), lower post-treatment self-efficacy (Allsop et al., 2000), higher baseline levels of drug use, decreased use of coping responses (Gossop et al., 1997), subscales on a measure of abstinence self-efficacy (Relapse Self-Efficacy Questionnaire; RSEQ; Gwaltney et al., 2001), a higher number of reasons to quit, higher levels of work strain, having smoked cigarettes with higher levels of nicotine at baseline, and having higher levels of psychological symptoms after quitting (Swan & Denk, 1987). In contrast, predictors of relapse included total RSEQ score (but not the subscales; Gwaltney et al., 2001), decreases in self-efficacy after a lapse (Shiffman et al., 2000), being unemployed, the presence of abnormal respiratory symptoms, daily alcohol consumption at intake, work strain, and change in body mass during the quit attempt. The only variable that predicted both lapse and relapse was post-treatment self-efficacy, and this finding was unique to a single study (Allsop et al., 2000). Changes in the magnitude of prediction for post-treatment self-efficacy at lapse and relapse may have existed, but this comparison was not reported.

A good illustration of differential prediction of outcome at the milestones comes from research on naltrexone, a pharmaceutical agent designed to help problem drinkers (Volpicelli et al., 1992; 1995; 1997; O'Malley et al., 1995). Naltrexone may improve end-state outcomes specifically by preventing lapses from progressing to relapse, not by decreasing risk for lapse (study participants were already abstaining; Volpicelli et al., 1992; 1995). The hypothesized mechanism for this effect is that naltrexone blocks endogenous opiate receptors, thus preventing alcohol consumed during a lapse from activating endogenous opioids, making consumption of alcohol less rewarding (Volpicelli et al., 1992). Pharmacological interventions that improve end-

state outcomes may not be effective for promoting abstinence equally at all milestones, but may be limited to affecting processes specific to individual milestones. Distinguishing between treatments affecting outcomes at specific milestones may lead to more systematic, targeted treatment administration.

1.4.2. Sequential Influence of Earlier Outcomes on Subsequent Milestones

The effects of outcomes at earlier milestones can influence outcomes at later milestones. For example, difficulty achieving initial abstinence, such as failure to achieve initial abstinence on target quit day (TQD), predicts shorter time to lapse (Westman, Behm, Simel & Rose, 1997). Similarly, depressed mood, craving, anger, self-reported difficulty not smoking, and more time spent with urges to smoke during initial periods of abstinence have all been shown to predict shorter time to lapse (West, Hajek, & Belcher, 1989; Swan, Ward, & Jack, 1996). This suggests that the characteristics of the attempt to achieve initial abstinence may predict lapse. As predicted by the RP model, characteristics of lapses predict relapse. Reports of cravings, urges, and guilt reactions associated with lapsing have been related to relapse (Baer et al., 1989). Similarly, using near real-time data collection techniques, Shiffman and colleagues (1996) have found that lapses reportedly triggered by stress or mood (positive or negative) lead to faster relapse, whereas lapses occurring during alcohol consumption or eating progressed more slowly to relapse (Shiffman et al.,1996). AVE variables were found to have no effect on progression to relapse. Overall, these data suggest that key processes contributing to outcomes at the milestones may not be set in motion until the challenges associated with earlier milestones have been attempted.

In sum, findings from studies of a variety of drugs of abuse suggest that factors associated with abstinence differ between the milestones, with some processes not being initiated until previous milestones have been met. Important information about the processes contributing

to end-state outcomes, therefore, may be gained by assessing outcomes and related predictors at intermediate points throughout the cessation process.

1.5. Operationalizing the Milestones

Researchers have used varied definitions for the milestones and significant controversy exists regarding how best to define the constructs of initial abstinence, lapse, and relapse (Ossip-Klein et al., 1986; Ockene et al., 2000). Although differences in operational definitions could affect research findings guided by the framework, accepting the definitions of the milestones proposed below is not necessary for acknowledging the utility of the framework itself. To date, insufficient research has clearly stated which definitions best capture the essence of initial abstinence, lapse and relapse. Therefore, acknowledging the utility of the milestones framework only implies accepting the idea that important information about processes contributing to end-state outcomes can be gained by assessing outcomes at the milestones. The operational definitions of the milestones described below, therefore, reflect the author's best approximation of professional consensus, practicality, and the scientific utility of the constructs and are provided under the assumption that these milestone definitions could be revised should future data emerge to justify their improvement.

1.5.1. Initial Smoking Abstinence

I, like others, propose that initial smoking abstinence be defined as 24h of no smoking (Ockene et al., 2000; Shiffman et al., 1986; U.S.Department of Health and Human Services, 1989). An operational definition of initial abstinence is important for the completeness of the milestones framework because an initial abstinence milestone distinguishes individuals who have quit from those who have not (Ossip-Klein et al., 1986). A clear definition of abstinence is also necessary to distinguish ongoing smoking from early lapse or relapse (Shiffman et al., under review). The

initial abstinence milestone may be useful for identifying subjects who are not likely to benefit from treatments that produce their therapeutic effects at the lapse or relapse milestones. For example, the achievement of initial abstinence has been used as an entry criterion to some studies (Mothersill et al., 1986; Killen and Fortman, 1997; Volpicelli et al., 1995), presumably because participants who never achieve abstinence do not generate lapse or relapse data.

Although current research is insufficient for drawing conclusions about which definition of initial abstinence is best, preliminary evidence suggests 24h of abstinence is at least as appropriate as other competing definitions. In a series of three studies investigating the predictive power of craving on prolonged abstinence, measurements of craving following 24h of abstinence predicted abstinence at 1-year post-quit as well as data following a 48h period of abstinence (Killen et al., 1997). Therefore, although future research may ultimately suggest that one definition is more appropriate than another, current research supports a 24h definition of initial abstinence. 24h of abstinence appears to be the more popular of the two definitions (Ockene et al., 2000), thus it is adopted in the milestones framework.

Although nicotine dependence is commonly defined as a "relapsing disorder" (e.g. Brownell et al., 1986; Fagerström, 2003; Shiffman, 1989), because relapse is what occurs when quit attempts fail, data also suggest that quit attempts can fail when individuals do not achieve initial abstinence. Studies have shown that about 1 in 6 prospective quitters are unable to achieve initial smoking abstinence (Garvey et al., 1992; Shiffman et al., under review). An initial abstinence milestone describes individuals whose most significant barrier to abstinence is not encompassed by the "relapsing disorder" definition.

Similarly, some individuals who eventually abstain from smoking (about 1 in 4) are unable to do so on their Target Quit Day (TQD; Shiffman et al., under review; Brown, Strong et

al., 2001; O'Connell & Martin, 1987). Thus, achieving initial abstinence may only be possible after some abstinence-initiating processes have been activated. If specific processes must be activated for initial abstinence to be achieved, information about the processes ultimately contributing to end-state outcomes may be gained by studying factors that make initial abstinence possible.

1.5.2. Lapse

Lapse, the second proposed milestone, is defined in the framework as any smoking after initial abstinence (including a single puff). This definition of lapse is well established (Marlatt & Gordon, 1985; Shiffman et al., 1986; Ossip-Klein et al., 1986; Ockene et al., 1986; Brownell et al., 1986; Ockene et al., 2000; Brandon et al., 1990). The inclusion of a lapse milestone is important because it represents the first return to smoking after initial abstinence (Shiffman et al., 1996), and possibly a significant change in the factors affecting smoking abstinence. Indeed, several theories suggest that reinitiating smoking after a period of abstinence sets new psychological and physiological processes in motion. For example, the RP theory posits that the AVE occurs after abstinence has been achieved and subsequently violated (Marlatt & Gordon, 1985). Others describe processes that begin as a result of priming or reinforcement from re-exposure to nicotine after a prolonged abstinence. Perkins et al (2001) have demonstrated that chronic tolerance to nicotine is not lost after weeks of abstinence, and that re-exposure to nicotine after a period of abstinence (i.e. a lapse), can prime a quick return to heavy smoking. Indeed, any smoking (including a single cigarette) during a quit attempt is associated with a 90% chance of returning to regular smoking (Brandon et al., 1986; Kenford et al, 1994).

Although lapses are significant indicators of later relapse, not all lapses result in relapse (Kenford et al., 1994; Garvey et al., 1992). Some smokers are able to experience brief periods of smoking and quickly regain smoking abstinence while others are not (Kenford et al., 1994;

Garvey et al., 1992; Brandon et al., 1990; Brownell et al., 1986; O'Connell & Martin, 1987; Ossip-Klein et al., 1986; Baer et al., 1989; Curry et al., 1987). These findings suggest that important individual differences may exist in factors contributing to end-state outcomes after a lapse has occurred. The lapse milestone, therefore, is conceptually important for distinguishing isolated episodes of smoking within a quit attempt from a resumption of regular smoking.

1.5.3. Relapse

Relapse marks the last phase of a failed quit attempt. A single quit attempt often includes periods of both smoking and abstinence (Swan et al., 1987; Brandon et al., 1990); therefore, a concise, operational definition of relapse can distinguish between multiple lapses within a single quit attempt and a resumption of regular smoking. In addition, reliable reporting of end-state outcomes, such as tallies of the number of participants who are "quit" vs. "smoking" at the end of a study depends upon how effectively those individuals who are still working on an initial quit attempt can be distinguished from those who have failed and will need to try again.

Little controversy exists about the meaning of the term relapse, at least for describing samples of daily smokers (a resumption of regular smoking; Ockene et al., 2000; Ossip-Klein et al., 1986). Operationally, relapse is often defined by seven consecutive days of any smoking after a period of seven days of abstinence (Ossip-Klein et al., 1986). A more stringent definition, and the definition tentatively included in the milestones framework, is smoking at least five cigarettes a day for three consecutive days (Shiffman et al., 1996). Some authors have suggested that, intuitively, participants who smoke on three consecutive days generally have resumed the habit (Brandon et al., 1990), but available research does not support one definition over the other.

1.6. Testing the Utility of the Milestones as an Organizational Framework

Studies predicting smoking cessation outcomes from pretreatment characteristics have provided valuable information about who is likely to achieve end-state abstinence (e.g. Shiffman, 1989;

Shiffman et al., 1997; Curry et al., 1989). Pretreatment characteristics including age, sex, self-efficacy, alcohol use, length of longest prior smoking abstinence, nicotine dependence, and number of past quit attempts have all been associated with risk for cessation failure (see Persico, 1992 for a review). Pretreatment characteristics, however, are typically presumed to exert a stable, "atemporal" influence on failure risk throughout the course of a quit attempt (Shiffman, 1989). For example, although baseline motivation to quit smoking has been shown to affect end-state outcomes, few researchers have explored the possibility that differences exist in the importance of motivation for achieving initial abstinence compared to that for preventing relapse. One way to demonstrate the utility of the milestones framework, therefore, would be to show that variables known to affect end-state outcomes do so differentially at each milestone.

In this study, I investigate whether participants' baseline characteristics differentially predict outcomes at the milestones. Below, relationships between various individual differences in baseline characteristics and outcomes at the milestones are hypothesized. The list of hypotheses described below is not meant to be exhaustive; rather, it is meant to introduce the reader to the idea of learning about processes contributing to end-state outcomes by assessing the relationship between baseline characteristics and outcomes at the milestones.

1.6.1. Nicotine Dependence

Nicotine dependence, an index of how essential smoking is to maintaining a comfortable state, is assessed with well-validated questionnaires (Heatherton et al., 1991; Fagerström, 1978; Shiffman et al., 1995). High scores on measures of nicotine dependence may include high self-reported craving during periods of abstinence (Shiffman et al., 1995), and willingness to smoke despite illness or environmental smoking restrictions (Fagerström, 1978). Nicotine dependence has been reliably associated with end-state outcomes (e.g. Heatherton et al., 1991).

Smoking cessation is associated with an abstinence syndrome that is ameliorated by the administration of nicotine (Balfour & Fagerström, 1996; Benowitz, 1996). Given that the abstinence syndrome is most acutely felt by the most dependent smokers, smoking during an unaided quit attempt (lapse) is expected to provide the most negative reinforcement for the most dependent smokers, thereby increasing the risk for more smoking (i.e. relapse). Nicotine dependence is therefore hypothesized to be most predictive of relapse. Although withdrawal symptoms associated with high levels of nicotine dependence are felt during abstinence and may promote lapses, shorter latency to lapse is expected to be predicted more accurately by motivational and coping variables than by nicotine dependence, because unlike relapse, lapse represents a shift from abstinence to smoking (if only temporarily) rather than persistence with already re-initiated smoking behavior as is the case necessary for relapse.

1.6.2. Previous Quit Attempts and Abstinence Self-Efficacy

Smoking history variables such as length of longest prior smoking abstinence have been associated with end-state outcomes (e.g. Stapleton et al., 1995). Length of longest prior smoking abstinence has been associated with time to first lapse (Garvey et al., 1992). Alternatively, simply having had any prior quit may increase confidence in ability to abstain ("I've done it before, I can do it again.") and may therefore predict achievement of initial abstinence. Self-efficacy theory (Bandura, 1977, 1982, 1997) and supporting research (Gwaltney et al., 2002), however, suggests that self-efficacy is specific to particular contexts and challenges, not to smoking cessation in general. Therefore, self-efficacy for achieving initial abstinence may predict the achievement of initial abstinence but not lapse or relapse. Instruments for assessing self-efficacy tend to assess self-efficacy for avoiding lapses (e.g. Gwaltney et al., 2001), thus current measures of abstinence self-efficacy are expected to predict lapse. Instruments designed

to measure self-efficacy for relapse avoidance, for example, may predict risk for relapse but not for lapse and initial abstinence. These milestone-specific relationships have not been evaluated.

1.6.3. Stress and Affect

Although high levels of negative affect have been related to cessation failure, a number of hypotheses could potentially explain the relationship between affect and end-state failure via effect on the milestones. Smokers report higher overall levels of anxiety, stress, and discomfort than do nonsmokers (e.g. Billings & Moos, 1983), and they may use nicotine to reduce these symptoms temporarily (Kendler et al., 1993; Pomerleau & Pomerleau, 1991). One possibility, therefore, is that high baseline levels of stress, anxiety and discomfort put individuals at risk for lapse because cigarettes are a known tool for medicating these symptoms when they emerge after cessation. Another possibility is that baseline levels of negative affect will be less important for lapse and more closely associated with failure to achieve initial abstinence. For example, smokers with high negative affect response may react with greater distress to nicotine withdrawal and therefore choose to smoke on the target quit day (Piasecki, Fiore, et al., 1998). However, negative affect has also been associated with relapse. Shiffman, Hickox et al (1997) have suggested that, although some individuals may find effective temporary means of coping with negative mood early in a cessation attempt, those who do not have effective coping strategies may later succumb and resort to smoking as a reliable means of improving their mood. The milestone at which negative affect will be most predictive of outcome is unclear.

1.6.4. Demographics

Demographic variables such as age, sex, marital status, education, household composition, and income have been associated with end-state outcomes and may be differentially associated with outcomes at each milestone. Living with a partner who is a smoker, for example, is associated with marked decreases in cessation (Jarvis et al., 2002). One possible effect is that living with a

partner who smokes increases cessation failure by increasing risk for lapse. Individuals who live with smokers may have more exposure to smoking cues and easier access to cigarettes, both of which have been associated with risk for smoking during a quit attempt (Perkins et al., 1994; Lazev et al., 1999; Balfour, 2003). Alternatively, living with a current smoker may increase risk for relapse, because after a lapse has occurred, the presence of cigarettes and other smoking cues may overshadow the salience of means for re-establishing abstinence.

Women may have less success quitting smoking than men do (Scharf & Shiffman, 2004). Women are more likely than men to enlist in formal cessation treatments, and in this setting, worse outcomes for women have frequently been observed (e.g. Stapleton et al., 1995). Among smokers in general, however, most of whom quit without formal treatment, there is little evidence that women overall are any less likely to quit (Jarvis, 2003). Cessation rates are significantly higher in women than in men during the childbearing years, higher in men than in women in middle age, and equal between the sexes in the oldest age groups (Jarvis, 1994). Therefore, the relationship between gender and outcomes at the milestones may be complicated by different processes at each stage in life. Nonetheless, women and men may differ in terms of their degree of risk for failure at the milestones overall, for example, because of differences in risk for depression and concerns about weight-gain. Depressive tendencies may make women more sensitive to the effects of withdrawal, thus impeding initial abstinence. Alternatively, women may be at greater risk for relapse if they ruminate about the negative implications of having lapsed (AVE, Marlatt & Gordon, 1985). Women may also be at greater risk for relapse than men if they are more averse to weight-gain associated with abstinence, returning to smoking to manage their weight. This hypothesis may be especially relevant for younger women.

In sum, numerous pharmacological, social, and psychological variables have been associated with smoking cessation outcomes, but the focus has generally been on end-state abstinence, with the result being that we know little about the particular process by which these variables influence outcome. The degree to which each variable contributes to abstinence at particular milestones is unclear. By investigating the role of these variables, new insight can be gained into the processes contributing to success or failure at each milestone, and simultaneously to the processes contributing to end-state outcomes in smoking cessation.

1.7. Problem Statement

Although available pharmacological and behavioral smoking cessation aids double quit rates relative to placebo, the most common outcome of a quit attempt is failure. Smoking cessation outcomes might be improved if more were known about the processes contributing to failure and success. Current methods for assessing outcomes are not amenable to a systematic study of the *processes* contributing to success or failure. Typically, studies tally outcomes (i.e. abstinence) at a specified time point, and information about how outcomes are achieved is obscured. One way to promote a systematic study of the processes contributing to end-state outcomes is to promote the assessment of intermediate outcomes at milestones throughout the process of smoking cessation. Assessing multiple, targeted outcomes will help researchers identify where in the cessation process important changes in risk and protective factors occur, and ultimately, how these changes can be used to inform more efficient, targeted interventions.

I propose that three behavioral milestones--initial abstinence, lapse and relapse--serve as an organizational framework for the studying and reporting of outcomes within the process of smoking cessation. Several existing theories (implicitly or explicitly) distinguish these milestones and posit unique processes operating at each. Preliminary empirical evidence

suggests that the milestones segment the process of smoking cessation in a meaningful way. Practically, using observable changes in smoking behavior to operationalize the milestones will facilitate reliable measurement and reporting of outcomes. In addition, an organizational framework of the process of smoking cessation can provide researchers with a standardized format for reporting study outcomes. Standardized reporting of outcomes could facilitate systematic integration and interpretation of data from investigators working on the problem of tobacco dependence from diverse perspectives (Piasecki & Baker, 2001).

In this study, I will test the utility and validity of the milestones as an organizational framework by determining if pretreatment characteristics known to predict end-state outcomes can be used to differentially predict outcomes at the milestones. This approach is fairly atheoretical in that I will be examining an array of available variables collected from an earlier study, not all of which are subjects of theory-based hypotheses for differential prediction. These analyses, however, will serve as preliminary evidence for the utility of the framework, and suggest the importance of assessing outcomes at the milestones for future theory-based research.

2. METHODS

2.1. Participants

This study uses an existing data set of 260 male and female smokers enrolled in a research smoking cessation clinic (Shiffman, Gnys et al., 1996). Participants were recruited by advertisements for smoking cessation treatment and were paid $50. To qualify, participants needed to have smoked at least ten cigarettes per day for at least two years and report high motivation and efficacy to quit (sum of 150 on two 100-point scales). Fifty-eight percent of the participants were female, and 92% were Caucasian. Participants' average age was 44.3 (SD=10) years. Sixty-eight percent had some post-secondary education; 34% had completed college. At enrollment, participants reported smoking 26.7 (SD=11) cigarettes per day, having their first cigarette of the day 16.5 min after waking; 90% smoked within the first 30 minutes. Their baseline motivation to quit smoking averaged 85.9 (SD=12.4) on a scale from 0 to 100. Most participants (83%) had a history of failed quit attempts, averaging 3.4 (SD=3.0) previous attempts.

2.2. Procedures

2.2.1. Baseline Phase

Upon enrollment, participants completed a battery of questionnaires and were trained to use an electronic diary (ED) to monitor their smoking. Participants were then instructed to smoke as usual during a two-week baseline period prior to the cessation program's onset.

2.2.2. Target Quit Day and Follow-up Phase

The cessation program set a Target Quit Day (TQD) to fall at the end of the baseline phase. EDs were set to switch modes when participants awoke on the morning of the TQD and begin monitoring participants' ongoing experiences as part of the quit attempt for up to four weeks.

Participants were directed to record any episodes of smoking, which could encompass more than one cigarette if several were smoked at one sitting. Sixty-seven percent of participants smoked during the ED monitoring period. Overall, participants showed good compliance with the protocol. For example, during the first week after TQD, participants responded to the ED's prompts within two minutes, 88% of the time.

2.2.3. Assessment of Outcomes

2.2.3.1. Traditional Outcomes

Traditional outcomes, continuous abstinence and 7-day point prevalence, were assessed to compare and contrast findings related to outcomes at the milestones. Continuous abstinence was defined as the percentage of former smokers who did not smoke at all after TQD (Velicer & Prochaska, 2004). Participants lost to follow-up were counted as smoking. Seven-day point-prevalence abstinence was defined as the percentage of participants not smoking at all during the last seven days of observation (Velicer & Prochaska, 2004; Hughes et al., 2004). Violation of biochemical verification and loss to follow-up were both used to indicate an unsuccessful quit attempt.

2.2.3.2. Milestones Definitions

Progression to the milestones was calculated by the ED according to the time at which participants made entries of smoking episodes. Initial abstinence was determined by ED entries indicating 24h of no smoking after TQD, and rate of progression from TQD was assessed by computing how many days passed until 24h of abstinence was first achieved. Seventeen percent of participants (17%, n=44) did not reach initial abstinence on TQD, and an additional 5% (n=12) of participants did not achieve initial abstinence at all during the duration of the study.

A lapse was considered to be any smoking entry after ED had determined that the initial smoking abstinence milestone was achieved. Progression to lapse from initial abstinence was

computed by how many days had passed from initial abstinence until the first smoking episode. Sixty percent (60%, n=149) of participants who achieved initial abstinence lapsed. On average, the initial lapse occurred 5.1 days (SD=5.7) after initial abstinence, and half of those who lapsed did so within three days of initial abstinence. Seventy-five percent lapsed within eight days of abstaining. In the present sample, 70.1% of participants reported smoking less than one cigarette during the first lapse; 16.2% smoked one cigarette; 8.5% smoked two cigarettes, and 5.1% smoked more than two cigarettes.

Relapse was defined as three consecutive days of smoking five or more cigarettes per day. Progression from the first lapse to relapse was assessed by ED computing how many days passed until relapse (last day of a string of lapses sufficient to count as relapse). In this study, when relapse occurred, it fell 14.7 (SD=6.6) days after quitting and 9.6 (SD=5.9) days after the first lapse. Approximately 15% of the initial sample relapsed (n=40). Half of those who relapsed did so within two weeks of achieving initial abstinence.

2.2.4. Treatment

Subjects received eight 1-hour sessions of non-pharmacological treatment in groups of 8 to 16. Four sessions were held prior to the TQD, one on the TQD, and the others were held 5, 12, and 26 days thereafter. Treatment took a behavioral-psychoeducational approach with strong emphasis on providing a supportive group environment. Group leaders facilitated discussion of tobacco dependence, reasons for smoking and quitting, health benefits of quitting, and instruction in the following topics: relaxation techniques, eliciting social support, exercise, and weight control. Some homework was assigned. Minimal coping information was provided beyond the leader's discussion of simple coping responses (6 behavioral and 4 cognitive, e.g., drinking water, leaving the scene, deep breathing, reviewing reasons for quitting and benefits of quitting).

2.3. Assessment of Baseline Characteristics

Participants completed the questionnaire battery during the baseline assessment phase of the study. Questionnaires were counterbalanced and completed by participants at the research facility.

2.3.1. Demographics

At baseline, participants completed an extensive battery of demographic questionnaires assessing variables including gender, marital status, partner's smoking behavior, age, income, and education. Numerous demographic variables have been identified as predictors of end-state outcomes, as well as potential predictors of outcome at the milestones (see section 1.6.4.)

2.3.2. Nicotine Dependence

Total scores and scores on subscales of nicotine dependence measures have been repeatedly associated with end-state outcomes (e.g. Heatherton et al., 1991). Assessment of nicotine dependence at baseline included the following:

a) Baseline smoking rate was measured by self report (M= 28.7 cigarettes per day, SD=14.10).

b) Fagerström Tolerance Questionnaire (FTQ; Fagerström, 1978) is a standard tool for assessing nicotine dependence (M=5.9, SD=2.2). This measure has been used extensively in psychological and pharmacological research and has well-established psychometric properties (Fagerström & Schnieder, 1989). Like other versions of the FTQ (e.g. Heatherton et al., 1991), the variant used in this study included expanded scaling to yield more variance; this version also included variations on items. Consistent with Payne et al's (1994) report, factor analysis yielded two factors, morning smoking and difficulty refraining (M=0.1, SD=.99, M=0.05, SD=.95, respectively).

c) Fagerström Test of Nicotine Dependence (FTND; Heatherton et al., 1991). Scores on the FTND range from 0 to 10 with higher values indicating greater dependence on nicotine.

Using this scale, smokers can also be categorized as low (scores from 0 to 4), medium (4 to 7), or high (8 to 10) nicotine dependent. Test-retest reliability for the FTND is high (r=0.88; Pomerleau et al., 1994), and scores on the FTND correlate with cotinine levels (r=.39) and years smoked (r=.57) (see Currie, 2004).

d) Nicotine Dependence Syndrome Scale (NDSS; Shiffman, Hickox, Gnys, Paty & Kassel, 1995) is a more recent nicotine dependence measure incorporating a broader concept of dependence than previous measures, including DSM criteria. The NDSS was developed on the basis of Edward's (1986) concept of a dependence syndrome (z- scores: M=0.0 SD=0.98) consisting of a cluster of symptoms, and is correlated with other nicotine dependence measures. The NDSS also captures some dependence-relevant variance over and above the FTQ (Shiffman et al., 1995). NDSS factors include: Smoking Drive, Behavioral Priority, Tolerance, Continuity, and Stereotypy.

e) Baseline levels of salivary cotinine (ng/mL) were assessed while participants were still smoking regularly (M=319.07 ng/ml, SD=165.02). Large inter-individual differences exist in nicotine metabolism (Tyndale et al., 1999). Cotinine is nicotine's major metabolite, and because the half-life of nicotine is short (<2 hrs), cotinine levels are reliably used to reflect each smoker's nicotine intake (Benowitz et al., 1982).

2.3.3. Affect

Baseline affect was assessed with several questionnaires:

a) Affect Intensity Measure (AIM; Larsen, 1984). The Affect Intensity Measure (AIM), developed by Larsen (1984), is a 40-item instrument that measures a uni-dimensional construct known as Affect Intensity, which describes the intensity of emotional experience.

b) State-Trait Anxiety Inventory (STAI), Trait portion (M=2.11, SD=0.42, on a 1-4 scale; Spielberger, Gorsuch, Luschene, Vagg & Jacobs, 1983). The STAI has been used extensively in psychological research to capture enduring characteristics and patterns of anxiety, such as neuroticism.

c) Speilberger Trait Anger Scale (STAS; trait portion, M= 2.01, SD=0.47; Speilberger, Jacobs, Russell, & Crane, 1983). Similarly, the Speilberger Trait Anger measure yields a report of an individual's characteristic level of anger and hostility. Individuals experiencing high levels of anger may be more motivated to smoke to reduce the aversive state of anger. Tension, annoyance, irritation, fury and rage are components of the STAS and are designed to reflect the frequency of anger over time.

d) History of Major Depression (HMD, Shiffman et al, unpublished work). The HMD is a self-report questionnaire designed to reflect DSM-III-R and the Structured Clinical Interview for the DSM-III-R (American Psychiatric Association, 1987) criteria for a lifetime history of major depression (46% of participants met this criteria). History of major depression is related to an increased incidence of smoking, increased daily smoking rate, nicotine dependence, and poorer smoking outcomes (Fergusson, Goodwin, & Horwood, 2003; Persico, 1992).

2.3.4. Smoking Motives and Typology

The following questionnaires include assessments of what participants perceived as factors motivating them to smoke and to quit. Researchers have hypothesized that people with different motives may have varying degrees of success quitting when using different types of cessation interventions (Leary, Tchividjian & Kraxberger, 1994), and different smoking motives have been associated with variability in end-state outcome (Berlin et al., 2003). The importance of different

motives may vary by milestone, but research is not available to either support or refute this hypothesis.

a) Reasons for Smoking Scale (RFSS; Russell, Peto & Patel, 1974). The RFSS is based on Tomkins' affect management model (Tomkins, 1966) which hypothesizes that people smoke to manage positive and negative affect. The scale contains six factors (three items per scale) that examine different motives for smoking. The factor structure of the RFSS has been assessed in eight published studies (see Currie, 2004), which support the six factor model: Negative-affect reduction, psychological addiction smoking, habit smoking, pleasure-relaxation, stimulation, and sensorimotor manipulation. Factor scores derived from this measure include: Indulgent, Negative-affect, Sensorimotor, Addictive, Automatic, Stimulation, Psychosocial, and Psychomotor.

b) Occasions for Smoking Questionnaire (OFS; McKennell, 1970) assesses under what circumstances individuals believe they are most likely to smoke. Scores for the following seven factors were calculated for the OFS (McKennell, 1970): Nervous Irritation, Relaxation, Smoking Alone, Activity Accompaniment, Food Substitution, Social, and Social Confidence. Higher-order pharmacological and non-pharmacological factors from the OFS were also included.

2.3.5. Stress

a) Perceived Stress Scale (PSS; M=2.78, SD=0.54, on a 1-6 scale; Cohen & Williamson, 1988). The PSS measures the degree to which events are perceived as stressful. It is reported to tap how unpredictable, uncontrollable, and overloaded people find their lives. The PSS has 14 items that are not specific to particular situations, and it is easily applied to diverse populations. High scores on the PSS have been shown to correlate with depressive symptoms and physical symptoms such as headache, acid stomach, and

muscle tension (Cohen, Kamarck, & Mermelstein, 1983). Higher levels of perceived stress have been associated with poorer smoking cessation outcomes in studies assessing stress at baseline, and/or repeatedly throughout a quit attempt (e.g. Carey, Kalra, Carey, Halperin, & Richards, 1993).

b) Life situations. The Life Situations Questionnaire (LSQ) was constructed to measure primary appraisal in each of 21 life situations, rating each in terms of the amount of challenge and threat they posed.

c) General Life Questionnaire: The General Life Questionnaire (GLQ) is a 33-item instrument for assessing stressors associated with four domains of daily life: finances, employment, romantic relationships, and children.

2.3.6. Coping

The following measures assess what coping methods participants have used or propose that they would use in a variety of situations. Certain kinds of coping have been associated with lapses (Shiffman, Paty et al., 1996), and how an individual copes with lapse is a predictor of further smoking (e.g. Shiffman, Hickox et al., 1997).

a) Daily Coping Inventory (DCI; Stone & Neale, 1984) includes eight items representing eight intended categories of coping based on Lazarus' Transactional Model of Coping (Lazarus, 1966): distraction, positive reappraisal, planning/taking direct action, catharsis, seeking social support, relaxation, turning to religion. Participants read about a broad type of coping (a definition) and are then asked if they did or thought anything with the intention of functioning according such a definition (e.g. relaxing one's self) to cope with the "most bothersome" event of the day. DCI items and coping definitions have been validated extensively (Stone & Neale, 1984). Coping strategies in this measure are

dichotomous and tend to be consistent between similar situations. This instrument, however, was designed for daily assessment.

b) Ways of Coping Checklist (WCCL; Vitaliano, Russo, Carr, Maiuro, & Becker, 1985) is a questionnaire derived from Lazarus' Transactional Model of Stress (Flockman & Lazarus, 1980). Scales in this measure are related to appraisal and distress. The revised version used here contains 42 items and five dimensions of coping: problem focused, seeking social support, blaming self, wishful thinking, and avoidance (Folkman & Lazarus, 1980; Vitaliano, Russo, Carr, Mairuo, & Becker, 1985).

2.3.7. Abstinence Self-Efficacy

Participants described conditions under which they were likely to have smoked in the past, as well as under what conditions they anticipated having difficulty maintaining abstinence during the present quit attempt. They also reported the amount of time they expected that they could remain abstinent. Conditions across measures include environmental, psychological and physical states. Recent data suggest that people can predict under what circumstances they are likely to lapse (Gwaltney et al., 2002).

a) Confidence Questionnaire assesses confidence in one's ability to remain abstinent under 46 specific circumstances (CQ; 0-100% scale in increments of 10, Condiotte & Lichtenstein, 1981). This item yields a single summary score.

b) Relapse Situation Efficacy Questionnaire (RSEQ; Gwaltney et al., 2001) is a tool for assessing participants' confidence in their ability to resist smoking in various contexts via 75 items where ASE is rated on a 4-point scale. Confirmatory factor analysis has produced seven context-specific factors: negative affect, positive affect, social-food situations, idle time, restrictive situations (to smoking), low arousal, and craving. The RSEQ also yields a total summary score. Mean RSEQ subscale scores were calculated for

each individual. On average, participants reported a moderate level of confidence in abstaining for all items = 2.67 ± 0.46. Average RSEQ scores ranged from 1.65 to 3.95 (see Gwaltney et al., 2001).

2.4. ED System Hardware and Software

The ED system was implemented on a PSION Organizer II LZ 64 (PSION, Ltd.; London, England), a hand-held computer with a four-line, 20 character-per-line LCD screen, a clock-calendar, and an audio speaker. The computer was 5.6 x 3.1 x 1.1 in., weighed 8.8 oz., and was powered by a 9-volt battery. Data were recorded on computer chips in the ED. Software was developed specifically for this project. The user interface was very simple, using scrolling menus with on-screen prompts. Participants had access to only six keyboard keys (ON, ENTER, and four arrow keys). All assessment data were collected by means of structured input. For each question, the ED displayed a context (e.g. "for this smoking episode"), a question (e.g. how many cigarettes did you smoke?), and allowed the user to use arrow keys to scroll through a series of response alternatives (e.g., a numeric scale). The ED prompted participants to continue if they paused within an assessment for more than two min. The ED software prevented omissions (missing data) and entry of formally incorrect responses (e.g., "6" on a scale ranging from 1 to 5), and performed other data quality checks. Participants could correct keying errors within the current assessment but had no access to previous assessments. All entries were tagged with date and time.

2.5. Biochemical Verification

Participants provided breath samples (for carbon monoxide [CO] analysis) and saliva samples (for cotinine analysis) at every clinic visit before and after TQD. Some also provided CO measures one day post-quit. A combination of CO ≤ 10ppm and cotinine ≤ 46ng/ml was

considered validating (Cummings & Richard, 1988). For participants who reported quitting briefly but lapsing before their next session, we used saliva samples they provided "in the field;" for detecting 24 hr abstinence, the ED prompted participants to expectorate a saliva sample. The sample was considered to verify abstinence if the cotinine concentration was ≤ 6% of the participant's baseline saliva cotinine; this was based on the half-life of cotinine and its 95% confidence interval (Benowitz et al., 1982). Data from participants failing validation were handled differently depending on where in the analyses they failed to meet abstinence criteria. Participants who reported abstinence at all assessment points but who consistently failed to meet criteria were counted as failing to achieve initial abstinence (n=0). Participants who had verified periods of abstinence but failed to meet CO criteria on a single occasion (followed by at least 1 subsequent period of verified abstinence) were counted as lapsing (n=4). To avoid bias, lapse time for these participants was assigned at random within the period since the last assessment. Participants who had at least one assessment including CO-verified abstinence (e.g. TQD) but who failed to meet CO criterion at two or more proceeding, consecutive assessments were counted as relapsed (n=14). Although the infrequency of biochemical assessments in this study design does not permit us to distinguish lapses from relapse, in the absence of reliable self-report data, this measure can serve as a crude approximation of smoking behavior during the trial.

3. DATA ANALYSIS

3.1. Primary Analysis

Progression to the milestones was analyzed using Cox proportional hazards analysis of the survival function (Allison, 1988), with days as the unit of time. Survival analyses assess changes in risk for an event (traditionally death) by analyzing the incidence of events over the period of the study. Each time period contains a "risk set" of those people at risk of experiencing the event, and a hazard; i.e. the proportion of the risk set who experience the event in that period. Results of survival analyses are summarized in a hazard function, a chronological profile of these ratios.

Survival analyses improve upon traditional methods for studying changes in risk over time. As described by Willett and Singer (1993), survival analyses document variations in risk over time; therefore, estimates are not inextricably linked to the particular time frame chosen for data collection. Rates of relapse, for example, would be lower if recorded closer to the TQD. Second, survival analyses improve upon traditional analytical methods by offering methods for dealing with censored data (points at which individuals are no longer available for observation, but the reason for their absence is unknown, e.g. illness), thus providing estimates unbiased by length of observation or attrition. Unlike group comparisons, survival analyses take into account the reality that we cannot determine smoking status after participants were last observed (Allison, 1988; Curry et al., 1988). Third, if censoring times vary across individuals, people followed for longer periods of time have more opportunity to experience the target event than do those followed for shorter periods of time. Observed differences in rates of event occurrence in traditional analytical methods may be artifacts of the length of the period of observation, while censoring in survival analyses account for this difficulty. Survival analyses have been used

successfully to predict end-state outcomes (i.e. relapse) in numerous published reports of smoking cessation and other drugs of abuse (e.g. Stevens & Hollis, 1989).

Survival analysis is used here to model the risk of the defining events for the three proposed stages of the cessation process: TQD to initial abstinence, initial abstinence to lapse, and lapse to relapse. Cox proportional hazards analysis was chosen above the log-rank procedure primarily because the Cox model is based on probabilities rather than ratios between observed and expected values, which can be biased by changes in sample size. Further, although they make more assumptions (i.e., the analyses will be limited by the assumption of proportional hazards) than the log-rank test, Cox analyses are more robust when multiple covariates are entered into the model, preserving a larger number of participants within each cell.

The results of the survival analyses are reported as hazard ratios (HRs), representing increases in risk of failure on each subsequent day resulting from a one-unit increase in the independent variable (baseline characteristic). In order to compare the magnitude of prediction (the HR) across different baseline characteristics, all continuous variables were standardized prior to analysis. Thus the HR expresses the change in risk associated with a 1 standard deviation (SD) change in the predictor. As described above, the analyses considered cases where participants were not observed to abstain, lapse, or relapse before the end of the study to be censored as of their last day of observation.

Power for the survival analyses was calculated using PASS software (Hintze, 2004), that uses an algorithm developed by Schoenfeld (1983) and Hsieh (2000). This method is more robust than earlier techniques because the only assumptions it requires are about the distributions of survival time and predictor variables, not that of proportional hazards.

3.1.1. Univariate and Multivariate Models

Baseline variables were tested as predictors at each milestone. Variables that predicted outcome with HRs ≠ 1.00 and 95% CIs not including 1.00 were considered to have predicted outcome above a threshold suitable for interpretation (i.e. findings are considered predictors). Although a test producing similar results would typically be labeled "statistically significant", due to the multiplicity of tests in this design, alternate language (i.e. level of interpretation) was chosen so as not to imply an equivalent standard of statistical interpretation.

Univariate predictors of outcome meeting this level were entered into multivariate models. Each model included multiple univariate predictors within the same conceptual class. For example, if cigarettes smoked per day, FTND, HSI, gender, and age all predicted lapsing, then cigarettes per day, FTND and HSI would be entered into a "nicotine dependence" model, while gender and age would comprise a separate "demographics" model. The rationale for using this strategy was twofold. First, this strategy was used to help determine which variables incrementally contributed to outcome prediction above other predictors within the same class, so that the unique influences on outcome within a single class could be identified. Second, this method was chosen because multivariate models with variables from multiple classes (e.g. demographics, nicotine dependence, coping) cannot be informative about the underlying processes contributing to outcomes at a milestone without *a priori* theories for explaining possible interactions between them. Analyses of interactions between the large numbers of predictors examined in this project are beyond the scope of this report. Analyses of predictors are intended simply to highlight possible differences in underlying processes contributing to outcomes at the milestones, rather than to identify *the* specific processes which do so. Multivariate CPH models were built using SAS (v.8.1; 2001). The default entry procedure was used so that all predictors were simultaneously forced into the model. This method was selected

above other entry procedures (e.g. stepwise) because it would allow for the influence of all contributing variables to be examined simultaneously. The goal of building multivariate models was not to make the most parsimonious prediction model, but rather to investigate the nature of the relationships between a predictor variable in the context of other variables known to affect outcome.

3.2. Assessing Evidence of Differential Prediction Across the Milestones

Differential prediction across the milestones was assessed in three ways. First, in instances where a particular baseline characteristic predicted outcomes at more than one milestone, differences in the *magnitude* of the association may indicate that the variable has differential effects at different milestones. For example, coping style may mildly predict initial abstinence (e.g. HR=1.2), but may highly predict lapse (e.g. HR=7.0); therefore, the magnitude of the HRs for each baseline characteristic was compared across milestones. There is no established way to make this kind of comparison, so I used a threshold of 33% difference in HRs to represent a meaningful difference between milestones. That is, I regarded differences of this magnitude as interpretable.

Second, trends across groups of predictors were examined to determine whether multiple variables within a certain class uniquely predicted outcomes at one milestone and not the others. For example, if four out of five scales on a questionnaire assessing coping style predicted initial abstinence and no similar pattern of results was found for lapse or relapse, this would be considered evidence of differential prediction.

Finally, changes in the direction of prediction across milestones were considered to add weight to evidence of differential prediction first established with either of the first two criteria. If results suggested that female gender, for example, put participants at increased risk for lapse but decreased risk for relapse, differences in the direction of prediction between gender and

lapse, and gender and relapse, would be considered to suggest differential prediction of outcome at the lapse and relapse milestones.

3.3. Secondary Analyses: Assessment of Sequential Filtering Effects

The proposed cessation milestones are sequential and cascading: Only those participants who pass a prior milestone (e.g., initial quitting) become eligible (at risk) for the following one (e.g., lapsing). Thus, each step of the analysis focuses on a progressively smaller, less representative subset of the original sample (Willett & Singer, 1993; Shiffman et al., under review). For example, if the most dependent smokers do not achieve initial abstinence, then the analysis of lapses (i.e. those who achieved initial abstinence) is limited to a less dependent sample. As a result, while dependence might have predicted lapse if the entire sample had abstained (for example, if participants had received a treatment improving rates of initial abstinence), analyses of the filtered sample would not reveal this relationship. Indeed, 'filtering' at each step may affect the sample studied at each milestone, as well as the baseline characteristics that predict outcomes at subsequent milestones. Although the difficulties associated with analyzing sequential outcomes has been recognized in other literatures (Meyer, 1990; Dekimpe, Van de Gucht, Hanssens, & Powers, 1998; Hser, Anglin & Liu, 1991), no accepted practical solution has emerged.

I used two complimentary procedures to test for the effects of "filtering". I first examined the degree to which the means and standard deviations of predictor variables changed across milestones to determine whether subsets of the sample (e.g. the oldest participants) were systematically being removed. I then examined trends in patterns of predictive strength across the milestones to determine if filtering effects were making prediction progressively weaker at later stages in the cessation process. Consider a situation in which progressively lower levels of

nicotine dependence emerged after each milestone (i.e. the most nicotine dependent participants failed at earlier milestones), but in which nicotine dependence continued to predict outcomes at relapse. According to the first criterion, filtering effects would have occurred, as evidenced by systematic changes in the mean and SD of scores on the measure of nicotine dependence. However, in this case, nicotine dependence would still be considered important for predicting outcomes independent of the filtering process because it predicted relapse even after the most dependent participants were removed from the sample.

In contrast, patterns of findings that would be most troubling would be those in which variables that predicted earlier milestones failed to predict later milestones. In other words, the strength of prediction of a baseline characteristic would decrease as more participants were eliminated through filtering. For example, if nicotine dependence strongly predicted initial abstinence, moderately predicted lapse, and did not predict relapse, its failure to predict relapse could be attributed to the fact that the most dependent subjects were no longer in the sample. Under these circumstances, no conclusion about the suspect variable's status as a non-predictor of relapse could be drawn.

3.3.1.1. Power for Survival Analyses

Analyses were run to determine the power of this study for detecting a variety of effect sizes at each milestone (see Figure 1). Power for observing predictors of initial abstinence was based on a Cox regression of the log hazard ratio on standardized covariates (i.e. SD=1.00), with sample size of n=260, and event rate of 0.05. Using these parameters, a HR of 2.20 could be detected with 80% power (a *large* effect size, see Cohen, 1988). Power for predicting lapse was based on the same model, but with sample size of n=248 and event rate of 0.60. This resulted in 80% power for detecting a HR of 1.26 (a small effect size). Power for predicting relapse was based on

a sample size of n=149 and event rate of 0.27. Using these parameters, a HR of 1.55 (a medium effect size) could be detected with 80% power. Overall, power was greatest for detecting predictors of lapse, followed by relapse, and initial abstinence, respectively. While power for effects on initial abstinence was modest, power for detecting predictors of lapse and relapse was considered adequate.

4. RESULTS

4.1. Sample Characteristics

Participants enrolled in the study at the Target Quit Date (TQD) were predominantly Caucasian (92%), female (59%), and averaged 34 (SD=10.9) years of age (see Table 1). Participants were moderately nicotine dependent (mean FTND = 5.9) and smoked approximately 27 cigarettes per day.

4.2. Milestones as Outcomes

The majority of participants (n=248, 95%) achieved initial abstinence during the study period. Sixty percent (60%; n=149) of those who abstained recorded at least one lapse, and 27% (n=40) of those who lapsed also met criteria for relapse.

4.2.1. Initial Abstinence

Figure 2 presents the survival curve for all participants (n=260) who completed the baseline phase of the study and were still enrolled on the TQD. The survival curve shows an initial steep drop, followed by a relatively flat line indicating that most participants quit shortly after TQD. Ninety-five percent of participants successfully quit for 24h (n=248), with 77% doing so on TQD (see Table 2). Of the 23% of participants who did not abstain on TQD, 92% did so within 2 days of TQD, and 100% of those who eventually abstained did so by 13 days post TQD.

4.2.2. Lapse

Figure 3 presents the survival curve for all participants who successfully quit (as described above, n=248). In Figure 3, the scale on the X-axis is days since quit. Like Figure 2, the shape of the survival curve shows a negatively decelerating shape, indicating that many participants lapsed shortly after quitting, with 50% lapsing within the first 11 days after quitting. A total of 60% (n=149) of participants lapsed within four weeks after the TQD (Table 2).

4.2.3. Relapse

Figure 4 presents the survival curve for all participants who quit and lapsed and were therefore eligible to relapse (n=149). The scale on the X-axis is days since first lapse. Of the participants reporting a lapse, 27% (n=40) reported relapsing (i.e. smoking at least 5 cigarettes per day for three consecutive days) during the four weeks post TQD (Table 2). The first relapse occurred four days after the participant's first lapse. Subsequent to the first relapse, rates of relapse remained roughly constant until the end of the observation period.

4.3. Traditional Outcomes

Thirty-three percent (33%; n=85) of participants in the original sample (n=260) met criteria for continuous abstinence and 41% (n=106) met criteria for 7-day point prevalence abstinence (see Table 2).

4.3.1. Continuous Abstinence

Continuous abstinence reflects the percentage of former smokers who did not smoke since TQD (Velicer & Prochaska, 2004). Using observations recorded during the 4 weeks of ED monitoring following the TQD, 67% of the sample (n=175) either reported some smoking (n=149), failed to meet biochemical criteria for abstinence (n=11), or were lost to follow-up (n=15).

4.3.2. Seven-Day Point Prevalence

Point-prevalence abstinence is defined as the percentage of former smokers who are abstinent at a particular point in time (Velicer & Prochaska, 2004), typically for a period of 7 days (Hughes et al., 2004). Seven-day point-prevalence was calculated for the fourth week of ED observation. Any smoking, violation of biochemical verification of abstinence, or loss to follow-up was used to indicate an unsuccessful quit attempt. According to this definition, 59% (n=154) of participants were counted as failed

4.4. Predicting Outcomes at the Milestones

4.4.1. Filtering Effects

To determine whether participants were systematically removed from the sample after each milestone, the means and standard deviations of standardized (mean = 0, SD = 1) predictor variables were compared across the samples eligible to quit, to lapse, and to relapse. Means and standard deviations of predictors were very similar across all three samples (Figures 5 and 6), suggesting that filtering effects did not greatly affect the sample composition as participants moved through milestones.

Trends in predictor strength across the milestones were also examined to detect any possible filtering effects. Decreases in strength (magnitude) of prediction across the milestones indicated filtering effects. Trends in this direction across all three milestones (initial abstinence, lapse and relapse) were generally not observed. However, where filtering was expected to be the greatest (i.e. moving from lapse to relapse), there were instances where the strength of prediction for relapse was notably less (> 33%) than the strength of prediction for lapse. These differences (detailed in 4.2.2.2), however, did not tend to cluster within a particular class of variables (e.g., filtering out the most nicotine dependent subjects), again suggesting that overall, filtering did not greatly affect the results of this study.

4.4.2. Predictors of Outcome at the Milestones

Predictors of outcome were derived from univariate survival analyses, in which a single baseline characteristic was used to predict outcome at a single milestone. Figure 7 shows the hazard ratios (HRs) of predictor variables at each milestone (a version including CIs is included in the Appendix). Very few predictors of outcome were identified. Consequently, there was little differential prediction between milestones. This was true whether considering the 33% difference criterion (see section 3.2), changes in the direction of prediction, or by considering groups of predictors representing a particular conceptual class. However, a few trends towards specificity

of prediction (i.e. consistency in directionality of findings for individual predictors within a certain conceptual class) should be noted. Higher scores on measures of nicotine dependence and stress were strongly associated with relapse but not with initial abstinence or lapse. Similarly, indices of smoking motives related to nicotine dependence were also associated with relapse, and not the other milestones. Below, results of the univariate analyses are reviewed.

a) Demographics: None of the demographic variables assessed predicted initial quit. Living with other smokers increased participants' risk of lapsing χ^2 (1, N = 248) = 5.26, p<0.02, HR=1.27, CI = 1.04 – 1.56). No demographic variable predicted relapse. Although gender did not predict outcome at any of the milestones, the difference in risk for failure associated with female gender was greater than 33% between lapse (HR = 1.14, CI = .82 – 1.58) and relapse (HR = .85, CI = .46 – 1.59), and the direction of prediction was reversed. Specifically, women were more likely to lapse, but (once lapsed) less likely to relapse. Similarly, participants living with another smoker were more likely to lapse, but (once lapsed) were less likely to relapse (33% difference in HRs; and change in direction of prediction; relapse, HR = .82, CI = .55 – 1.22, and lapse HR = 1.27, CI = 1.04 – 1.56). The magnitude of prediction (HRs) across milestones did not differ by 33% for any other variable in this class.

b) Nicotine Dependence: No measure of nicotine dependence predicted initial abstinence. Participants with higher total scores on the NDSS were more likely to lapse χ^2 (1, N = 248) = 3.83, p<0.05, HR=1.24, CI = 1.04 – 1.48). Participants reporting higher number of cigarettes smoked per day (CPD) χ^2(1, N = 149) = 10.37, p<0.001, HR = 1.57, CI = 1.16 – 2.12) and higher scores on the Heaviness of Smoking Index (HSI, χ^2 (1, N = 149) = 4.52, p<0.03, HR=1.45, CI = 1.03 – 2.03), were more likely to relapse. Of note, both of

these indices represent higher rates of daily smoking. CPD was the only variable in this class that was a stronger (>33%) predictor of relapse than of lapse (HR relapse = 1.57 > HR lapse = 1.18). Univariate predictors of relapse were entered into a multivariate model. This model included measures of nicotine dependence and smoking motives (also reflecting nicotine dependence). Results of this model are described in section c – Smoking Motives and Typology (see also Table 3).

c) Smoking Motives and Typology: Smoking motives and typology did not predict initial abstinence or lapse. Participants scoring higher on the Addictive Smoking factor from the Russell Reasons for Smoking Scale (RFSS; Russell et al., 1974) and the higher-order Pharmacological Smoking factor from the McKennell Occasions for Smoking Scale (OFS; McKennell, 1970) [χ^2 (1, N = 149) = 8.40, p<0.004, HR=1.57, CI = 1.11 – 2.23) and χ^2 (1, N = 149) = 10.08, p<0.002, HR=1.55, CI = 1.10 – 2.21, respectively] were more likely to relapse. Participants with higher social smoking motives (as on the OFS) were more likely to lapse (HR = 1.11, CI = 0.94 – 1.31), but once lapsed, were less likely to relapse (HR = .83, CI = .60 – 1.16). This difference, however, did not meet the 33% difference criterion. A multivariate model including the Addictive Smoking and Pharmacological Smoking factors, as well as cigarettes smoked per day and the HSI, was built to predict relapse (Table 3). Only the Addictive Smoking factor maintained an interpretable level of prediction in the multivariate model.

d) Abstinence Self-Efficacy (ASE): Participants with lower scores on the Confidence in Smoking Situations (CSS) questionnaire χ^2 (1, N = 260) = 4.01, p<0.05, HR = 0.88, CI = 0.77 – 1.00) and the Low Arousal factor from the RSEQ were less likely to achieve initial abstinence χ^2 (1, N = 260) = 6.06, p<0.01, HR=0.85). The CSS and the Low Arousal

factor were entered into a multivariate model to predict initial abstinence. Only the Low Arousal factor predicted outcome at an interpretable level in the multivariate model (see Table 3). Participants scoring lower on the CSS χ^2 (1, N = 248) = 9.07, p<0.003, HR=0.78, CI = 0.67 – 0.92), and the Craving (χ^2 (1, N = 248) = 6.53, p<0.01, HR=0.81, CI = 0.69 – 0.95), Negative Affect χ^2 (1, N = 260) = 8.69, p<0.003, HR=0.78, 0.66 – 0.92), Social-Food χ^2 (1, N = 248) = 5.08, p<0.02, HR=0.83, CI = 0.71 – 0.98), Low Arousal χ^2 (1, N = 248) = 5.42, p<0.02, HR=0.82, CI = 0.70 – 0.97), and Idle Time χ^2 (1, N = 248) = 3.96, p<0.05 HR=0.85, CI = 0.73 – 1.00) factors of the RSEQ were more likely to lapse. A multivariate model predicting lapse showed that the CSS was the most important independent predictor of outcome, followed by the Idle Time and Negative Affect RSEQ subscales (see Table 3). The only ASE variable affected risk for relapse was the CSS χ^2 (1, N = 149) = 4.22, p<0.04, HR=0.69, CI = 0.49 – 0.95). The CSS predicted outcome at all three milestones and the HRs for each milestone did not differ by 33%. This suggests that the relationship between scores on the CSS and outcomes were similar across the milestones. Similarly, the Low Arousal factor of the RSEQ predicted outcome both at initial abstinence and lapse, and the HRs at initial quit and lapse did not meet the 33% difference criterion. Again, suggesting similarities rather than differences in the association between the ASE variables and outcomes across the milestones. The magnitude of prediction (HRs) across milestones did not differ by 33% for any other variable in this class.

e) Affect: A history of major depression did not predict quit, lapse or relapse. None of the items used to assess other affective traits (Spielberger Trait Anger and Anxiety inventories, the Affect Intensity Measure) predicted outcome at any milestone. The

magnitude of prediction (HRs) across milestones did not differ by 33% for any of the variables in this class.

f) Perceived Stress: Measures of perceived stress (PSS, General Life Questionnaire, Life Situations Questionnaire, Partner Interaction Questionnaire) did not predict initial abstinence or lapse. Participants reporting higher scores on the Job subscale of the Life Situations Questionnaire (LSQ; χ^2 (1, N = 149) = 4.10, p<0.04, HR = 1.44, CI = 1.01 – 2.08), subscales from the General Life Questionnaire (GLQ), including the Job Load subscale (χ^2 (1, N = 149) = 5.11, p< 0.02, HR= 1.43, CI = 1.05 – 1.96), the Social Equality subscale (χ^2 (1, N = 149) = 4.00, p<0.05, HR=1.69, CI = 1.01 – 2.78), and the Child Discipline subscale (χ^2 (1, N = 149) = 4.86, p<0.03, HR=1.70, CI = 1.06 – 2.76) were more likely to relapse. Moreover, higher ratings of stress related to participants' jobs (lapse HR = 1.12, CI = 0.96 – 1.33; relapse HR = 1.45, CI = 1.01 – 2.08), child discipline (lapse HR = 1.25, CI = .98 – 1.39; relapse HR = 1.69, CI = 1.06 – 2.70), and perceived social equality (lapse HR = 1.02, CI = 0.78 – 1.11; relapse HR = 1.69, CI = 1.01 – 2.78) put participants at increased risk for relapse above (33%) risk for lapse. Social equality, child discipline, job stress, and job load subscales of the GLQ were entered into a multivariate model for predicting relapse. Social equality, child discipline and job load all maintained an interpretable level of prediction in the multivariate model (see Table 3).

g) Coping: Measures of coping (DCI, WOCS) did not predict outcome at any of the milestones. The magnitude of prediction (HRs) across milestones did not differ by 33% for any of the variables in this class, nor did the direction of prediction change across milestones.

4.5. Predictors of Traditional Outcomes

Logistic regression analyses were used to determine predictors of traditional outcomes. Very few predictors of traditional outcomes were identified. Demographic, stress and ASE variables predicted continuous abstinence. Specifically, participants living with another smoker $\chi^2(1, N=260) = 4.85$, $p = 0.03$, OR=0.65, CI = 0.44 – 0.95), reporting non-Caucasian ethnicity $\chi^2(1, N=260) = 4.25$, $p = 0.04$, OR=0.38, CI = 0.15 – 0.95), higher levels of stress from child discipline (GLQ, $\chi^2(1, N=260) = 5.45$, $p = 0.02$, OR=1.69, CI = 1.09 – 2.62), and lower levels of ASE on the CSS $\chi^2(1, N=260) = 11.19$, $p = 0.007$, OR=1.48, CI = 1.11 – 1.98), RSEQ (total score; $\chi^2(1, N=260) = 7.18$, $p = 0.09$, OR=1.26, CI = 0.97 – 1.65), RSEQ Negative affect $\chi^2(1, N=260) = 9.55$, $p = 0.002$, OR=1.55, CI = 1.17 – 2.05), RSEQ Idle time $\chi^2(1, N=260) = 9.34$, $p = 0.002$, OR=1.58, CI = 1.18 – 2.12), RSEQ Social and food $\chi^2(1, N=260) = 5.10$, $p = 0.02$, OR=1.37, CI =1.04 – 1.79), RSEQ Low arousal $\chi^2(1, N=260) = 7.98$, $p = 0.005$, OR=1.49, CI = 1.13 – 1.96), and RSEQ Craving subscales $\chi^2(1, N=260) = 7.34$, $p = 0.007$, OR=1.47, CI = 1.11 – 1.95) less likely to abstain. No measure of nicotine dependence, affect, or coping predicted continuous abstinence.

Measures of demographics, stress and ASE also predicted failed 7-day point prevalence abstinence. Participants living with another smoker $\chi^2(1, N=260) = 8.83$, $p = 0.003$, OR=0.60, CI = 0.43 – 0.84), reporting higher levels of stress on the Partner Interaction Questionnaire $\chi^2(1, N=260) = 5.12$, $p = 0.02$, OR=1.35, CI = 1.04 – 1.74), and lower levels of ASE on the CSS $\chi^2(1, N=260) = 12.02$, $p = 0.0005$, OR=1.60, CI = 1.23 – 2.09), Low Arousal $\chi^2(1, N=260) = 5.38$, $p = 0.02$, OR=1.36, CI = 1.05 – 1.76) and Craving subscales of the RSEQ $\chi^2(1, N=260) = 3.00$, $p = 0.08$, OR=1.26, CI = 0.97 – 1.64) were less likely to be abstinent during the last week of observation. No measure of nicotine dependence, affect, coping, or smoking motivations predicted 7-day point prevalence.

5. DISCUSSION

This study tested the utility of the milestones as an organizational framework for the process of smoking cessation. Results of this study demonstrated that all three milestones were significant barriers in the process towards successful smoking cessation, in that some participants failed at each milestone – some did not attain abstinence, some lapsed, and some relapsed.

This study aimed to test the utility of the milestones framework by identifying pretreatment characteristics that could differentially predict outcomes at the milestones. Differential prediction was to suggest different processes contributing to outcomes at each milestone. Few predictors of any outcome were identified. As a consequence, few *differential* predictors of outcome were identified. Accordingly, the study did not provide a context in which differential prediction could be evaluated as an indicator of the milestones framework's utility for studying changes in the cessation processes. Therefore, findings did not support (or refute) differential prediction of outcome across the milestones. Possible explanations and implications of these null results are discussed below.

5.1. Findings

5.1.1. Milestones as Barriers to Successful Smoking Cessation

Results of this study suggest that each of the milestones represents a significant barrier to successful smoking cessation. The proportion of participants failing to achieve 24h of smoking abstinence was 5% overall, and is in agreement with studies of treated (Shiffman et al., under review) and untreated (e.g. Garvey et al., 1992) samples. Although the proportion of participants who were unable to surpass the initial abstinence milestone was small, almost one quarter (23%) of the sample was unable to quit on the scheduled target quit day (TQD), despite quitting later. Failing to quit on TQD would lead to a "failed" designation in some studies where continuous abstinence was the outcome criteria. Thus, it is possible that in previous reports, up to a quarter

of prospective quitters earned a "failed" designation because they did not achieve initial abstinence. Further, it could be expected that in other studies, larger numbers of participants may have "failed" at the initial abstinence milestone, especially if participants were selected independent of high motivation and self efficacy to quit.

More than 60% of those who quit reported a lapse. The finding that more than half of the participants lapsed within the first four weeks is in agreement with other reports. Despite participants' best efforts and intentions, the majority of smokers are not able to maintain abstinence from cigarettes even for a few weeks (Garvey et al., 1992; Shiffman & Waters, 2004). This finding is also in agreement with a recent review of published survival curves of self-quitters. Hughes, Keely and Naud (2004) found that in 7 of the 8 relapse curves they examined, the majority of smokers lapsed within the first 8 days post TQD. In this sample, as in others (Garvey et al., 1992; Shiffman et al., under review), not all participants who lapsed reported a relapse. In short, many participants likely earned a "failure" designation in previous smoking cessation trials by lapsing, even though they never reported a full-blown relapse.

Approximately one third of participants who lapsed reported a relapse during the study period. The number of relapses reported here is lower than in other studies (e.g. Jarvis et al., 2003) for at least three reasons: (1) The follow-up interval in this study was very brief, giving participants less of an opportunity to relapse while under observation; (2) participants who never quit were removed from the pool of possible relapsers; and (3) lapse was distinguished from relapse. Nonetheless, investigating relapse independent of the other two milestones demonstrates that during the early stages of a quit attempt (i.e. the first 4 weeks), many highly motivated participants resume smoking cigarettes multiple times per day.

In sum, each milestone represents a subset of participants who, using traditional, end-state outcome criteria, would be counted as "failed." Using the milestones, however, it is possible to see that these participants earn this designation as a result of varying degrees of success with smoking abstinence (e.g. failing to achieve initial abstinence vs. having had only a single lapse). Thus, these findings suggest that the milestones have some conceptual utility for distinguishing between multiple outcomes falling under the umbrella of end-state failure or success.

5.1.2. Prediction of Outcomes at the Milestones

Despite the large number of baseline characteristics examined, very few predictors of any outcome were identified. One possibility is that by dividing end-state outcomes into three separate outcomes (i.e. the milestones), sample size, event rate and power for detecting potential predictors were reduced and potential predictors of outcome were overlooked. Analyses of predictors of traditional outcomes (continuous abstinence and 7-day point prevalence) that included the entire original sample and substantial failure rates (67% continuous abstinence, and 59% 7-day point prevalence), however, produced similar findings with a similar dearth of significant predictors. This suggests that the segmentation of the outcome into three milestones (and consequent loss of power) did not account for the lack of prediction. Further, as illustrated in Figure 1, analyses for detecting predictors at all three milestones were generally adequately powered, at least for detecting large effects.

More likely, however, stringent recruitment criteria may have limited the variance of a number of baseline characteristics that might have otherwise predicted outcome within the sample. For example, participants were selected for high levels of perceived motivation and self-efficacy for quitting. Participants were also educated, willing to endure a challenging research protocol, and were treatment-seeking, suggesting that they were not representative of the general

population of smokers. Participant characteristics previously associated with end-state outcomes, such as coping style (Kamarck & Lichtenstein, 1988), may have been somewhat uniform across the sample (e.g. with participants primarily reporting effective coping styles), and thus did not contain sufficient variance to emerge as predictors of any outcome. Indeed, predictors of outcome in a highly motivated, confident, and educated sample (as was the case in this study) may not generalize to typical community samples of prospective quitters, and vice versa.

Overall, the magnitude of prediction by baseline characteristics at all three milestones was generally modest (see Figure 7). If the level of interpretability was adjusted to account for the multiplicity of tests in this design (e.g. with a Bonferroni adjustment), all of the interpreted effects would be considered non-significant. Based on the number of findings relative to the number of tests, it could be argued that predictors of traditional and milestone outcomes are merely statistical artifacts, rather than evidence of conceptual relationships. However, the results of exploratory studies that include multiple statistical tests should not be interpreted based on statistical significance alone. Tests of statistical significance are designed to provide evidence for or against a specific hypothesis, which was not the intended goal of this study. Rather, this study was a preliminary investigation of trends towards differential prediction across the milestones. Examinations of trends in the data can suggest areas in which future theory-driven, hypothesis-based investigations might be fruitful. Failure to identify predictors of outcomes based on tests of statistical significance, therefore, does not negate the results suggested by other methods of assessment used in this study.

In any case, the analysis found few predictors, and modest magnitude of prediction at the milestones. Consequently, this study failed to provide a context in which the utility of the

milestones framework could be tested based on differential prediction. Thus, findings from this study cannot be used to support the use of the milestones framework as a tool for identifying processes contributing to end-state outcomes.

5.1.3. Differential Prediction of Outcome at the Milestones

A consequence of identifying only a few predictors of milestones is that it limits the extent to which differential prediction across the milestones can be established. Indeed, little differential prediction of outcome was found in this study (though there was some; see below). Thus, the findings of this study do not support the utility of the milestones framework. However, the results of this study also do not refute the utility of the framework for identifying different processes contributing to the milestones, either. Rather, results suggest a number of methodological limitations of this study design that may have prevented the identification of predictors of outcome, especially for initial abstinence and lapse.

5.1.3.1. Evidence for Differential Prediction of Relapse?

Two classes of variables, nicotine dependence and stress showed reasonably consistent trends towards predicting relapse, but not initial abstinence or lapse. Specifically, relapse seemed to be predicted by variables associated with nicotine dependence or stress, but not those related to coping, affect or demographics. The addictive and pharmacological smoking motives of the Occasions for Smoking Scale (OFS) have been shown to be associated with components of nicotine dependence, such as smoking rate, craving, and withdrawal (see Shiffman, 1993). Participants reporting higher daily smoking rates, higher scores on the HSI, and higher scores on the pharmacological and addictive smoking motives of the OFS were at increased (> 33%) risk for relapse, as compared to failing to abstain or lapsing. Where differences in the magnitude of prediction between milestones were identified, other variables in the same class (i.e. nicotine dependence) tended to demonstrate trends towards differential prediction for relapse (see Figure

7). For example, participants scoring higher on the NDSS Total score and NDSS Tolerance subscales appeared to be more likely to relapse (but not to fail to abstain or lapse), with HRs falling just below the level of interpretation. Thus, evidence from two distinct methods for assessing differential prediction (representing magnitude and frequency of occurrence), suggest that nicotine dependence may differentially predict relapse.

Recent research by Shiffman et al (under review) also supports the notion that nicotine dependence is particularly important in relapse. Treatment with high-dose (35mg) nicotine patches had the greatest effects (more than 3-fold the effect sizes at other milestones) on progression from lapse to relapse. Since nicotine replacement specifically targets nicotine dependence processes, this is consistent with the notion that nicotine dependence is particularly important in promoting progression to relapse.

The finding that nicotine dependence predicted relapse and not initial abstinence or lapse is not unexpected. Participants with the highest levels of nicotine dependence typically experience the most severe abstinence syndromes. Lapsing may provide higher levels of negative reinforcement, thus increasing the likelihood of further smoking (i.e. relapse; Hughes, 1993). While it is possible that a severe abstinence syndrome could be associated with shorter latency to lapse, this seems less likely because nicotine withdrawal symptoms, such as craving, decrease over time (Scharf et al., 2005). In other words, if participants achieved initial abstinence despite symptoms of withdrawal, the risk of withdrawal predicting lapse should only continue to decrease over time.

Like nicotine dependence, measures of stress taken at baseline demonstrated some evidence of differential prediction of relapse. Participants with higher scores on three subscales from the General Life Questionnaire (GLQ) (stress from work, child discipline, and perceived

social inequality), and the Job subscale from the Life Situations Questionnaire (LSQ) were more likely to relapse (>33%) than they were to fail to initially abstain or lapse. Trends towards prediction by other measures of stress (e.g. the Perceived Stress Scale, other GLQ and LSQ subscales) also suggested that increased levels of stress put participants at greater risk for relapse, while the effects of stress on the other milestones were considerably less clear (see Figure 7).

Existing literature provides some support for baseline measures of stress as predictors of relapse. Previous research has demonstrated that continuous efforts at self-control, such as efforts to cope with on-going stressors, can degrade over time (Muraven & Baumeister, 2000). One possibility, therefore, is that participants with high levels of stress, such as stress associated with the workplace, may have the least resources for coping with a lapse and for ultimately regaining abstinence. While it could be argued that baseline measures of stress should predict lapsing as reliably as relapse, participants reported high levels of abstinence self-efficacy related to lapsing at baseline, despite high levels of stress. Similarly, achieving initial abstinence demonstrates that prospective quitters can abstain from smoking despite high levels of baseline stress. Decreases in self-efficacy after each successive lapse (Abstinence Violation Effect; Marlatt & Gordon, 1985), however, may represent a novel stressor not present at baseline that cause individuals to relinquish self control and ultimately relapse.

Similarly, chronic stress assessed at baseline may predict relapse more reliably than initial abstinence or lapse because relapse is a chronic smoking behavior, while initial abstinence and lapse status can be determined by an isolated event (i.e. a single puff on a cigarette). Relapse is comprised of multiple samples of smoking behavior occurring over several consecutive days. As a consequence, levels of stress assessed at baseline, particularly by instruments designed to

capture typical levels of daily stress (rather than the highest or lowest levels participants have experienced) may be more reliable predictors of relapse. In contrast, initial abstinence and lapse are determined by a single puff on a cigarette. A single puff is an isolated event which may not accurately represent an individual's typical behavior (especially if the single puff does not proceed to relapse). Prediction of behavioral anomalies (such as the first lapse) by baseline levels of stress is unlikely. Alternatively, *changes* in levels of stress may be more likely to predict changes in smoking behavior. Indeed, some research suggests that lapses can be predicted by dynamic shifts in factors affecting smoking behavior (Shiffman, Paty et al., 1996; Shiffman, Hickox et al., 1997; Shiffman & Waters, 2004). In any case, results of this study suggest that stress may be associated with increased risk for relapse, more so than failure to achieve initial abstinence or lapsing.

Finally, it is worth noting that a large number of abstinence self-efficacy (ASE) variables predicted lapse, but not initial abstinence or relapse. However, several lines of evidence suggest that these findings do not represent differential prediction of lapse. First, the direction of prediction across all three milestones was consistent, such that higher levels of ASE appeared to be related to abstaining, avoiding lapses, and avoiding relapse. In particular, scores on the Confidence in Smoking Situations (CSS) questionnaire predicted outcome at interpretable levels at all three milestones. Second, although numerous ASE variables reached interpretable levels for predicting lapse while fewer ASE variables predicted initial abstinence or relapse, power for detecting predictors of lapse was greater than for the other two milestones. If power for identifying predictors of outcome was equivalent across all three milestones, many ASE predictors of lapse would have also likely predicted outcomes at initial abstinence and relapse.

Thus, despite the large number of ASE variables predicting lapse, the data do not support differential prediction of lapse.

5.1.3.2. Failing to Find Differential Prediction for Initial Abstinence and Lapse

No class of variables differentially predicted initial abstinence or lapse, but stress and dependence variables seemed to predict progression to relapse. This may indicate that stress and dependence are truly unique predictors of relapse, but we also need to consider methodological reasons why relapse was the only outcome associated with apparently unique predictors. The failure to find unique predictors of lapses was surprising for two reasons: 1. Most prior prediction studies using continuous abstinence measures were essentially lapse prediction studies; 2. The power of the analyses were greatest for predicting lapses (see Figure 1).

With this as background, why did relapse seem to be more "predictable?" One possibility is that relapse was measured more precisely than initial abstinence or lapse. This, however, seems unlikely because operational definition of relapse is the most complex and artificially derived of the three milestones (e.g. three consecutive days of smoking five or more cigarettes per day, as opposed to seven consecutive days of any smoking, etc.). However, relapse may inherently be a more robust outcome, since it depends on subjects' consistent behavior over multiple days, whereas initial abstinence and lapse are determined by a single puff on a cigarette, which may not represent an individual's typical behavior (especially if a lapse does not proceed to relapse).

Alternatively, failure to find predictors of initial abstinence and lapse could be related to the way in which predictors were assessed. Assessments were taken once at baseline, and questionnaires were designed to capture participants' general psychological states (e.g. *Quite often* I cannot overcome unpleasant thoughts that bother me) and behaviors (e.g. How many cups

of coffee do you consume on an *average* day?), rather than extremes in their experiences. Indeed, some research suggests that lapses can be predicted by dynamic shifts in factors affecting smoking behavior (Shiffman, Paty et al., 1996; Shiffman, Hickox et al., 1997; Shiffman & Waters, 2004). In contrast, relapse represents a larger, drawn-out sample of smoking behavior that is less likely to be swayed by unpredictable proximal events. Because relapses are more prolonged and stable, they may be more reliably predicted by measures of general psychological states and behaviors than isolated smoking events are. Failure to find predictors of initial abstinence and lapse, therefore, may be related to the way in which predictors were assessed.

5.1.4. Summary of Evidence for Differential Prediction between the Milestones

Overall, as a consequence of the paucity of predictors of initial abstinence and lapse, the findings of this study do not support the utility of the milestones framework for identifying differential predictors (and thus, processes) contributing to outcomes at different stages of the cessation process. Although some evidence from this study suggests that nicotine dependence and stress differentially predict relapse, these findings would need to be confirmed by additional studies. Thus, at present, the goal of demonstrating the utility of the milestones framework for identifying differential prediction between outcomes has not been achieved.

5.1.5. Multivariate Predictor Models

There were instances where multiple variables from a single conceptual class (e.g. nicotine dependence) predicted outcome at the same milestone (e.g. relapse). When this occurred, all of the predicting variables were entered into a multivariate model. This strategy was intended to investigate the relative importance of each variable in the context of other variables known to affect outcome. Unfortunately, the multivariate models constructed in this study could not contribute to the overall interpretation of the data.

An important limitation of the multivariate models is that because the models were constructed based on conceptual class, there is necessarily a high degree of multicollinearity within each model. Multicollinearity occurs when the explanatory variables in a multivariate regression are so highly correlated with one another that it becomes very difficult (if not impossible) to disentangle their influences and obtain a reasonably precise estimate of each one's effects. If the effects of multicollinearity are extreme, suppressor effects can occur such that one variable substantially increases the multiple correlation when combined with another variable that is only modestly correlated with outcome (Sithisarankul, Weaver, Diener-West, & Strickland, 1997). Increases in multiple correlation can also complicate the interpretation of findings by changing the direction of prediction. Examination of the Variance Inflation Factors (VIF's) in Table 3 confirms that multicollinearity within the multivariate models in this study was high (for example, a VIF of 2.5 = an R^2 of 0.6). For these reasons, the results of the multivariate models cannot be reliably used to meet their intended goal of identifying meaningful associations between variables within a single class evidencing differential prediction at the milestones. Nevertheless, in the multivariate nicotine dependence model, the Addictive Smoking Motive of the Smoking Motives Questionnaire was the only predictor to maintain an interpretable level of prediction in the multivariate model. This could suggest that a subjective feeling of being "addicted" is more important for predicting risk of relapse than objective indices of nicotine dependence (e.g. daily smoking rate). In contrast, three of the four items entered into the multivariate stress model maintained an interpretable level of prediction. Results suggest that stresses associated with different domains of daily living (e.g. social inequality, disciplining children, and the workplace) have different qualitative associations with risk for relapse.

5.2. Study Limitations

5.2.1. Original Study Design

The sample of baseline characteristics selected as predictors of outcome was limited by the design of the original study from which the data was taken. The list of baseline characteristics to be tested was not based on any unifying psychological theory. The theory in this investigation is in the structure of the analysis; the baseline characteristics selected reflected hypotheses based on the available literature as well as the author's perceived need for an investigation into the strength of particular predictors at the milestones. This may be one explanation for why so few predictors of outcome were identified.

5.2.2. Length of Observation Period

Four weeks of ED monitoring is a relatively short period of observation compared to other outcome studies (e.g. 12 months follow-up - Jorenby et al., 1999; Hurt et al., 1997; Jamerson Hays et al., 2001). The follow-up period was limited in this study by the burden imposed on participants of carrying EDs. However, data suggest that the majority of initial abstinences, lapses, and relapses will typically occur within the time frame of this study. For example, data show that most relapse occurs soon after quitting: 65% of subjects relapse within 30 days, and nearly 85% of initial lapses occur within 30 days (Garvey et al., 1992; Shiffman et al., under review). Nonetheless, an extended observation period would have been beneficial for this study so that conclusions could be drawn about predictors of early and late (rather than just early) events.

5.2.3. Variations in the Length of the Observation Period

One outcome of the sequential and cascading nature of the milestones framework is that the timing of earlier events affects the length of observation for later events. For example, how long participants were observed after they achieved initial abstinence depended in part on when they initially abstained; participants who abstained later were eligible to lapse under observation for a

shorter period of time than participants who quit on the TQD. Although survival analyses adequately account for this limitation in designs where only one interval of time is studied, investigating multiple, sequential outcomes within a single study resulted in variable lengths of successive observation periods (and sample sizes eligible to meet each milestone) as determined by the timing of each event. One result of this is that more participants would likely record relapses if the observation period were longer. Differences among participants who relapsed earlier rather than later could affect which baseline characteristics ultimately predicted relapse.

5.2.4. Protocol Noncompliance

One possible limitation of this study is that participants could have been noncompliant and failed to record every cigarette smoked because the protocol was burdensome. Because data are electronic and time-tagged, noncompliance necessarily affects when milestone events are recorded. Failure to record smoking episodes could muddy the sample of participants suspected of having a smoking event at each milestone, thus obscuring predictors and processes of outcomes at the milestones. Although biochemical verification could not guarantee accurate reporting of individual cigarettes, it was helpful in verifying, in general, whether participants were being honest about their reported smoking status.

5.2.5. Sample

An additional limitation is that sampled participants were more motivated to quit than is typical in the general population. All of the participants were willing to endure a difficult protocol and to attend regular counseling sessions. For these reasons, smokers who are either less motivated or less confident that they can quit may be under-represented in this study. It is possible that less motivated and less confident quitters would have different predictors of outcome, and that the processes leading to successful outcomes at the milestones would be more strongly affected by different factors. One possibility, for example, is that this sample of committed participants

overwhelmingly reported high rates of self-efficacy for quitting. Limiting the variability of other variables associated with a motivated and self-efficacious sample could reduce the likelihood that they would emerge as predictors of outcome.

5.2.6. Power

A related limitation of this design was that variations in power for detecting predictors of outcomes across the milestones led to variations in the amount of noise associated with estimates of HRs at each milestone. When power is low, statistical estimates of HRs are variable and the certainty with which evidence of prediction can be interpreted is reduced. Although power for detecting large effects was generally adequate across the milestones, power at the initial abstinence milestone was less than the lapse and relapse milestones (Figure 1) because very few participants failed to abstain (e.g., 95% of participants eventually achieved initial abstinence). Similarly, power for detecting predictors of relapse was less than lapse because of a smaller sample size and lower event rate. Power in this study was a limitation in the design, not because there were inadequate levels of power for detecting effects, but because differences in power across the milestones made it difficult to conclude whether predictors of initial abstinence or relapse failed to emerge because of lower levels of power, or because they truly did not predict outcome.

5.2.7. Multiplicity of Tests

Efforts to be inclusive in terms of a wide variety of baseline predictors may have had the unwanted effect of producing spurious associations between variables and outcomes (i.e., increased Type I error). In other words, some of the reported predictors of outcome may reflect statistical artifacts rather than accurate reflections of underlying cessation-related processes. For example, if the level of interpretation (e.g., the alpha level) was adjusted to control for the number of tests (e.g., Bonferroni adjustment of alpha levels) virtually all of the interpretable

findings would disappear. Patterns of emergent predictors, however, suggest that many of the findings are not random. Specifically, multiple variables within a particular class tended to predict outcome (e.g. multiple ASE variables predicted lapse), while few single variables within a particular class emerged as the sole predictor of outcome. Replication would lend considerable weight to findings suggesting differential prediction in this study.

5.2.8. Criteria for Establishing Differential Prediction

Although there were multiple criteria used in this study for establishing differential prediction, the criteria that were used were somewhat arbitrary. No established method for detecting meaningful differences in HRs across milestones was identified. Thus, a difference of 33% was used to determine whether a variable that predicted outcomes at two milestones did so with sufficient differences in magnitude as to signal differential prediction. Although the 33% difference criterion was loosely based on Cohen's (1988) definition of a small effect size, future research investigating differential prediction of outcomes across the milestones would benefit from analyses that allowed some statistical comparison of differential associations across two or more milestones so as to facilitate interpretation of potentially ambiguous results.

5.3. Directions for Future Research

Future research for testing the utility of the milestones framework as a tool for identifying differential prediction should proceed in two ways. First, investigators should select potential predictors of outcome based in psychological theory. Since this was an exploratory investigation of the milestone framework, theory directed the structure of the analysis, not the selection of predictors. One consequence of this strategy was that predictors were chosen from what was available in an existing study design, and not on the basis of strong theoretical rationale. Studies using predictors based in psychological theory could extend the findings of this report to include tests of specific hypotheses about differences in the processes contributing to outcomes at each

milestone. In sum, selection of predictors based in psychological theory may lead to more parsimonious investigations, as well as higher numbers of identified predictors of outcome.

Second, future research should consider how differences between the milestones themselves may suggest methodological strategies for improving prediction and differential prediction of outcomes. For example, the relapse construct represents multiple samples of smoking behavior occurring over several consecutive days. Essentially, it represents a return to participants' regular patterns of smoking. As a consequence, participant characteristics assessed at baseline, particularly by instruments designed to capture patterns (rather than anomalies) in psychological states and behaviors may be, as was suggested by the results of this study, reliable predictors of relapse. In contrast, initial abstinence and lapse status are determined by a single puff on a cigarette. A single puff is an isolated event which may not accurately represent an individual's typical behavior, especially if the single puff does not proceed to relapse. Prediction of behavioral anomalies by chronically-present influences (e.g. such as levels of nicotine dependence or chronic stressors) is unlikely. Alternatively, *changes* in the factors affecting smoking may be more likely to predict changes in smoking behavior. Indeed, some research suggests that lapses can be predicted by dynamic shifts in factors affecting smoking behavior (Shiffman, Paty et al., 1996; Shiffman, Hickox et al., 1997; Shiffman & Waters, 2004).

More generally, investigators should consider using dynamic assessments of predictors to determine how they change over the course of a quit attempt and how these changes may affect outcomes. For example, Shiffman & Waters (2004) showed that changes in mood can affect trajectory towards a successful or unsuccessful cessation attempt. Further, researchers have demonstrated that some predictors may change as a consequence of moving through the milestones. For example, in a previous report, my colleagues and I (Scharf et al., 2005)

demonstrated that self-reported craving increases after a lapse. Static, baseline assessments of predictor variables, such as self-reported estimates of craving, may not reflect the proximal changes in processes that are ultimately most influential on outcome. Therefore, dynamic assessments of predictor variables may ultimately lead to greater identification of predictors of initial abstinence and lapse.

6. SUMMARY AND CONCLUSIONS

This study presented a milestones framework of the process of smoking cessation. The framework was designed to facilitate the assessment, reporting and integration of data from multiple, targeted outcomes so that researchers could begin to identify where in the cessation process important changes in risk and protective factors occur. The utility and validity of the milestones as an organizational framework was supported insofar as all of the milestones represented significant barriers to successful smoking cessation. However, few predictors of any outcome were identified, and consequently, differential prediction of outcome at the milestones was largely unobserved. Although there was some evidence to suggest differential prediction of relapse by nicotine dependence and stress, this study did not provide an adequate context for testing this. Future research should consider examining more focused theory-driven hypotheses positing differential prediction of particular milestones. Similarly, investigating the utility of the milestones framework using dynamic predictors of outcome may be a fruitful area of research.

Table 1. Participant characteristics

		Sample			
Baseline Characteristic		Entire Sample (n=260)	Quit (n=248)	Lapsed (n=149)	Relapsed (n=40)
Demographics					
Age		44.3 (10.0)	44.2 (9.92)	43.21 (10.09)	43.97 (9.27)
Education, at least some college		69.6%	65.32%	65.77%	33.50%
Ethnicity, Caucasian		92.3%	92.34%	94.63%	95.00%
Gender (% female)		58.5%	57.66%	59.73%	55.00%
Household Income > 29,999		34.44%	34.43%	33.43%	42.00%
Married or living with a partner		46.2%	45.97%	44.96%	33.50%
Live with at least one other smoker		32.16%	31.16%	36.15%	32.44%
Partner is also a smoker		20.8%	20.99%	22.45%	20.00%
Nicotine Dependence					
Cigarettes per day		26.70 (11.4)	26.47 (11.50)	27.47 (12.79)	32.4 (16.3)
NDSS	Total score	-0.01 (0.98)	-0.04 (0.98)	0.07 (1.00)	0.26 (0.95)
Drive		0.01 (1.00)	0.01 (1.01)	0.07 (0.99)	0.05 (0.90)
Priority		-0.03 (1.01)	-0.05 (1.01)	0.04 (1.03)	0.02 (0.87)

Tolerance		-0.04 (1.02)	-0.07 (1.01)	0.01 (1.00)	0.27 (0.99)
Continue Smoking		-0.01 (0.99)	0.01 (1.01)	0.06 (1.03)	-0.16 (1.01)
Stereotyped Smoking		-0.03 (1.00)	-0.02 (0.99)	-0.03 (1.05)	-0.4 (1.24)
FTQ	Total score	6.24 (1.80)	6.20 (1.81)	6.31 (1.81)	6.48 (1.92)
FTND	Total score	5.90 (2.19)	5.81 (2.19)	5.97 (2.29)	6.30 (2.51)
	Morning smoking	-0.03 (0.99)	-0.05 (0.99)	-0.04 (0.98)	-0.01 (1.06)
	Difficulty refraining	-0.02 (0.99)	-0.04 (1.00)	0.03 (0.97)	0.15 (0.93)
HSI		4.06 (1.36)	4.01 (1.36)	4.07 (1.42)	4.40 (1.58)
Smoking Motivations					
SMQ	Indulgent	2.67 (0.45)	2.66 (0.45)	2.65 (0.47)	2.58 (0.41)
Negative affect		3.06 (7.12)	3.05 (0.72)	3.09 (0.73)	3.21 (0.61)
Sensory-motor		1.94 (0.70)	1.95 (0.70)	1.96 (0.71)	2.00 (0.62)
Addictive		2.98 (0.63)	2.97 (0.63)	3.0 (0.65)	3.23 (0.50)
Automatic		2.35 (0.84)	2.33 (0.84)	2.35 (0.87)	2.54 (0.84)
Stimulation		2.66 (0.54)	2.66 (0.53)	2.69 (0.53)	2.72 (0.48)
Psychosocial		1.93 (0.59)	1.92 (0.60)	1.96 (0.63)	1.87 (0.54)
OFS	Pharmacological	2.66 (0.49)	2.65 (0.49)	2.68 (0.50)	2.83 (0.47)
Non-pharmacological		2.18 (0.40)	2.18 (0.40)	2.19 (0.41)	2.15 (0.33)
Food substitute		3.29 (1.02)	3.27 (1.02)	3.33 (1.00)	3.39 (1.07)
Nervous irritation		4.35 (0.55)	4.35 (0.56)	4.37 (0.51)	4.39 (0.47)
Social smoking		3.70 (0.60)	3.70 (0.60)	3.74 (0.59)	3.68 (0.59)
Smoke alone		3.92 (0.63)	3.92 (0.63)	3.95 (0.59)	3.98 (0.60)

Relaxation		3.78 (0.82)	3.78 (0.83)	3.83 (0.86)	3.93 (0.83)
Accomplish activities		3.55 (0.90)	3.54 (0.91)	3.58 (0.88)	3.49 (0.90)
Abstinence Self-Efficacy					
CSS		2.68 (0.53)	2.70 (0.52)	2.63 (0.48)	2.46 (0.52)
RSEQ	Negative affect	2.04 (0.63)	2.06 (0.63)	1.97 (0.61)	1.93 (0.56)
Positive Affect		3.21 (0.56)	3.23 (0.56)	3.24 (0.55)	3.16 (0.51)
Restrict		3.23 (0.56)	3.24 (0.56)	3.23 (0.55)	3.21 (0.53)
Idle time		2.42 (0.69)	2.45 (0.68)	2.37 (0.63)	2.35 (0.65)
Social and food		2.21 (0.64)	2.24 (0.63)	2.18 (0.61)	2.10 (0.61)
Low arousal		2.79 (0.60)	2.83 (0.59)	2.78 (0.57)	2.74 (0.59)
Craving		2.34 (0.71)	2.37 (0.72)	2.28 (0.67)	2.15 (0.69)
Total RSEQ		2.61 (0.48)	2.63 (0.47)	2.59 0.42)	2.54 (0.41)
Affect					
SCID		33.10%	32.26%	35.57%	42.50%
DSM3		40.00%	38.71%	42.95%	52.50%
AIM		3.73 (0.58)	3.73 (0.58)	3.72 (0.58)	3.66 (0.54)
STAS		1.94 (0.45)	1.94 (0.46)	1.97 (0.48)	1.95 (0.53)
STAI		2.14 (0.41)	2.14 (0.41)	2.14 (0.42)	2.18 (0.42)
Stress					
PSS		2.81 (0.53)	2.79 (0.52)	2.79 (0.53	2.77 (0.58)

LSQ	Friends	11.80 (7.18)	11.85 (7.22)	11.94 (6.77)	11.77 (5.64)
Relationships		20.00 (11.50)	20.20 (11.51)	21.49 (11.76)	23.79 (13.49)
Children		11.22 (15.79)	17.59 (15.34)	17.38 (13.56)	19.41 (14.67)
Family		11.80 (7.13)	11.94 (7.14)	11.97 (7.05)	12.26 (7.10)
Health		11.01 (7.79)	10.75 (7.07)	10.49 (7.17)	10.18 (7.33)
Job		14.60 (11.13)	15.01 (11.15)	14.32 (11.32)	11.08 (8.01)
Finance		12.62 (7.94)	12.74 (7.88)	12.52 (8.04)	11.51 (7.01)
PIQ		3.41 (0.56)	3.42 (0.55)	3.37 (0.56)	3.33 (0.56)
GLQ	Poverty	1.89 (0.77)	1.90 (0.77)	1.91 (0.77)	1.88 (0.68)
Job condition		1.62 (0.71)	1.62 (0.73)	1.66 (0.76)	1.72 (0.92)
Like job		1.65 (0.65)	1.65 (0.64)	1.69 (0.70)	1.72 (0.56)
Job load		2.25 (0.80)	2.25 (0.81)	2.29 (0.81)	2.02 (0.74)
Satisfaction from job		2.02 (0.84)	2.01 (0.84)	1.95 (0.88)	2.12 (1.01)
Social acceptance		1.84 (0.75)	1.84 (0.75)	1.85 (0.69)	1.83 (0.63)
Socially equal		2.26 (0.88)	2.26 (0.87)	2.25 (0.88)	1.85 (0.82)
Social roles		1.77 (0.70)	1.78 (0.68)	1.75 (0.68)	1.63 (0.69)
Disciplining Children		2.52 (0.72)	2.52 (0.72)	2.41 (0.76)	2.14 (0.65)
Hopes for Children		2.81 (0.84)	2.80 (0.85)	2.76 (0.88)	2.70 (0.95)
Children Honor for Parents		5.26 (3.23)	5.28 (3.25)	5.20 (3.26)	4.91 (3.27)
Coping					
WOCS	Self control	2.72 (0.39)	2.72 (0.39)	2.71 (0.38)	2.68 (0.40)
Seek support		2.98 (0.46)	2.98 (0.46)	3.01 (0.48)	3.08 (0.45)

Blame self		2.89 (0.50)	2.89 (0.51)	2.90 (0.52)	2.90 (0.50)
Wishful thinking		2.61 (0.60)	2.60 (0.61)	2.62 (0.63)	2.66 (0.60)
Problem focused		3.14 (0.33)	3.15 (0.33)	3.13 (0.33)	3.12 (0.39)
DCI	Avoidance	2.44 (0.45)	2.44 (0.46)	2.45 (0.48)	2.49 (0.51)
Divert Attention		2.08 (0.85)	2.07 (0.85)	2.08 (0.83)	2.08 (0.84)
See things in a different light		2.59 (0.77)	2.59 (0.77)	2.61 (0.81)	2.54 (0.91)
Emotions		2.62 (0.90)	2.63 (0.90)	2.61 (0.94)	2.67 (0.90)
Accept Situation		1.97 (0.79)	1.96 (0.79)	2.00 (0.81)	1.95 (0.69)
Seek Support		2.62 (0.92)	2.62 (0.91)	2.65 (0.96)	2.77 (0.93)
Relax		2.60 (0.82)	2.62 (0.83)	2.62 (0.85)	2.77 (0.90)
Seek Spiritual Guidance		2.24 (1.09)	2.23 (1.10)	2.18 (1.11)	2.36 (1.16)

AIM = Affect Intensity Measure, *CPD* = Cigarettes per day, *CSS* = Confidence in Smoking Situations, *DCI* = Daily Coping Inventory, *FTND* = Fagerström Test of Nicotine Dependence, *FTQ* = Fagerström Tolerance Questionnaire, *GLQ* = General Life Questionnaire, *HSI* = Heaviness of Smoking Index, *LSQ* = Life Situations Questionnaire, *NDSS* = Nicotine Dependence Syndrome Scale, *OFS* = Occasions for Smoking Scale, *PIQ* = Partner Interaction Questionnaire, *PSS* = Perceived Stress Scale, *RSEQ* = Relapse Self Efficacy Questionnaire, *SMQ* = Smoking Motivations Questionnaire, *STAI* = Speilberger Trait Anxiety Inventory, *STAS* = Speilberger Trait Anger Scale, *WOC* = Ways of Coping scale.

Table 2. Participants meeting criteria for a "failed" quit attempt using traditional and milestone criteria

	Traditional		Milestone		
Failures	Continuous abstinence (Wks. 1-4)	7-day Point Prevalence (Wk. 4)	Not Quit	Lapse	Relapse
N (%)	175 (67)	154 (59)	12 (5)	149 (60)	40 (27)

Table 3. Individual variables as predictors of outcome at the milestones. Results from univariate (unadjusted ORs) and multivariate (adjusted ORs) analyses

		Quit			Lapse			Relapse		
Class	Item	Uni-var.	Multi-var.	VIF	Uni-var.	Multi-var.	VIF	Uni-var.	Multi-var.	VIF
ASE	CSS	0.88	0.92	1.70	0.78	0.69*	2.68	0.69	N/A	N/A
RSEQ	Low Arousal	0.85	0.80*	1.70	0.82	1.12	1.77			
	Negative Affect				0.78	0.86*	1.71			
	Idle time				0.81	0.84*	2.06			
	Social/ Food				0.83	1.02	2.48			
	Craving				0.81	1.01	1.92			
Nicotine Dependence	CPD							1.57	1.03	2.17
NDSS	Total score				1.24	N/A	N/A			
HSI	Total score							1.45	1.03	2.37
Motives for Smoking	Pharmac-ological (higher-order)							1.55	1.05	2.81

	Addictive				1.57	1.77*	2.37
Stress	Social Equality				1.69	2.70*	1.03
	Child Stress				1.69	2.13*	1.02
	Job				1.45	0.97	1.29
	Job Stress				1.43	1.72*	1.31
Demogr-	#smokers/						
aphics	household	1.27	N/A	N/A			

*CIs do not include 0.00

VIF = Variance Inflation Factor

ASE = Abstinence Self-Efficacy, *C.P.D.* = Cigarettes per day, *CSS* = Confidence in Smoking Situations, *GLQ* = General Life Questionnaire, *HSI* = Heaviness of Smoking Index, *LSQ* = Life Situations Questionnaire, *NDSS* = Nicotine Dependence Syndrome Scale, *RSEQ* = Relapse Self Efficacy Questionnaire.

Figure 1. Power curves for predicting outcomes at the milestones

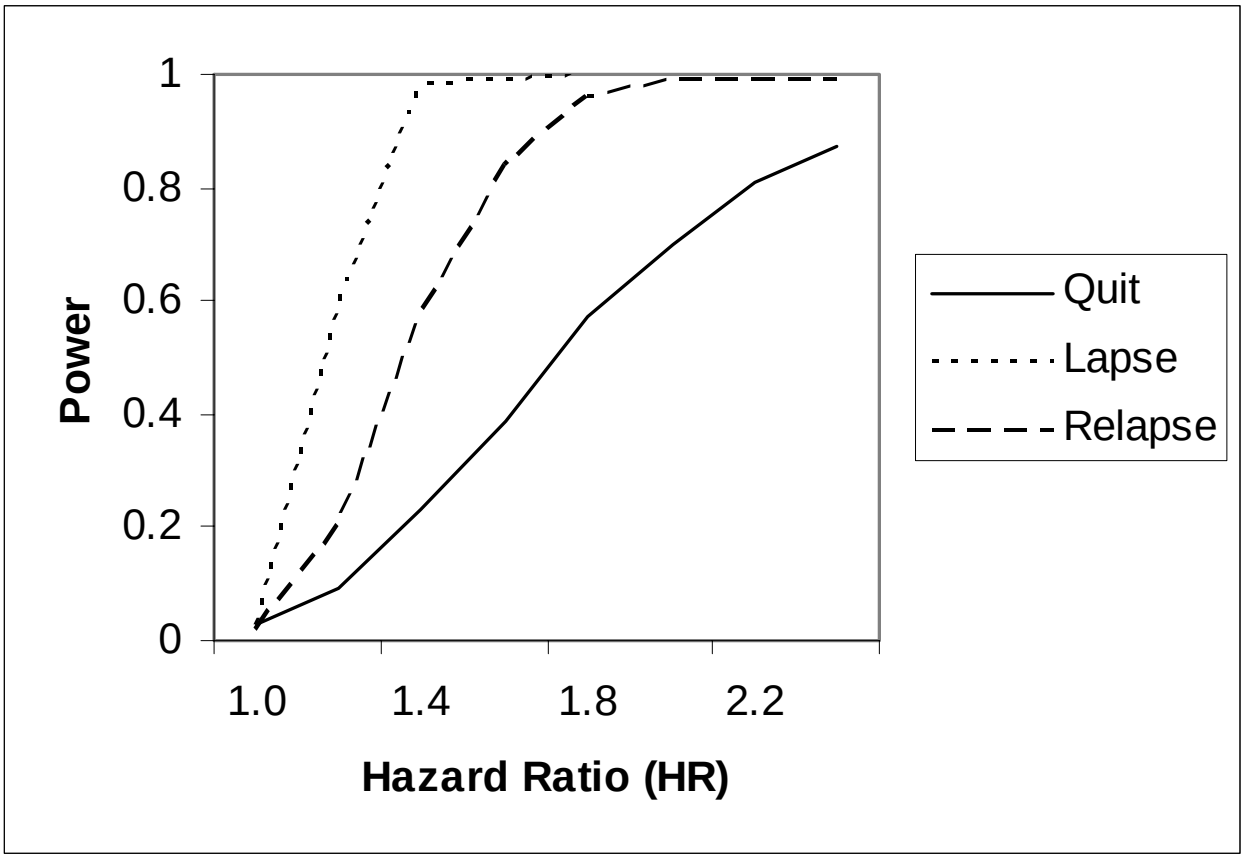


Figure 2. Survival curve for time to initial abstinence

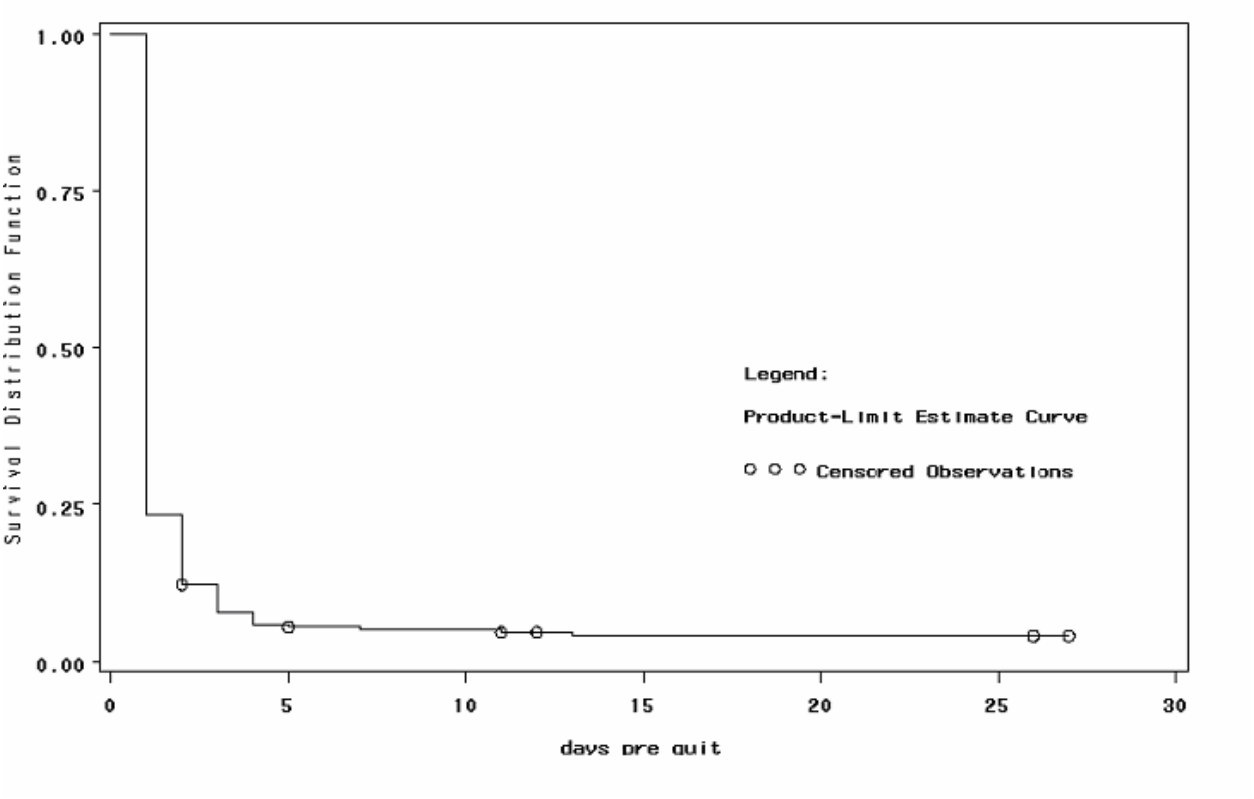


Figure 3. Survival curve for initial abstinence to lapse

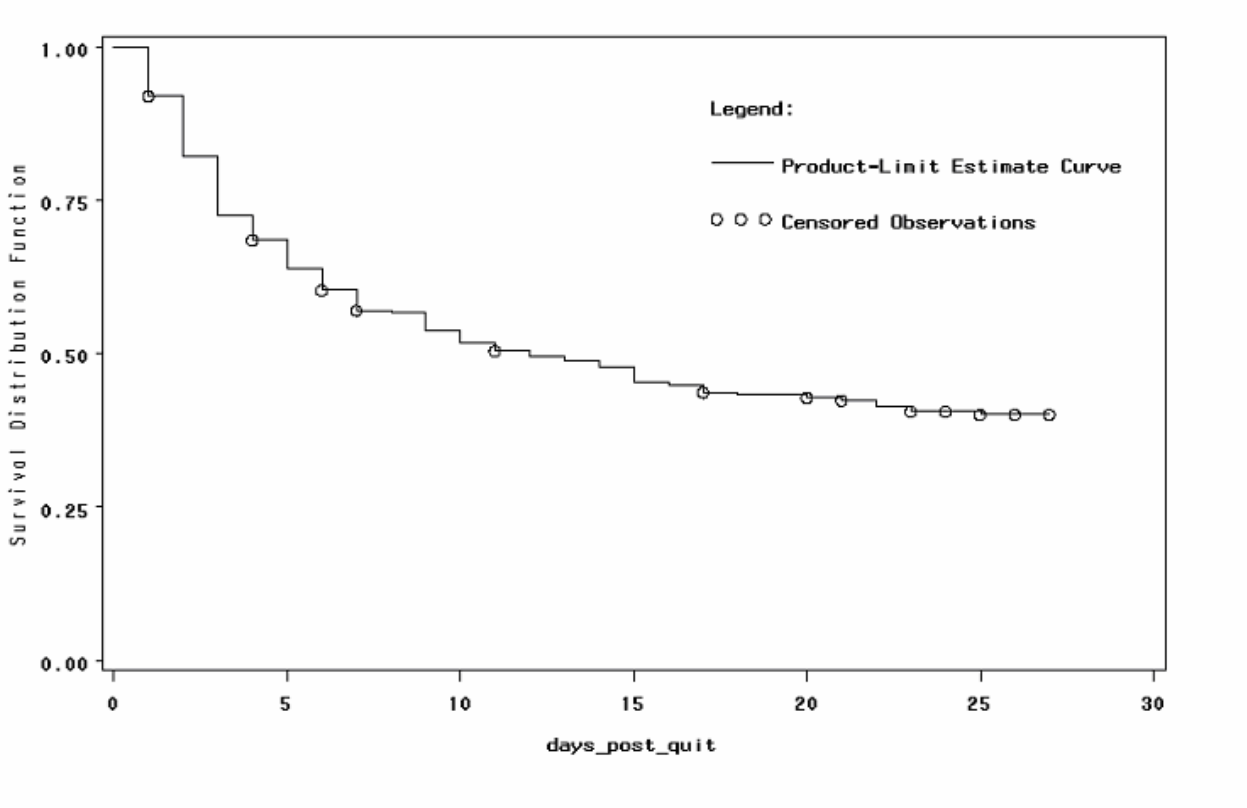


Figure 4. Survival curve for lapse to relapse

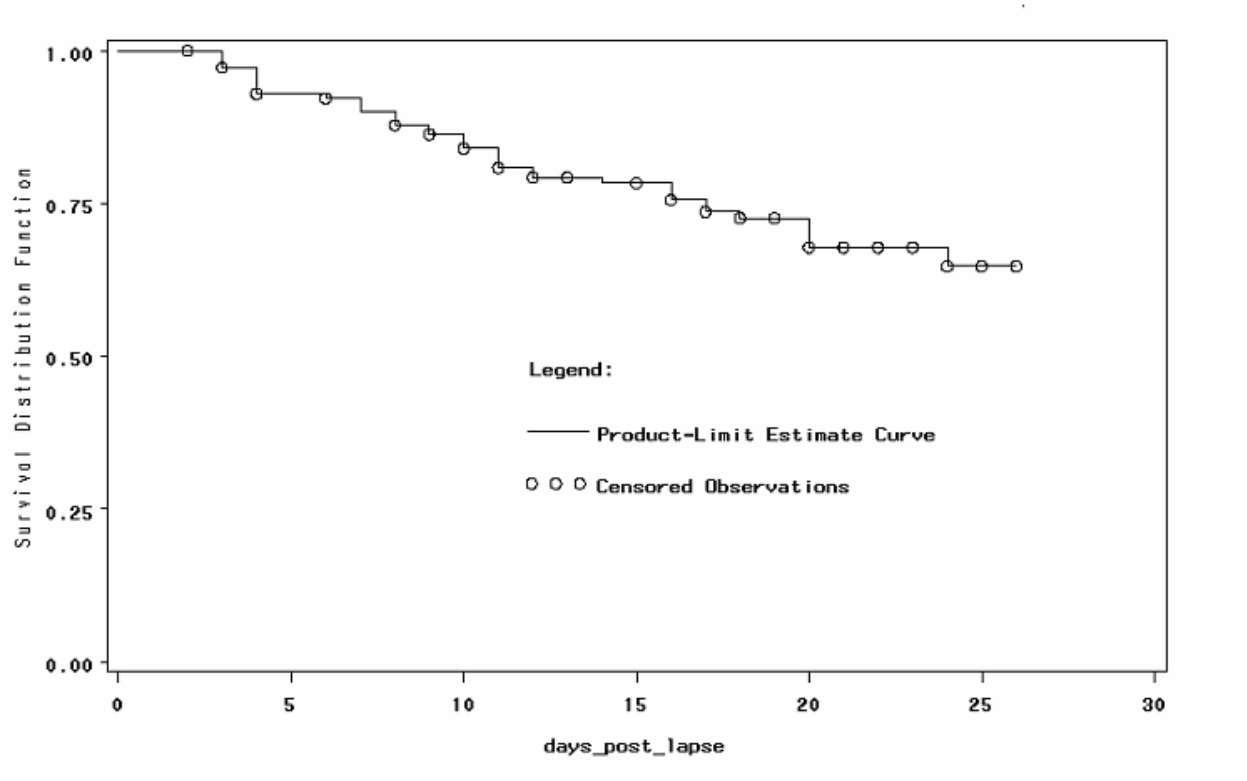


Figure 5. Testing for effects of filtering: Mean values from classes of standardized predictors were largely unaffected by changes in sample composition across the milestones

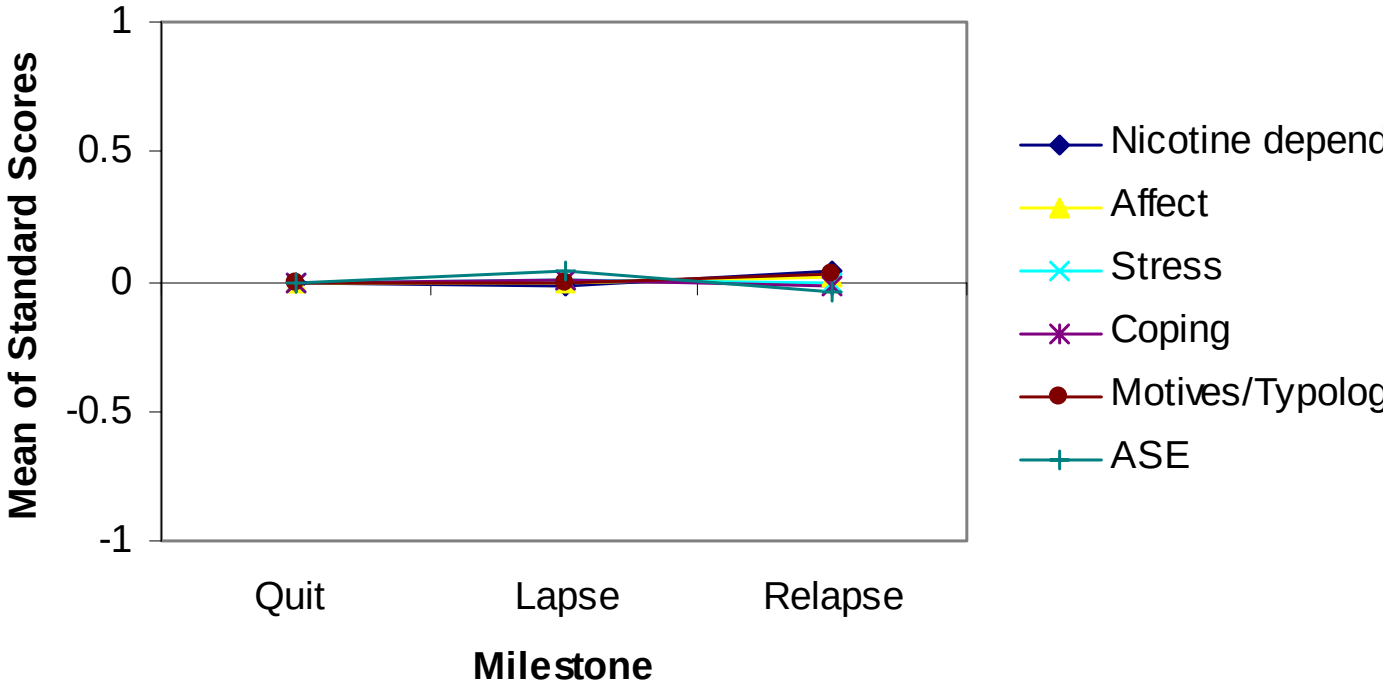


Figure 6. Testing for effects of filtering: Mean estimates of variance from classes of standardized predictors were largely unaffected by changes in sample composition across the milestones

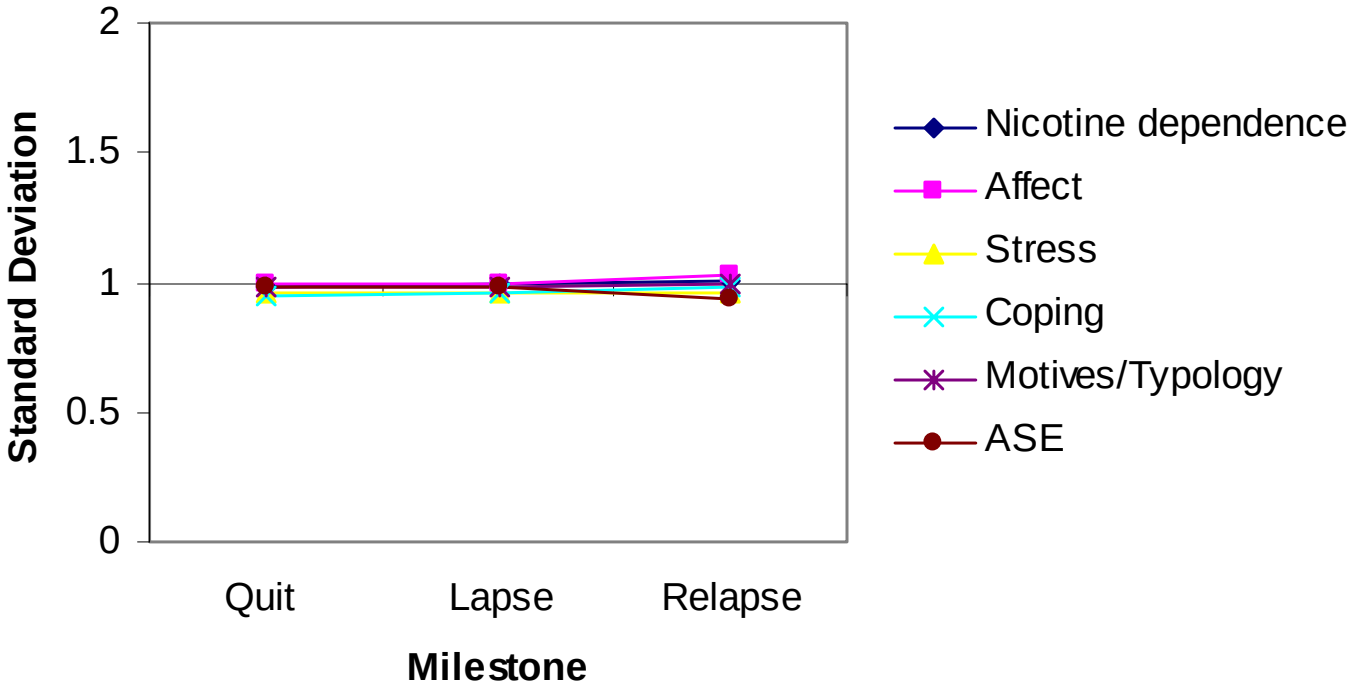
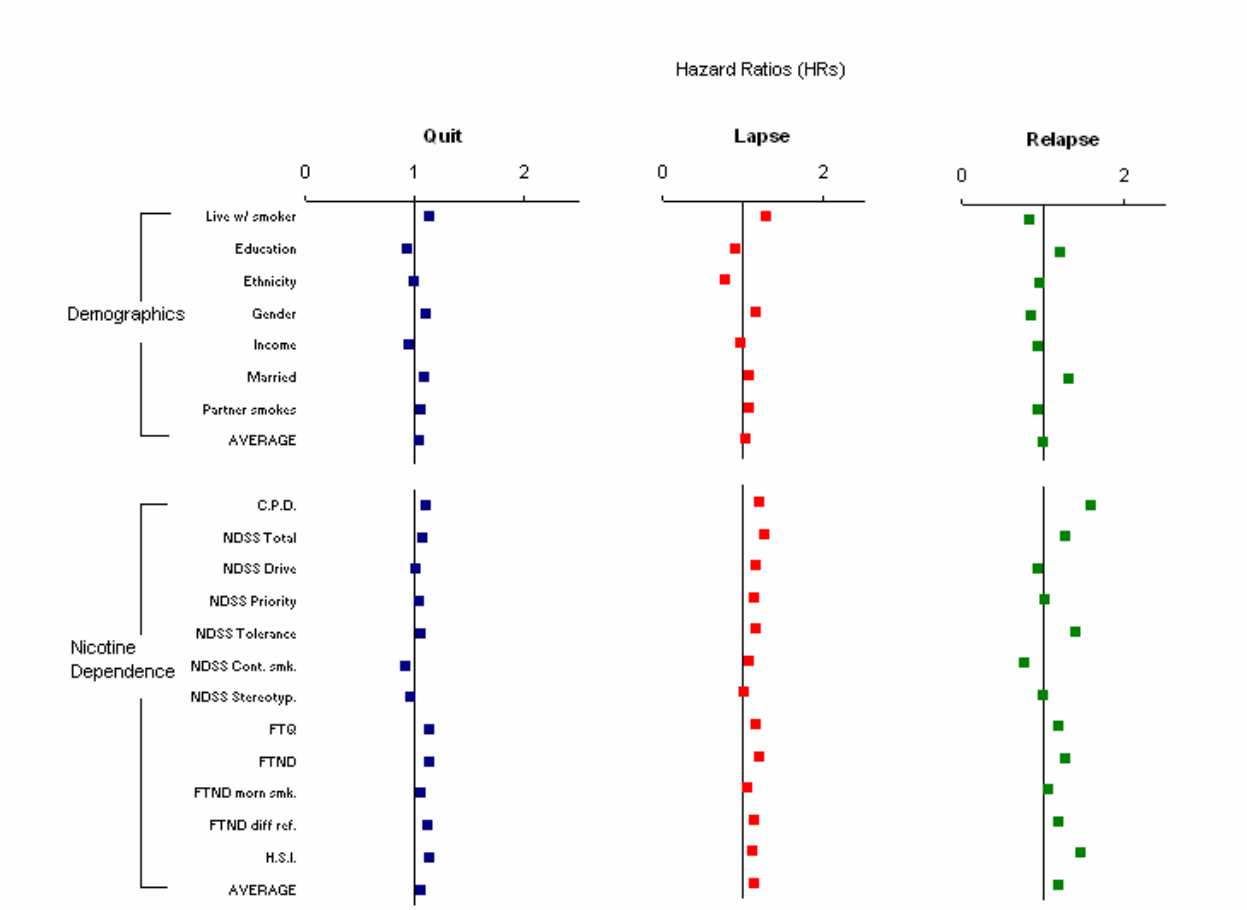
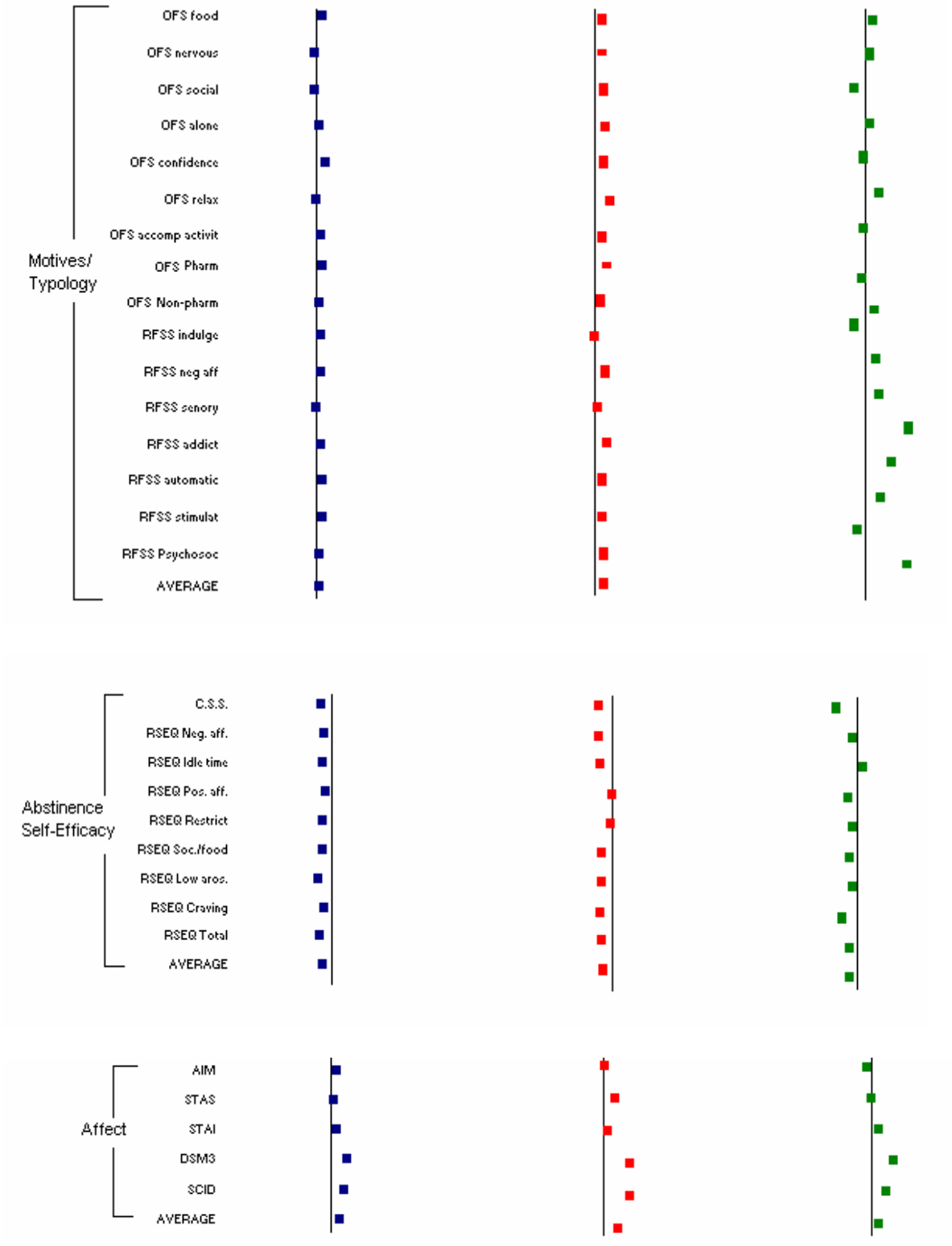
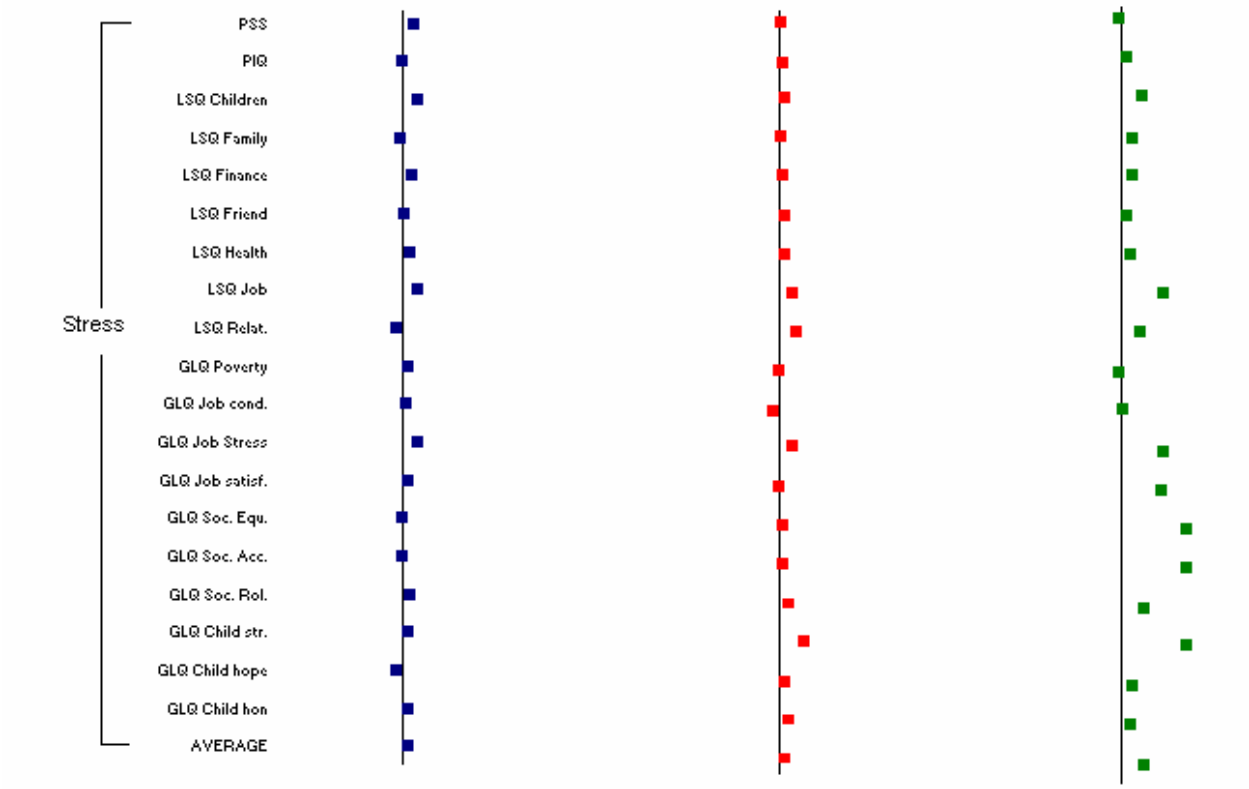
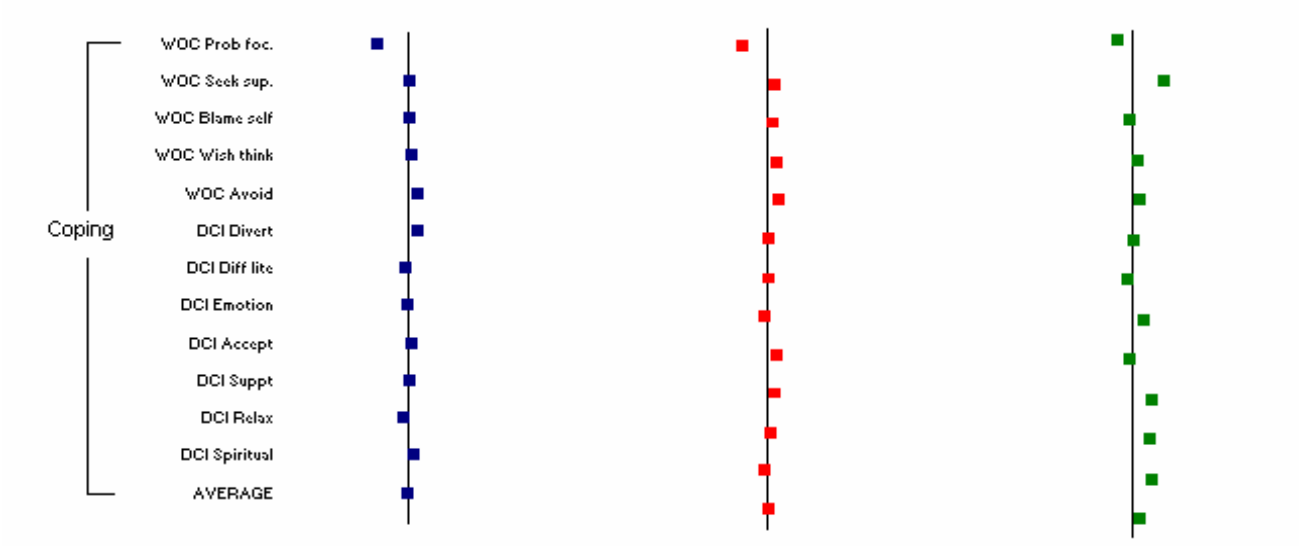


Figure 7. Predictors of outcome at the milestones




Motives/ Typology
OFS food
OFS nervous
OFS social
OFS alone
OFS confidence
OFS relax
OFS accomp activit
OFS Pharm
OFS Non-pharm
RFSS indulge
RFSS neg aff
RFSS senory
RFSS addict
RFSS automatic
RFSS stimulat
RFSS Psychosoc
AVERAGE
Abstinence Self-Efficacy
C.S.S.
RSEQ Neg. aff.
RSEQ Idle time
RSEQ Pos. aff.
RSEQ Restrict
RSEQ Soc./food
RSEQ Low aros.
RSEQ Craving
RSEQ Total
AVERAGE
Affect
AIM
STAS
STAI
DSM3
SCID
AVERAGE


Stress
PSS
PIQ
LSQ Children
LSQ Family
LSQ Finance
LSQ Friend
LSQ Health
LSQ Job
LSQ Relat.
GLQ Poverty
GLQ Job cond.
GLQ Job Stress
GLQ Job satisf.
GLQ Soc. Equ.
GLQ Soc. Acc.
GLQ Soc. Rol.
GLQ Child str.
GLQ Child hope
GLQ Child hon
AVERAGE


Coping
WOC Prob foc.
WOC Seek sup.
WOC Blame self
WOC Wish think
WOC Avoid
DCI Divert
DCI Diff lite
DCI Emotion
DCI Accept
DCI Suppt
DCI Relax
DCI Spiritual
AVERAGE

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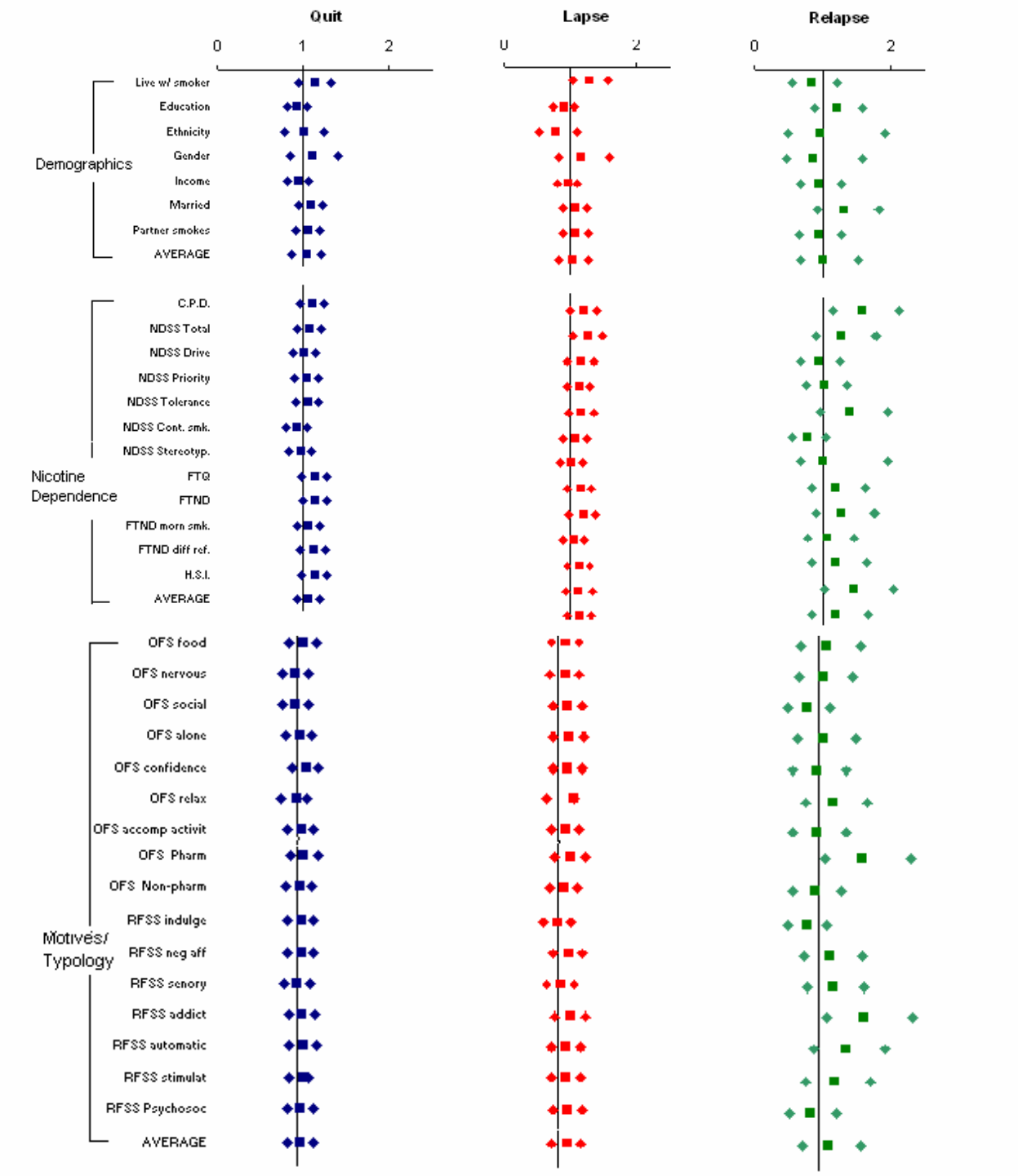
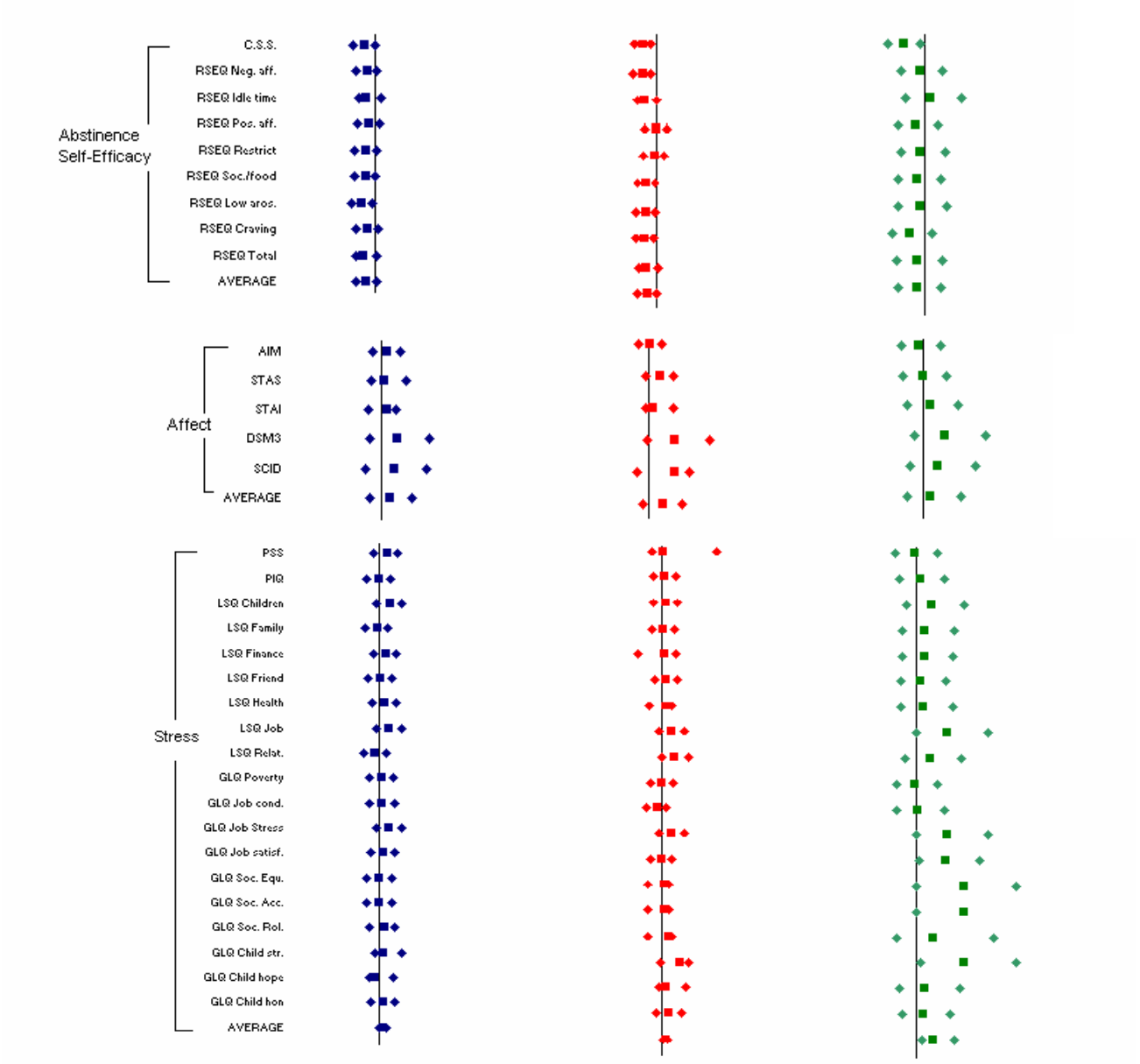
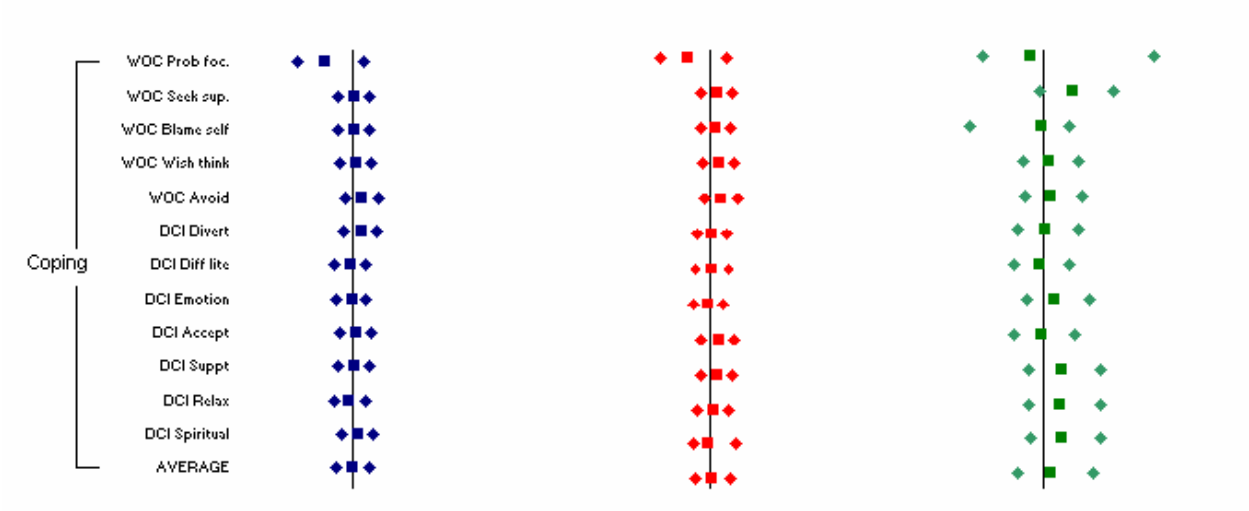
Appendix

HAZARD RATIOS (HRS)




Abstinence Self-Efficacy
C.S.S.
RSEQ Neg. aff.
RSEQ Idle time
RSEQ Pos. aff.
RSEQ Restrict
RSEQ Soc./food
RSEQ Low aros.
RSEQ Craving
RSEQ Total
AVERAGE
Affect
AIM
STAS
STAI
DSM3
SCID
AVERAGE
Stress
PSS
PIQ
LSQ Children
LSQ Family
LSQ Finance
LSQ Friend
LSQ Health
LSQ Job
LSQ Relat.
GLQ Poverty
GLQ Job cond.
GLQ Job Stress
GLQ Job satisf.
GLQ Soc. Equ.
GLQ Soc. Acc.
GLQ Soc. Rel.
GLQ Child str.
GLQ Child hope
GLQ Child hon
AVERAGE


Coping
WOC Prob foc.
WOC Seek sup.
WOC Blame self
WOC Wish think
WOC Avoid
DCI Divert
DCI Diff lite
DCI Emotion
DCI Accept
DCI Suppt
DCI Relax
DCI Spiritual
AVERAGE