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# The Effect of Exercise on Cigarette Craving and Withdrawal Symptoms While Using a Nicotine Lozenge

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A thesis submitted in partial fulfillment of the requirements for the Master of Arts degree in Kinesiology

# THE EFFECT OF EXERCISE ON CIGARETTE CRAVING AND WITHDRAWAL SYMPTOMS WHILE USING A NICOTINE LOZENGE

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by

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**Abstract**

It is imperative that smoking cessation aids effectively alleviate cigarette craving and withdrawal symptoms because their intensity has shown to predict relapse. The nicotine lozenge is a pharmacotherapy that has shown to reduce symptoms of craving and withdrawal. Research has also shown that a single session of exercise can provide temporary relief from craving and withdrawal for smokers who are both temporarily abstaining and undergoing a real quit attempt. Applying two efficacious monotherapies concurrently may provide additive benefit and greater symptom relief. Thirty recently quit smokers were randomized to either the experimental (exercise and lozenge) or control (lozenge alone) condition. While both conditions demonstrated reductions in craving, the reduction was significantly greater for the experimental group. These findings demonstrate that an acute bout of exercise provides additional craving relief to the nicotine lozenge in recently quit smokers.

*Keywords:* smoking, nicotine lozenge, acute exercise, craving, withdrawal symptoms

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# Chapter One: Literature Review

## Introduction

Cigarette smoking continues to be the leading cause of preventable death in the world today (World Health Organization [WHO], 2011), accounting for more than 37,000 deaths each year in Canada alone (Baliunas et al., 2007). The negative health consequences of smoking have been thoroughly researched. While lung cancer has long been identified as the disease of smokers, the detriments of smoking are much more broad. Several other cancers have been linked to smoking as well, including: mouth, larynx, throat, esophagus, bladder, kidney, cervix, pancreas, and stomach. Furthermore, smoking has shown to lead to cardiovascular diseases such as stroke and coronary heart disease. In general, smoking harms nearly every organ in the body and affects a person's overall health (U.S. Department of Health and Human Services [USDHHS], 2014).

Despite the unfavourable morbidity and mortality outcomes associated with smoking, a significant proportion of the population continues to engage in this behaviour. It is estimated that approximately 16% of Canadians aged 15 years or older smoke (Health Canada, 2012). Fortunately for these individuals, it is never too late to reap the benefits of quitting. The risks associated with many of the aforementioned diseases can be reduced or largely removed by stopping smoking. These benefits commence almost immediately, with a decrease in heart rate occurring within 20 minutes of abstinence. Other short-term benefits of quitting include: removal of carbon monoxide (CO) from the blood and improved

lung function and blood circulation. The long-term benefits are even more motivating. For example, the risk of coronary heart disease is cut in half after 1 year of quitting and can drop to the level of a non-smoker after 15 years. In addition, the risk of stroke can be reduced to that of a non-smoker within 5 to 15 years of quitting. After 10 years of being smoke-free, the risk of several cancers (i.e., mouth, throat, esophagus, bladder, and cervix) decrease and one's lung cancer death rate becomes approximately half that of a smoker's (USDHHS, 2004). Although stopping smoking at a younger age reduces health risks to a greater degree, quitting at any age is beneficial and can give back years of life that would be lost by continuing to smoke.

Given these health benefits, it may come to no surprise that the majority of smokers want to quit. Unfortunately, only 3 to 5% of those who quit unassisted remain smoke-free after 6 to 12 months (Hughes, Keely, & Naud, 2004) and nearly half of those who undergo surgery for early-stage lung cancer return to smoking (Walker et al., 2006). These findings are not only discouraging but also indicative of the degree of difficulty that presents itself when trying to quit. So, what makes quitting smoking so challenging? The answer to this question is multifaceted and requires an understanding of the factors that contribute to nicotine dependence.

**Nicotine Dependence**

As reported by the Royal College of Physicians of London (2000), nicotine is a highly addictive drug on par with heroin and cocaine. Nicotine is recognized as a substance that meets the criteria for dependence defined in the *International*

*Classification of Diseases,* tenth edition (ICD-10; WHO, 1992). These symptoms include: tolerance, withdrawal, impaired control, neglect of activities, time spent in substance-related activity, continued use despite problems, and compulsion. The criteria described in the ICD-10 are similar to those found in the *Diagnostic and Statistical Manual of Mental Disorders,* fourth edition (DSM-IV; American Psychiatric Association, 2000); with the exception that the DSM-IV does not explicitly state the compulsion criteria (i.e., strong desire or sense of compulsion to use). Both systems require at least three co-occurring criteria within a 12-month period to diagnose dependence (Hasin, Hatzenbuehler, Keyes, & Ogburn, 2006).

Nicotine is the major psychoactive constituent in tobacco (Karan, Dani, & Benowitz, 2003) and can be found in various tobacco products. The cigarette is the most efficient device, delivering nicotine to the brain within 7 seconds of inhalation (Maisto, Galizio, & Connors, 2004). The average smoker absorbs 1 to 2 mg of nicotine per cigarette (Karan et al., 2003) and metabolizes the drug relatively quickly, with nicotine blood concentration levels dropping by half within 2 to 3 hours of smoking (Lynch & Bonnie, 1994). The neurological effect of nicotine serves as a powerful driving force of this disorder; however, behavioural, genetic, and socio-environmental factors contribute as well.

**Neurological factors.** Nicotine activates the mesolimbic pathway, known as the “reward centre” of the brain that controls feelings of pleasure and motivation (Gardner, 1997). The mesolimbic pathway originates in the midbrain and is composed of the ventral tegmental area (VTA) and nucleus accumbens (NAc). The VTA houses dopaminergic projections that extend to the NAc, limbic

brain regions, and the prefrontal cortex. Embedded on the plasma membrane of dopaminergic neurons are nicotinic acetylcholine receptors (nAChRs) that are activated by the neurotransmitter acetylcholine (ACh; Gardner, 1997). These receptors can also be stimulated by nicotine (Calabresi, Lacey, & North, 1989), which has particularly high-affinity to $\alpha_4\beta_2$ subunits (Lukas et al., 1999). When nicotine or ACh bind to nAChRs, the ion-gated channels open and a subsequent action potential is fired down the dopaminergic axons to the terminal found in the NAc. The neurotransmitter dopamine is then released from the synaptic vesicles and into the cleft. Dopamine elicits euphoric feelings and reinforces future engagement in smoking behaviour (Benowitz, 2010; Wonnacott, Sidhpura, & Balfour, 2005). The binding of nicotine stimulates the release of other neurotransmitters as well, which produce a range of psychoactive effects. These neurotransmitters and their associated responses include: ACh (arousal and cognitive enhancement), norepinephrine (arousal and appetite suppression), glutamate (learning and memory enhancement), serotonin (mood modulation and appetite suppression), β-endorphin (reduction in anxiety and tension), and GABA (reduction in anxiety and tension; Benowitz, 2008).

Prolonged nicotine exposure causes neuroadaptations (Wang & Sun, 2005) and leads to drug tolerance, where a higher nicotine dose is required to produce the same magnitude of effect (Smith & Stolerman, 2009). The exact adaptations the brain undergoes in response to nicotine have been debated, however, desensitization and upregulation seem most probable (Ortells & Barrantes, 2010). The desensitization-upregulation hypothesis is as follows: 1) Excess and chronic nicotine exposure saturates $\alpha_4\beta_2$ nAChRs and induces an

activated state. 2) The nAChRs become desensitized as binding-sites are occupied with high-affinity. 3) The homeostatic response to desensitization is upregulation, whereby a greater number of nAChRs are produced (Ortells & Barrantes, 2010). It has been suggested that during periods of nicotine abstinence, previously desensitized nAChRs become unoccupied and recover to a responsive state. Together, the increase in number of nAChRs and reactivation of desensitized receptors are thought to be responsible for cigarette cravings and the array of withdrawal symptoms (e.g., irritability, depressed mood, restlessness, anxiety, difficulty concentrating, increased hunger and eating, and insomnia) that emerge in nicotine-deprived smokers (Dani & Heinemann, 1996).

**Behavioural factors.** With habitual smoking, smokers become familiar with the pleasant state elicited by cigarettes and the unfavourable symptoms that accompany short-term abstinence. Becoming aware of, and ultimately learning, these consequences of smoking (or not smoking) impacts future behaviour. This method of learning is known as operant conditioning, where an individual's behaviour is influenced by its outcomes. These consequences (or reinforcements) can be positive or negative, and in turn, strengthen or weaken the behaviour accordingly (Skinner, 1938). For example, the psychoactive effects of nicotine serve as a reward, and thus, positively reinforce smoking (Glautier, 2004). Conversely, craving and withdrawal symptoms serve as a punishment, and as a result, negatively reinforce quitting (Eissenberg, 2004). Together, these behavioural consequences strengthen future smoking behaviour and reduce the likelihood quitting.

The average Canadian smoker consumes 15 cigarettes per day (Health Canada, 2012) and takes approximately 11 puffs per cigarette (USDHHS, 1988). This exposes smokers to more than 150 doses of nicotine daily. As a result, smokers are likely to develop associations with this drug because it is administered at such a high frequency. The repetitive nature of smoking and the associations that develop with this behaviour can be explained by Pavlov's (1927) classical conditioning theory. Classical conditioning occurs when an initially neutral stimulus produces the same response as an existing stimulus with which it has been paired. This process entails three stages (i.e., before, during, and after conditioning). Before conditioning, smoking serves as the unconditioned stimulus (UCS) and cigarette cravings and withdrawal symptoms serve as the unconditioned response (UCR). During the conditioning stage, a neutral stimulus becomes associated with the UCS. In regards to smoking, environmental stimuli that occur repeatedly in temporal proximity become conditioned stimuli (CS) and can include smoking paraphernalia (e.g., an ashtray), sensory aspects of smoking (e.g., cigarette smell or taste), and/or situational cues (e.g., smoking while drinking coffee). After conditioning, the mere presence of CSs alone can trigger craving and withdrawal symptoms, which now become a conditioned response (CR; Bevins & Palmatier, 2004; Niaura, 2000). Classical and operant conditioning are two behavioural theories that help explain the learned component of this disorder.

**Genetic factors.** Certain smokers may be at greater risk of becoming addicted to nicotine due to genetic predispositions. Nicotine is primarily metabolized into cotinine, and cotinine is metabolized into 3-hydroxycotinine by

the liver enzyme cytochrome CYP2A6. Research reveals that polymorphic variations of the CYP2A6 gene influence the rate at which nicotine is metabolized (high vs. low activity), which in turn, impact nicotine dependence, smoking behaviour, and withdrawal symptoms. For example, smokers with a high-activity variation of the gene have a tendency to smoke a greater number of cigarettes per day, intake more nicotine daily, and smoke their first cigarette earlier in the day compared to those with a low-activity variant. This heavy smoking behaviour translates into a higher nicotine (or cigarette) dependence score. In addition, among those attempting to quit, high-activity carriers report greater withdrawal symptoms than their low-activity counterparts (Kubota et al., 2006).

**Socio-environmental factors**. Many social and environmental factors contribute to the development and maintenance of nicotine dependence as well as the likelihood of relapse (WHO, 2010). Environmental influences, such as being in the presence of smokers (i.e., peers, family, or strangers), can encourage smoking behaviour. Furthermore, marketing, portrayal in the media, and brand preference of specific populations can influence the progression towards habitual smoking (Royal College of Physicians, 2007). However, environmental factors can also discourage tobacco use. Developing and enforcing smoke-free policies as well as increasing taxes can serve as barriers to smoking, and thus, reduce initiation rates and promote cessation attempts (WHO, 2010).

The interplay of these factors influences the development and resiliency of this disorder, as well as the challenges associated with quitting. A significant portion of tobacco control efforts has been directed towards developing

individual-based cessation interventions that facilitate quitting and remaining smoke-free. Of the various modalities and settings offered, behavioural counseling and pharmacotherapy, used alone or in combination, have shown to yield the greatest success (USDHHS, 2008). The effectiveness of some cessation strategies can be found in Table 1.

Table 1

*Abstinence at Six Months for Smoking Cessation Strategies (USDHHS, 2008)*

| Cessation strategies | % abstinent [95% CI] |
|---|---|
| Physician advice to quit | 10.2 [8.5, 12.0] |
| Behavioural interventions | |
| Proactive telephone counseling | 13.1 [11.4, 14.8] |
| Group counseling | 13.9 [11.6, 16.1] |
| Individual counseling | 16.8 [14.7, 19.1] |
| Pharmacotherapy interventions | |
| Nicotine patch (6 – 14 weeks) | 23.4 [21.3, 25.8] |
| Nicotine gum (6 – 14 weeks) | 19.0 [16.5, 21.9] |
| Nicotine lozenge (2 mg) | 24.2[a] |
| Nicotine inhaler | 24.8 [19.1, 31.6] |
| Bupropion SR | 24.2 [22.2, 26.4] |
| Varenicline (2 mg/day) | 33.2 [28.9, 37.8] |

*Note.* CI = Confidence Interval
[a]One qualifying randomized trial; 95% CI not reported

**Nicotine Replacement Therapy (NRT)**

Currently Health Canada's Therapeutic Products Directorate has approved six smoking cessation medications, including four NRT formulations (patch, gum, lozenge, and inhaler) and two non-NRT compounds (bupropion and varenicline

tartrate). It is imperative that cessation aids effectively manage craving and withdrawal symptoms because their intensity has shown to predict relapse (Swan, Ward, & Jack, 1996). NRT has been recognized as a first line treatment for smoking cessation, in part because it suppresses these symptoms. The fundamental mechanism by which all NRT formulations exert their effect is by binding to nAChRs that were formerly activated by nicotine obtained from cigarettes (Shiffman, Fant, Buchhalter, Gitchell, & Henningfield, 2005). The transdermal patch is an easy, convenient formulation that releases nicotine into the skin at a steady state (Shiffman et al., 2005). Research has shown that the patch effectively alleviates background cravings (Rose, Herskovic, Trilling, & Jarvik, 1985), which are constantly present and require no triggering stimuli (Shiffman, 2000). However, this passive modality does not protect users against episodic craving (Tiffany, Cox, & Elash, 2000; Waters et al., 2004). Episodic cravings are acute, intense, and typically provoked by environmental (e.g., someone smokers) or affective (e.g., emotional distress) stimuli (Shiffman, 2000). These acute craving episodes are particularly problematic because they are associated with a very high risk of relapse (Shiffman, Paty, Gnys, Kassel, Hickcox, 1996). Therefore, being able to quickly administer a dose of nicotine during an “at-risk” moment will help avoid a lapse (Shiffman et al., 2005).

**Oral NRT.** Several fast-acting oral NRT formulations are available in Canada, including the nicotine gum, lozenge, and inhaler. These products deliver nicotine through the oral mucosa membrane that lines the inside of the mouth. Orals NRTs offer the following advantages compared to the patch. Firstly, maximum nicotine blood concentrations are reached faster (in less than 1 hour;

McRobbie et al., 2010). Secondly, the user can control the amount and timing of dosing on an “as needs basis” (Shiffman et al., 2005). Lastly, the oral administration of these formulations mimics some of the sensory cues associated with the smoking behaviour (i.e., oral stimulation; Muramoto, Ranger-Moore, & Leischow, 2003).

A recent Cochrane review by Stead and colleagues (2012) revealed that the nicotine gum, lozenge/tablets, and inhaler are all effective smoking cessation aids, with respective pooled risk ratios of 1.49 (95% CI [1.40, 1.60], 55 trials), 1.95 ([1.61, 2.36], 6 trials), and 1.90 ([1.36, 2.67], 4 trials) compared to placebo or non-NRT control groups. While they exhibit comparable efficacy profiles, other factors must be weighed when selecting the most appropriate product for a single-dose randomized controlled trial. Two important factors to consider are: 1) standardization of the amount of nicotine consumed and 2) ease of drug administration. The lozenge allows for more consistent nicotine dosing, whereas, several confounding variables may influence amount of nicotine absorbed by the gum and inhaler modalities. For example, up to 50% of the nicotine can remain in the gum if not properly chewed (Benowitz, Jacob, & Savanapridi, 1987). In addition, the number and depth of inhalations as well as environmental factors, such as room temperature, impact the amount of nicotine absorbed from the inhaler (Lunell, Molander, & Andersson, 1997). The lozenge is also easier to administer and demands less activity (i.e., passively dissolves in mouth) than the gum (i.e., chew-and-park technique) or the inhaler (i.e., requires continuous puffing).

**Nicotine lozenge.** A single nicotine lozenge has shown to significantly reduce cigarette craving and withdrawal symptoms in temporarily abstaining smokers. In a double-blinded, placebo-controlled, randomized-controlled crossover trial, McRobbie and colleagues (2010) examined the effect of a 2.5 mg nicotine lozenge in the initial 60 minutes of product use. Cigarette craving and withdrawal symptoms were assessed on 100 mm visual analogue scales. The lozenge group reported a mean change craving score of -24.7 (*SE* = 2.8), which was significantly greater than that of the placebo group, $M_{diff}$ = -15.8, 95% CI [-23.7, -7.9], $p < .0001$. Significant group differences in craving were found within 10 minutes of product placement. In regards to withdrawal symptoms, the lozenge group reported mean reductions for irritability, restlessness, and poor concentration of 9.6 (*SE* = 2.2), 10.8 (*SE* = 2.0), and 7.1 (*SE* = 2.0), respectively. The lozenge group had significantly greater decreases than the placebo for irritability, $M_{diff}$ = -7.6, [-14.6, -.7], $p = .02$, restlessness, $M_{diff}$ = -10.0, [-16.5, -3.5], $p = .0006$), and poor concentration, $M_{diff}$ = -7.5, [-14.2, -.7], $p = .02$.

Shahab, McEwen, and West (2011) examined the effects of a 4 mg nicotine lozenge on cigarette craving and withdrawal symptoms in a single-blinded, randomized-controlled crossover trial. Significant decreases in craving (i.e., urge to smoke and desire for cigarette) were reported over the 20-minute assessment period. Of the five withdrawal symptoms assessed (i.e., depressed mood, irritability, restlessness, hunger, and poor concentration), significant reductions were found for poor concentration and restlessness from before to after NRT use. Similarly, Kotlyar and colleagues (2007) found that a 4 mg lozenge resulted in significant linear decreases in cigarette craving and

aggregated withdrawal symptoms from before to 5, 10, and 30 minutes after product placement.

These findings corroborate the efficacy of the nicotine lozenge and its ability to reduce craving and withdrawal symptoms. However, as advised by pharmaceutical companies, NRTs should be augmented with other treatments to maximize symptom relief. Applying two efficacious monotherapies concurrently may provide additive benefit and greater symptom relief. Meditation, deep breathing, cognitive relaxation techniques, and exercise are examples of acute strategies that have been postulated to relieve cravings and could be implemented with a nicotine lozenge. Of these adjunctive strategies, exercise is the strongest contender because its effects on craving and withdrawal symptoms have been most scientifically validated.

## Acute Effects of Exercise

The effects of acute exercise on nicotine-deprived smokers have been comprehensively studied and summarized in several systematic reviews (i.e., Hassova et al., 2013; Roberts, Maddison, Simpson, Bullen, & Prapavessis, 2012; Taylor, Ussher, & Faulkner, 2007).

**Cigarette craving.** Two meta-analyses (i.e., Hassova et al., 2013; Roberts et al., 2012) have quantified the effect of exercise on cigarette cravings. Roberts and colleagues used aggregate data to conduct their analyses, whereas Hassova et al. used individual participant data (IPD), which is a more rigorous statistical approach. The included studies used a temporary abstinence paradigm and involved different types (e.g., isometric, aerobic) and modes (e.g., cycling,

walking, running, and isometric) of exercise that ranged in intensity (light to vigorous) and duration (5 to 18 minutes). Craving was assessed using the 'desire to smoke' (DtS) and/or 'strength of desire to smoke' (SoD) item(s), both of which are rated on 7-point Likert scales.

The meta-analyses (Hassova et al., 2013; Roberts et al., 2012) concluded that a single bout of exercise has a positive effect on cigarette craving. Based on the aggregated data of 10 trials (Arbour-Nicitopoulos, Faulkner, Hsin, & Selby, 2011; Faulkner, Arbour-Nicitopoulos & Hsin, 2010; Janse Van Rensburg & Taylor, 2008; Janse Van Rensburg, Taylor, Bennattayallah, & Hodgson, 2012; Janse Van Rensburg, Taylor, & Hodgson, 2009a; Janse Van Rensburg, Taylor, Hodgson, & Benattayallah, 2009b; Scerbo, Faulkner, Taylor, & Thomas, 2010; Taylor & Katomeri, 2007; Taylor, Katomeri, & Ussher, 2006; Ussher, Nunziata, Cropley, & West, 2001), Roberts and colleagues (2012) calculated a weighted mean difference in DtS between exercise and control conditions of -1.90 points, 95% CI [-3.06, -.075], in favour of exercise. Similarly, the weighted mean difference in SoD of nine trials (Everson, Daley, & Ussher, 2006, 2008; Janse Van Rensburg et al., 2012; Scerbo et al., 2010; Taylor & Katomeri, 2007; Taylor, Katomeri, & Ussher, 2005; Ussher, Cropley, Playle, & Mohidin, 2009; Ussher et al., 2001; Ussher, West, Doshi, & Sampuran, 2006) favoured the exercise condition by -2.41 points, [-3.45, -1.37]. These findings are analogous to those reported by Hassova and colleagues who used individual participant data. For example, across 17 studies (Daniel, Cropley, & Fife-Schaw, 2006; Daniel, Cropley, Ussher, & West, 2004; Faulkner et al., 2010; Haasova, Oh, & Taylor, 2011; Janse Van Rensburg, Elibero, Drobes, Ehlke, & Watson, 2011; Janse Van

Rensburg & Taylor, 2008; Janse Van Rensburg et al., 2012, 2009a, 2009b; Katomeri, 2009; Oh, 2011; Scerbo et al., 2010; Taylor & Katomeri, 2007; Taylor et al., 2005; Thompson, 2009; Ussher et al., 2001, 2006), the weighted mean difference on DtS between exercise and control conditions was -2.04 points, 95% CI [-2.60, -1.46], in favour of exercise. Furthermore, their meta-analysis of 15 studies (Daniel et al., 2006, 2004; Everson et al., 2008; Faulkner et al., 2010; Haasova et al., 2011; Janse Van Rensburg et al., 2012; Katomeri, 2009; Oh, 2011; Scerbo et al., 2010; Taylor & Katomeri, 2007; Taylor et al., 2005; Thompson, 2009; Ussher et al., 2009, 2001, 2006) favoured the exercise condition by -1.91 points, [-2.59, -1.22] for SoD. The effect sizes found in these studies were moderate to large in size (ranging from $d$ = 0.4 to 1.9; Cohen, 1988). This is comparable to, or many cases exceed the effect sizes found with oral NRTs.

With respect to craving time effects, the magnitude of craving relief appears greatest during, or immediately after exercise. However, significant effects have been shown to last up to 30 minutes post-exercise (Scerbo et al., 2010; Ussher et al., 2009). The speed at which exercise relieves urges to smoke may be faster than that of the nicotine lozenge. While significant reductions have been reported within 3 to 5 minutes of administering a lozenge, maximal relief is not attained until after 30 minutes (Hansson, Hajek, Perfekt, & Kraiczi, 2012). The timing of this effect is in accordance with pharmacokinetic studies that reveal maximal blood nicotine levels at 25 (McEwen, West, & Gaiger, 2008) and 30 minutes (Kotlyar et al., 2007) post-administration.

Exercise-induced reductions in cigarette craving have been observed with various types of exercise and across all intensities. Even 10 minutes of isometric exercise (Ussher et al., 2009) or a low-intensity yoga session (Elibero, Janse Van Rensburg, & Drobes, 2011) have shown to significantly reduce craving relative to passive controls. However, recent work by Hassova and colleagues (2014) found that the benefits of exercise are significantly influenced by the intensity at which it is performed. Hassova et al. (2014) conducted a one-stage IPD meta-analysis on 930 subjects. They rescaled the DtS and SoD craving items from 0 to 100, thus a difference between groups of -10 indicated that post-intervention craving scores were 10% lower in the exercise group compared to the controls. The analysis revealed mean differences of -9.22, 95% CI [-15.24, -3.20], -34.56 [-2.59, -1.22], and -31.29 [-2.59, -1.22], for light-, moderate-, and vigorous-intensity exercise, respectively. Thus, as previously shown by Hassova et al. (2013), exercising at a light intensity results in craving reductions of a smaller magnitude compared to those resulting from moderate or vigorous intensities. However, no significant difference exists between the effects of moderate- and vigorous-intensity exercise on craving relief. In other words, there seems to be no additional benefit from engaging in vigorous as opposed to moderate-intensity exercise (Hassova et al., 2014). This finding is advantageous from a clinical standpoint because moderate-intensity exercise (e.g., brisk walking) is more convenient and tolerable than vigorous-intensity exercise. Therefore, quitters may be more likely to execute and adhere to this behaviour.

**Withdrawal symptoms.** Exercise has shown to reduce various withdrawal symptoms, including irritability, depression, tension, restlessness, difficulty

concentrating, and stress (Roberts et al., 2012). However, the effects of exercise on withdrawal symptoms are inconsistent compared to craving. As a result, less research has been devoted to examining withdrawal symptoms and no meta-analysis has been conducted on this outcome to date. The findings described below are based on the systematic review provided by Roberts and colleagues (2012). Three of the five studies (Arbour-Nicitopoulos et al., 2011; Daniel, Cropley, & Fife-Schaw, 2007; Everson et al., 2008; Ho, 2009; Ussher et al., 2009) that used the Mood and Physical Symptoms Scale (MPSS) and variations of the scale (i.e., included stress and tension items) found significant reductions in at least three withdrawal symptoms (Daniel et al., 2007; Ussher et al., 2009) and/or the composite MPSS score pre- to post-exercise (Everson et al., 2008). Two of these studies (Everson et al., 2008; Ussher et al., 2009) compared the effects of exercise to a passive sitting condition and found significant interaction (Time x Condition) effects. Ussher and colleagues (2009) found that a 10-minute bout of isometric exercise reduced levels of irritability, restlessness, and difficulty concentrating, as well as tension and stress. Everson and colleagues (2008) found that those cycling for 10 minutes at a moderate intensity (40 to 59% HRR) reported lower composite MPSS scores at the 5-minute mark compared to those sitting passively. However, pairwise comparisons revealed the vigorous-intensity (60 to 85% HRR) cycling condition reported significantly higher composite MPSS scores during exercise than the passive control.

The acute exercise and temporary smoking cessation literature is encouraging. A single bout of exercise has shown to consistently alleviate cigarette craving, and at times withdrawal symptoms. Therefore, future research

should continue to investigate the mediating mechanisms through which exercise exerts its acute effects.

## Possible Mechanisms of Acute Exercise Effects

As previously mentioned, the effect of acute exercise on craving has yielded more conclusive evidence than on withdrawal symptoms. Therefore, greater efforts have been devoted towards explaining the exercise-craving relationship. Understanding the mechanisms by which exercise influences craving will not only substantiate the causality of this relationship, but also provide insight for developing interventions that maximize craving relief (Taylor et al., 2007). The proposed mechanisms that will be reviewed below have been categorized into affect, biological, and cognitive hypotheses (Hassova et al., 2013, 2014; Roberts et al., 2012; Taylor et al., 2007).

**Affect hypotheses**. According to the circumplex model of affect (Russell, 1980), affective states are thought to arise from two dimensions: valence (pleasure-displeasure continuum) and arousal. Smoking cigarettes and exercise are two behaviours that influence both of these dimensions. For example, smokers report decreases in arousal and increases in emotional stress during periods of temporary abstinence. However, both of these levels return to normal values upon smoking a cigarette (Steptoe & Ussher, 2006). Furthermore, increases in affective valence (Ekkekakis, Parfitt, & Petruzzello, 2011) and activation (i.e., arousal; Reed & Ones, 2006) have been shown to occur following a single bout of exercise. Therefore, it has been proposed that changes in affect resulting from a bout of exercise may mediate its effect on cravings (Taylor et al.,

2007). In a seminal study, Taylor and colleagues (2006) showed that the moderating effect of acute exercise on craving and withdrawal symptoms was mediated only through reduced emotional stress (i.e., self-reported tension). In another study, Elibero et al. (2011) found that when positive affect was higher, cravings were lower. However, changes in positive affect did not mediate the exercise and craving relations. Hassova and colleagues (2014) recently tested this hypothesis across the IPD (372 observations) of eight studies. The included studies compared the effects of moderate-intensity exercise on cravings and dimensions of affect to passive controls. They found the exercise group reported higher levels of arousal and positive feelings (valence) post-intervention after adjusting for baseline values. This finding suggests that a bout of moderate-intensity exercise increases positive feelings and arousal in temporarily abstaining smokers. However, these changes in affect were not significantly associated with post-intervention craving values. In other words, neither arousal nor valence appeared to meditate the exercise-craving relationship. Despite evidence dismissing arousal and valence as potential mechanisms, other constructs of mood and affect still warrant investigation.

**Biological hypotheses.** Due to the brain's limited-processing capacity, it is thought that the additional strain of exercise requires a shift in attention from cognitive (i.e., cravings) to somatic (i.e., bodily) thoughts (Acevedo & Ekkekakis, 2006). This hypothesis was supported by Janse Van Rensberg et al. (2012, 2009b) who found that exercise reduced activation in areas of the brain associated with reward processing and increased activation in default mode areas of the brain (i.e., medial rostral prefrontal cortex) in temporarily abstinent

smokers. The next step is to test whether this attention-shift mediates the effects of exercise on craving.

Biological markers, such as cortisol, dopamine, catecholamines, heart rate variability (HRV), and nicotine metabolism have also been proposed as potential mechanisms of the exercise-craving relationship. Chronic smoking results in higher levels of plasma and salivary cortisol, a hormone that helps to cope with stress (Baron, Comi, Cryns, Brinck-Johnsen, & Mercer, 1995; Field, Colditz, Willett, Longcope, & McKinlay, 1994). These elevated cortisol levels drop after the first 2 weeks of quitting smoking (Cohen, al'Absi, & Collins, 2004; Frederick, Reus, Ginsberg, Hall, Munoz, & Ellman, 1998; Pomerleau C., Garcia, Pomerleau O., & Cameron, 1992; Pomerleau O., Pomerleau C., & Marks, 2000; Steptoe & Ussher, 2006). Greater reductions in cortisol have been associated with increases in craving and withdrawal (Steptoe & Ussher, 2006), higher levels of distress, and predictive of subsequent relapse (Frederick et al., 1998). One plausible explanation for this finding is that there is an increase in nicotine receptor sensitivity associated with a reduction in cortisol leading to an intensification of tobacco craving and withdrawal symptoms (Pomerleau O. & Pomerleau C., 1990). It is also possible that the stimulating effects of cortisol may contribute to the reinforcing properties of smoking, in which case a dramatic drop in cortisol might be distressing for the smoker (Steptoe & Ussher, 2006). Acute exercise in healthy humans has been shown to elevate cortisol levels (Mastorakos & Pavlatou, 2005). Through extension, exercise may help buffer both the desire to smoke and withdrawal symptoms by raising cortisol levels back to normal, thus regulating the body's emotional stress response in the absence of

nicotine. Scerbo and colleagues (2010) found that exercising at a vigorous intensity resulted in a smaller decline in cortisol levels compared to moderate-intensity exercise or sitting passively. However, this attenuated drop in cortisol did not translate into lower reported cravings by the vigorous-intensity exercise condition. This null effect may be due to the short abstinence period (3 hours) used, and in turn, producing cravings of only moderate degree. Therefore, the role of cortisol in the exercise-craving relationship should be examined using a longer abstinence period.

The remaining biological mechanisms (dopamine, catecholamines, HRV, and nicotine metabolism) are at the early stages of investigation, as described below. 1) Animal research has shown that exercise stimulates the release of dopamine in the striatum of rats (Hattori, Naoi, & Nishino, 1994); which may mimic the effects of nicotine on the mesolimbic pathway. However, research has not yet confirmed that exercise increases dopamine in the human brain (Taylor et al., 2007). 2) The presence of nicotine stimulates the release of adrenaline and noradrenaline, two catecholamines partially responsible for tobacco's mood-altering effect. As smoking increases levels of circulating adrenaline and noradrenaline (Laustiola, Kotamäki, Lassila, Kallioniemi, & Manninen, 1991), quitting smoking decreases both (Ward et al., 1991). A single bout of exercise has shown to increase the concentration of circulating adrenaline and noradrenaline (Richter & Sutton, 1994), which may explain the effect of exercise on craving. 3) Heart rate variability has shown to decrease with habitual smoking (Lucini, Bertocchi, Malliani, & Pagani, 1996; Niedermaier et al., 1993) and increase 4 to 6 weeks after cessation (Stein, Rottman, & Kleiger, 1996). The

effect of acute exercise on HRV for smokers is unknown. However, acute exercise may expedite this process and produce immediate increases in HRV, which in turn, may positively affect craving and withdrawal symptoms. 4) The speed at which an individual metabolizes nicotine influences smoking behaviour (e.g., number of cigarettes consumed per day) as well as the intensity and frequency of cravings experienced during periods of abstinence (Kubota et al., 2006; Lerman et al., 2006; Schnoll et al., 2009). The role of nicotine metabolism should be examined as it may influence the amount of craving relief exercise is capable of providing (e.g., may be less effective for smokers with a high nicotine metabolism).

**Cognitive hypotheses.** It was once suggested that the cognitive demands required to engage in exercise might distract individuals from thoughts pertaining to craving. However, the distraction hypothesis seems doubtful–as explained by Taylor and colleagues (2007). For one, exercise that requires minimal cognitive demands, such as walking, has shown to attenuate craving to a similar degree as vigorous-intensity exercise that demands greater resources (Scerbo et al., 2010). In addition, if exercise served as a distractor, one would expect its effect to dissipate once exercise stopped. However, this is not the case, as reductions in craving have shown to last 50 minutes post-exercise (Taylor & Katomeri, 2007). For these reasons alone, distraction does not appear to be a significant contributor to the effects of exercise on craving. Another cognitive mechanism that has been tested is treatment expectations. Patients' expectancy beliefs have been shown to influence treatment outcome in various psychotherapies, where individuals with higher expectations experience greater

treatment benefits (Constantino, Arnkoff, Glass, Ametrano, & Smith, 2011). Two studies (Daniel et al., 2007; Harper, Fitzgeorge, Tritter, & Prapavessis, 2013) examined if smokers' treatment expectations towards exercise influenced its effectiveness. Both studies revealed that expectancy levels (hi vs. low) did not correspond to the magnitude of symptom relief reported pre- to post-exercise.

**Combining Acute Exercise with a Nicotine Lozenge**

Ample research has confirmed that a single dose of exercise or nicotine consumed through a lozenge can effectively alleviate craving, and at times, withdrawal symptoms. Although both monotherapies have shown to produce greater relief compared to placebos, the adverse symptoms of nicotine deprivation persist and unfortunately cause the majority of individuals to return to smoking. Implementing these monotherapies together may provide additive relief and minimize cravings that linger.

Combining monotherapies with distinct mechanisms of action or therapeutic pathways has the potential to yield additive benefit (Ebbert, Hays, & Hurt, 2010). Apart from the dopamine hypothesis, the proposed mechanisms of acute exercise differ from the process by which the nicotine lozenge exerts its effect. Therefore, consuming a nicotine lozenge in adjunct with exercise may produce greater reductions in craving and withdrawal symptoms. To date, only one study has examined the acute effects of combining exercise and NRT on craving and withdrawal symptoms (Harper, Fitzgeorge, Tritter, & Prapavessis, 2012). In a 14-week exercise-aided NRT cessation program, Harper and colleagues (2012) found female quitters on the nicotine patch reported a

decrease in craving and withdrawal symptoms after a bout of moderate-intensity exercise. Significant reductions in craving pre- to post-exercise were found at all three assessment points of the program: 1) Week 5 (1 week after quitting while on the 21 mg NRT dose); 2) Week 11 (7 weeks after quitting while on the 14 mg NRT dose); 3) Week 13 (9 weeks after quitting while on the 7 mg NRT dose). In regards to withdrawal symptoms, significant reductions in psychological and sedation symptoms were shown at Week 5 and 11, but not at Week 13. Significant increases in physical symptoms were found at Week 5 and 11, but not at Week 13. No significant change in appetite was evident at any time point. In summation, Harper and colleagues found that exercise provided additional symptom relief while on an NRT. Although these findings are encouraging, it cannot be said for certain that these reductions in craving and withdrawal symptoms are specifically related to exercise because there was no control condition solely receiving the NRT patch. To validate this work, a more robust methodology must be used that compares the combined treatment to a control condition. Furthermore, the steady-release of nicotine from the transdermal patch alleviates background cravings; hence the instantaneous effect of both a nicotine lozenge and acute exercise on episodic cravings in recently abstinent smokers remains unknown.

## Purpose and Hypothesis

**Purpose.** The purpose of the present study was to examine whether an acute bout of moderate intensity exercise provides additional craving (primary outcome) and withdrawal (secondary outcome) relief to the NRT lozenge in recently quit smokers.

**Hypothesis.** It was hypothesized that participants in the treatment condition (acute exercise and nicotine lozenge) would report greater reduction in craving and withdrawal symptoms than those in the control condition (nicotine lozenge alone).

# Chapter Two: The Current Study

## Methods

The subsequent methods are reported in accordance with CONSORT principles (www.consort-statement.org). The conduct of this study adhered to the guidelines outlined in the Declaration of Helsinki (World Medical Association, 2013) and the Handbook for Good Clinical Research Practice (WHO, 2002). Ethical approval was granted from Western University's Health Sciences Research Ethics Board (#103508; Appendix A). All participants read the Letter of Information (Appendix A), had his/her questions answered, and signed a Consent Form (Appendix A) prior to participation in the study.

### Design

This research study used a two-group randomized controlled trial design. Randomization was accomplished using a computer-generated numbers table.

### Participants

Inclusion criteria included: (1) aged 18 to 65 years, (2) smoked a minimum of five cigarettes per day, (3) interested in quitting, (4) no contraindications to physical activity, and (5) no contraindications to NRT. Exclusion criteria included: (1) females who were pregnant, intending on becoming pregnant, or breast-feeding while in the study and (2) inability to abstain from smoking for a minimum of 15 hours without nicotine replacement aids. Thirty participants ($M_{age}$ = 40.24 years, *SD* = 10.36) who satisfied all criteria completed the study and were

randomized into one of two conditions: moderate intensity exercise (experimental arm) or passive sitting (control arm). Participants included 10 males and 20 females.

## Primary Outcome Measure

**Craving.** Cigarette craving was assessed using the "I have a desire to smoke" statement (Tiffany & Drobes, 1991). Desire to smoke was scored on a 7-point Likert scale, from 1 (*strongly disagree*) to 4 (*neither agree nor disagree*), and 7 (*strongly agree*).

## Secondary Outcome Measure

**Withdrawal symptoms.** Nicotine withdrawal symptoms were measured using the Moods and Physical Symptoms Scale (MPSS; West & Hajek, 2004). The MPSS contains five single-items that are believed to be part of the nicotine withdrawal syndrome, including depressed mood, irritability, restlessness, hunger, and poor concentration. In line with previous acute studies, the hunger and depression items were removed because of the short assessment period used (e.g., Kotlyar et al., 2007; McRobbie et al., 2010). In addition to the withdrawal symptoms described above, the MPSS assesses ratings of strength of urges to smoke and time spent with urges to smoke. These two items were also excluded because it has been suggested that they may not reflect withdrawal symptoms, but rather cigarette craving. The three remaining items were rated on a 5-point scale, ranging from 1 (*not at all*) to 5 (*extremely*). Separate change scores were calculated for each item.

## Other Measures

**Demographic and smoking behaviour.** The following information was collected: age, gender, smoking status (e.g., number of cigarettes smoked per day), and smoking history (e.g., number of years smoking regularly, number of previous quit attempts). In addition, height (m) and weight (kg) were provided and Body Mass Index (BMI: $kg/m^2$) was calculated.

**Physical activity.** The short-form International Physical Activity Questionnaire (IPAQ; Craig et al., 2003) was used to measure current levels of physical activity. The IPAQ assesses (1) walking, (2) moderate, and (3) vigorous physical activities. Participants were asked to estimate the amount of time (in minutes) they spent performing each type of physical activity in the previous 7 days. Time spent sitting was measured as well, however, given that this is an indicator of sedentary activity, it was excluded in the present study. Separate MET-minutes were computed for each level of physical activity by multiplying the MET score of an activity by the minutes performed weekly. The MET scores used in the calculation included: (1) walking = 3.3 METs, (2) moderate physical activity = 4.0 METs, and (3) vigorous physical activity = 8.0 METs. A total physical activity score was computed by summing the MET-minute scores for each activity. In line with the recommended scoring protocol, participants' physical activity levels were classified as low, moderate, or high.

**Cigarette dependence.** Perception of cigarette dependence was measured using the Fagerström Test for Cigarette Dependence (FTCD; Fagerström, 2012), formerly known as the Fagerström Test for Nicotine

Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991). The FTCD contains six items that were summed to yield a total score out of 10 points. A five-level categorization system was used ranging from very low to very high dependence. These classes have been scored as very low (0 to 2), low (3 to 4), medium (5), high (6 to 7), and very high (8 to 10). The FTCD has shown high internal consistency ($\alpha = .64$, $p < .001$) and adequate test-retest reliability ($r = .88$; Pomerleau C., Carton, Lutzke, Flessland, & Pomerleau O., 1994). In the current study, the Cronbach's alpha was slightly below the acceptable level ($\alpha = .619$), however, the mean inter-item correlation was adequate, falling within the range of .2 to .4 (Briggs & Cheek, 1986).

## Intervention

**Moderate intensity exercise.** The experimental condition completed a single bout of moderate intensity exercise. The session entailed a 2-minute warm-up, 15 minutes of moderate-intensity exercise, and a 3-minute cool-down on a Woodway PPS treadmill (Woodway, Waukesh, WI). Moderate intensity was defined as 45 to 68% of heart rate reserve (HRR; Karvonen, Kentala, & Mustala, 1957). Heart rate reserve was calculated using the formula: maximum heart rate ($HR_{max}$ = 220 − age) − resting heart rate ($HR_{rest}$). Resting heart rate was taken at Visit 1 because values can drop approximately 8.5 beats per minute upon 11 to 15 hours of abstinence (Perkins, Epstein, Stiller, Marks, & Jacob, 1989). Therefore, using $HR_{rest}$ values collected prior to quitting provided a more accurate indicator of a normal heart rate. The calculation for 45% HRR was: [($HR_{max}$ − $HR_{rest}$) × .45] + $HR_{rest}$. The calculation for 68% HRR was: [($HR_{max}$ − $HR_{rest}$) × .68]

+ $HR_{rest}$. Heart rate was monitored using the Polar RS100 heart rate device. The researcher controlled the incline and speed of the treadmill to ensure that participants were exercising in their target heart rate range.

**Passive sitting.** The control condition sat alone in a laboratory room for 20 minutes and had minimal contact with the researcher. Participants were allowed to read if they desired.

## Procedure

Male and female smokers from London, Ontario who were interested in quitting were recruited through several sources. Advertisement was exhibited in local newspapers, posters were placed at medical clinics, and a mass e-mail was sent to students of Western University and employees of the Middlesex London Health Unit (Appendix A).

Participants were initially screened for eligibility criteria by telephone or e-mail. Screening questions pertained to age (i.e., between 18 and 65 years), smoking status (i.e., number of cigarettes smoked per day), contraindications to NRT or exercise (i.e., capable of walking on a treadmill for 20 minutes at a moderate intensity), and for females, current pregnancy or breast-feeding statuses. For those eligible and interested, a first visit was scheduled where initial screening was confirmed and the Physical Activity Readiness Questionnaire (PAR-Q; Canadian Society for Exercise Physiology [CSEP], 2002) was completed. Participants who answered “yes” to any question on the PAR-Q were ineligible to participate. The study required participants to come to the Exercise and Health Psychology Laboratory (EHPL, www.ehpl.uwo.ca) at the University of

Western Ontario (London, Ontario) for two sessions, before (Visit 1) and after quitting (Visit 2). See Figure 2 for a flow diagram of participants.

Participants verified their smoking status at Visit 1 using the piCO+™ Smokerlyzer® carbon monoxide (CO) monitor (Bedfont Scientific, USA). In line with previous research (Faulkner et al., 2010), a breath CO reading greater than 10 parts per million (ppm) was considered the threshold for inclusion in the study. Resting heart rate was collected as well. Participants then completed the following questionnaires: (1) demographic and smoking behaviour, (2) IPAQ (Craig et al., 2003), (3) FTCD (Fagerström, 2012). All questionnaires can be found in Appendix B. Visit 1 took approximately 45 minutes to complete.

Visit 2 was scheduled within 1 week of the initial visit. Participants quit smoking cigarettes and refrained from using nicotine products 15 hours prior to the second visit. Upon arriving at the laboratory, participants provided another breath carbon monoxide (CO) sample to confirm their smoke-free status. A concentration reading of less than 6 ppm was deemed acceptable (as used in previous research). Participants who were unable to obtain a reading of less than 6 ppm were rescheduled for a second attempt. Those participants unable to abstain from cigarettes or nicotine products for the rescheduled appointment were deemed ineligible for the study. Once abstinence was confirmed, participants' heart rates were collected and questionnaires pertaining to cigarette craving (i.e., desire to smoke; Tiffany & Drobes, 1993) and nicotine withdrawal symptoms (i.e., Mood and Physical Symptoms Scale; West & Hajek, 2004) were completed. Those who reported craving scores of 1 or 2 (out of 7) were excluded

because these baseline values were too low to demonstrate a substantial decline.

All eligible participants were then randomized to the experimental or control condition and received a single dosage of the 2 mg NICORETTE® lozenge. The researcher instructed the participant to place the lozenge in his/her mouth and let it dissolve (approximately 20 minutes), occasionally moving the lozenge from one cheek to the other without chewing or swallowing it.

Immediately after administering the lozenge, participants commenced the 20-minute treatment they were allocated to (i.e., moderate intensity exercise or passive sitting). Cigarette craving and nicotine withdrawal symptoms were assessed during treatment (at 10 and 20 minutes). Following treatment, both conditions sat passively for 40 minutes. Post-treatment craving and withdrawal symptoms were assessed four times at 10-minute intervals. See Table 2 for the schedule of measures. After completing these assessments, the researcher provided participants with a set of smoking cessation aids that included 27 2 mg NICORETTE® Lozenges (expected to last 2 to 3 days), the Forever Free™: A Guide To Remaining Smoke Free, and direct access to the Smokers Help Line (1-877-513-5333). In addition, participants were invited to use the EHPL exercise facility over the next two weeks and were offered $50.00 of compensation. Visit 2 took approximately 90 minutes to complete.

Table 2

*Schedule of Measures*

| Variable | *1* | *2* | *3* | *4* | *5* | *6* | *7* | *8* |
|---|---|---|---|---|---|---|---|---|
| Expired CO | X | X | | | | | | |
| PAR-Q | X | | | | | | | |
| Demographic & smoking behaviour | X | | | | | | | |
| IPAQ | X | | | | | | | |
| FTCD | X | | | | | | | |
| Heart rate | X | X | X | X | X | X | X | X |
| Craving | | X | X | X | X | X | X | X |
| MPSS | | X | X | X | X | X | X | X |

*Note.* CO = carbon monoxide; PAR-Q = Physical Activity Readiness Questionnaire; IPAQ = International Physical Activity Questionnaire; FTCD = Fagerström Test for Cigarette Dependence; MPSS = Mood and Physical Symptoms Scale. 1 = Pre-quit (Visit 1) 2 = Baseline (Visit 2), 3 = 10-min of treatment, 4 = 20-min of treatment, 5 = 10-min post-treatment, 6 = 20-min post-treatment, 7 = 30-min post-treatment, 8 = 40-min post-treatment).

**Pilot sample.** A pilot sample (*n* = 10) was used to determine the optimal timing of administering the lozenge and commencing exercise to examine its additive effect. Previous research shows that maximum blood nicotine levels are reached 25 (McEwen et al., 2008) and 30 minutes (Kotlyar et al., 2007) after administering a lozenge. Exercise has shown a more rapid effect on craving, with reductions occurring almost immediately after onset. To account for the potential lag of the lozenge, a sequential approach was initially used where the experimental condition started exercising 10 minutes after administering the lozenge. However, preliminary data showed that the lozenge reduced cravings as early as 10 minutes after product placement (Figure 1). Therefore, the protocol was altered so the exercise and lozenge were administered simultaneously.

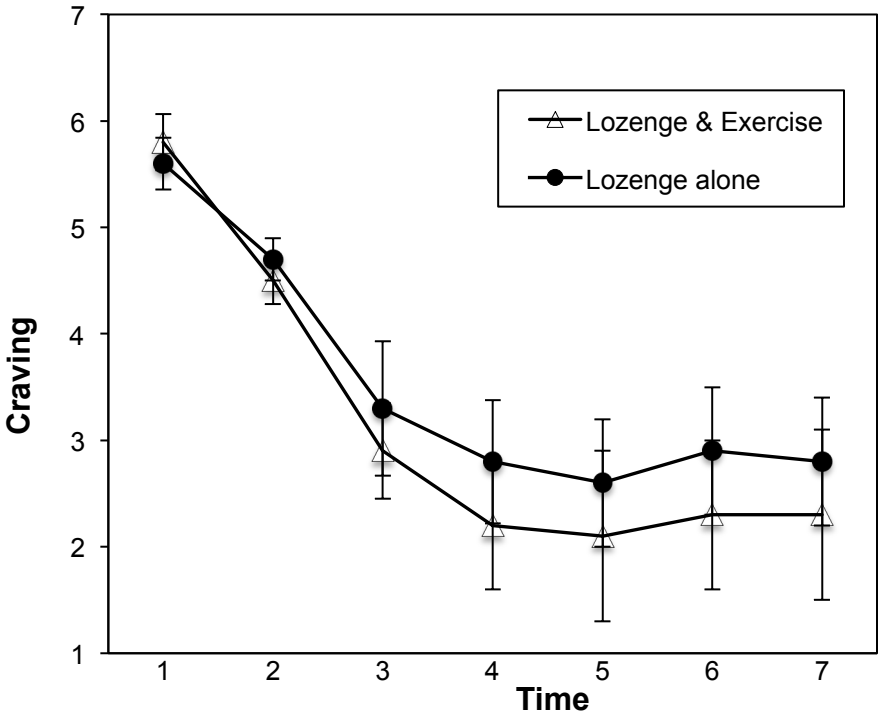


*Figure 1.* Pilot sample's craving relative to time (1 = baseline, 2 = 10-min of treatment, 3 = 20-min of treatment, 4 = 10-min post-treatment, 5 = 20-min post-treatment, 6 = 30-min post-treatment, 7 = 40-min post-treatment). Error bars represent standard errors.

## Sample Size Calculation

Muramoto and colleagues (2003) found that a single nicotine lozenge elicited a 1.43-point reduction in craving (desire to smoke) assessed on a 7-point scale. Roberts and colleagues (2012) calculated a weighted mean difference between exercise and control conditions of -1.90 points on the desire to smoke scale, in favour of exercise. If the effects of the nicotine lozenge and exercise were 100% additive, it would be expected that participants receiving both exercise and the nicotine lozenge would experience a larger reduction in craving (experimental mean = 3.33, *SD* = 1.0) compared to those receiving the nicotine lozenge alone (control mean = 1.43, *SD* = 1.0). Hence, in order to be adequately powered (power = .99) to detect this difference with the alpha set at .05, a sample size of 30 smokers was needed (SamplePower 3, IBM-SPSS).

## Statistical Analyses

**Fidelity check (exercise).** A one-way analysis of covariance (ANCOVA) was conducted to compare the groups' heart rate data collected after 20 minutes of treatment. Heart rate data collected immediately prior to treatment (i.e., baseline) were used as the covariate in this analysis.

**Group equivalency.** One-way analysis of variances (ANOVAs) and Chi-square tests were used to determine if any differences existed between groups for the following data: (a) demographic and smoking behaviour variables assessed at Visit 1 and (b) baseline (pre-treatment) craving and withdrawal symptoms scores and CO levels assessed at Visit 2.

**Primary and secondary outcome analyses.** A series of 2 (Condition: moderate intensity exercise vs. passive sitting) × 7 (Time: baseline, 10-min of treatment, 20-min of treatment, 10-min post-treatment, 20-min post-treatment, 30-min post-treatment, 40-min post-treatment) repeated measures ANOVAs were used to determine whether group differences could be seen across time for primary (i.e., craving) and secondary outcomes (i.e., restlessness, irritability, and poor concentration). As recommended by Thomson, Nelson, and Silverman (2005), significant interactions were described and main effects were only reported when no significant interaction was found.

Bivariate correlations were conducted on the variables of interest (i.e., craving, irritability, restlessness, and poor concentration). Standardized residual change scores were calculated for each variable using regression analysis, inputting the pre-treatment (baseline) value as the independent variable and the 20-min treatment value as the dependent variable (Schutz, 1989). The resulting residual or change score represents the degree of change over time, independent of the baseline value (Sallis, Alcarez, McKenzie, & Hovell, 1999).

The level of significance was accepted at $p < .05$ for all tests (Tabachnick & Fidell, 1996). Effect sizes ($\eta_p^2$, *phi*) accompany all reported findings. Data were analyzed using IBM SPSS Statistics (Version 21).

# Results

## Treatment of Data

**Missing data.** A pairwise deletion method was used to treat missing data. Ten data points were missing from Visit 1: one for age, one for height, two for weight, two for BMI, and four for the number of previous quit attempts. Two participants (one control, one intervention) were missing complete heart rate data collected at Visit 2.

**Outliers.** A boxplot technique was used to identify outliers. A datum point was considered an outlier if it extended more than 1.5 box-lengths from the edge of the box and an extreme outlier if it extended more than three box-lengths. Ten outliers were found at Visit 1: two for weight, two for BMI, one for CO level, four for number of quit attempts, and one for number of cigarettes smoked per day. No outliers were found at Visit 2. Outliers and extreme outliers were removed from the final data set.

**Assumptions of statistical techniques.** The following assumptions were satisfied in the present study. 1) The dependent variables assessed were interval or ratio (continuous). 2) A random sample from the population was used to obtain the data. 3) Each observation or measurement was independent from, or not influenced by, any other observation or measurement.

The assumption of normality was checked for the ANOVAs and ANCOVA. Normality was assessed in part using skewness and kurtosis values and histograms were used to check the shape of the distribution. The Kolmogorov-Smirnov statistic was also used to assess normality, where a significant value of

less than .05 indicated a violation of this assumption. These tests did not violate normality.

The assumption of homogeneity of variance was checked for the ANOVAs and ANCOVA using the Levene's test. A value of less than .05 was used to signify a violation of this assumption. No violations were found.

The assumption of homogeneity of intercorrelations was assessed for the repeated measures ANOVAs using Box's test of equality of covariance matrices. A significant value of less than .001 implied a violation of this assumption. Measures of poor concentration and restlessness violated this assumption, however, this was disregarded because the conditions were equal in size ($n$ = 15; Hakstian, Roed, & Lind, 1979).

The assumption of circularity was assessed for the repeated measures ANOVAs using Mauchly's test of sphericity. A significant value of less than .05 was used as an indicator of a violation of this assumption. Measures of craving, poor concentration, restlessness, and irritability were significant ($p$ < .05). Therefore, Multivariate statistics were reported to account for these violations (Stevens, 1996).

In regards to the bivariate correlations, the assumptions of linearity and homoscedasticity were checked through visual inspection of the distribution of data points in the scatterplots. No violations of assumptions were identified.

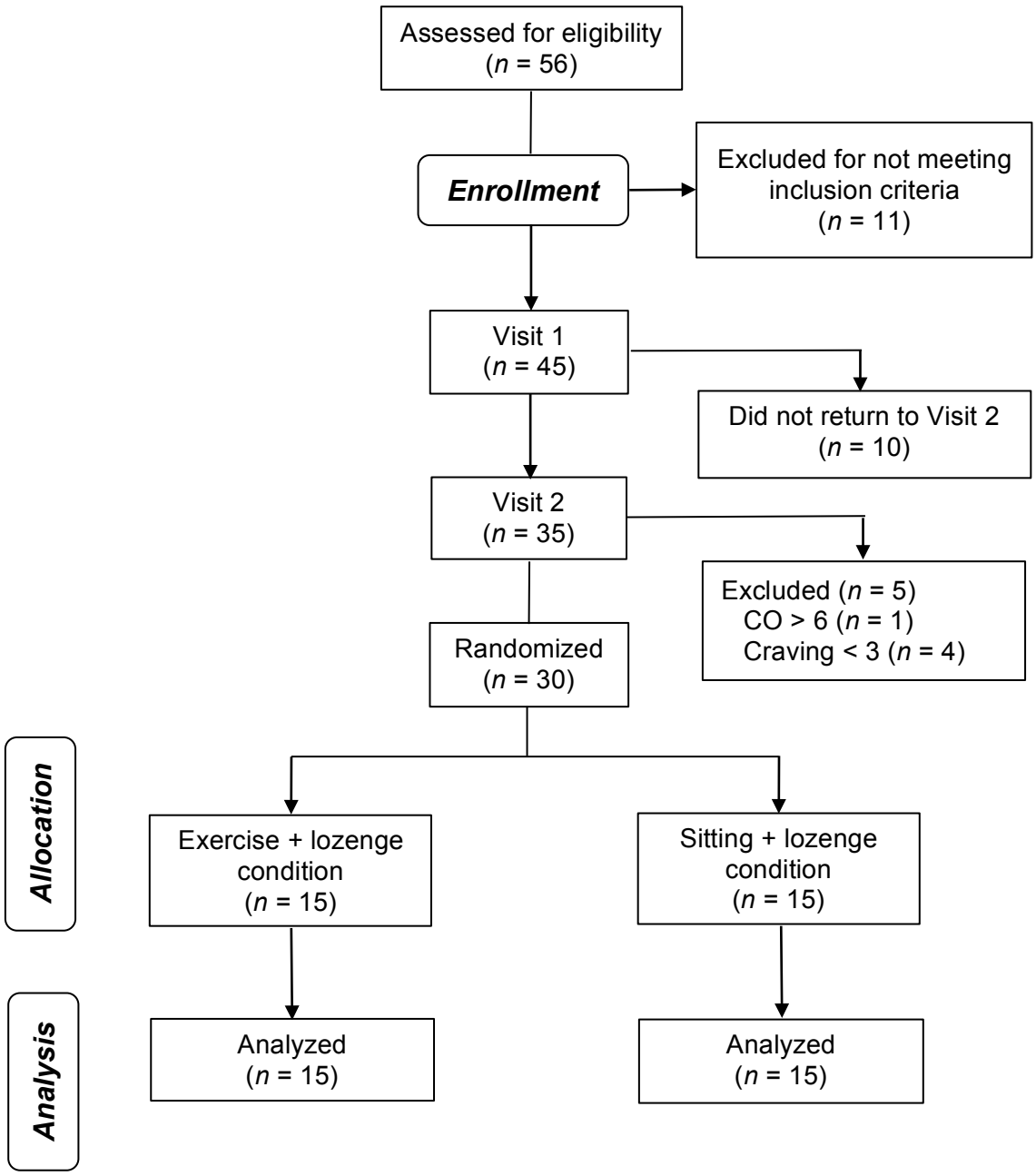


*Figure 2*. Flow of participants through the study.

**Fidelity Check**

After adjusting for pre-treatment values, those exercising ($n$ = 14, $M$ = 107.57, $SD$ = 6.97) had a significantly higher heart rates after 20 minutes of treatment compared to those sitting passively ($n$ = 14, $M$ = 79.50, $SD$ = 18.18), $F$ = 105.42, $p < .001$, $\eta_\rho^2 = .81$. All 14 participants in the exercise condition with complete heart rate data adhered to the moderate intensity prescription (45 to 68% HRR) while those in the control condition remained below this threshold.

**Group Equivalency at Baseline**

Demographic and smoking behaviour information is shown in Table 3. One-way ANOVAs revealed no significant group differences for age, $F(1, 27) = 0.64$, $p = .432$, $\eta_\rho^2 = .02$, weight, $F(1, 24) = 0.16$, $p = .690$, $\eta_\rho^2 = .01$, height, $F(1, 27) = 1.18$, $p = .287$, $\eta_\rho^2 = .04$, and BMI, $F(1, 24) = 0.99$, $p = .328$, $\eta_\rho^2 = .04$. Chi-square tests indicated no significant group differences for gender, $\chi^2$ (1, $n$ = 30) = 1.35, $p$ = .245, *phi* = -.28, or level of physical activity, $\chi^2$ (1, $n$ = 30) = 3.98, $p$ = .140, *phi* = .36.

No significant group differences were found for the following smoking behaviour variables assessed at Visit 1: CO level, $F(1, 27) = 3.28$, $p = .081$, $\eta_\rho^2 = .11$, number of cigarettes smoked daily, $F(1, 27) = 0.18$, $p = .673$, $\eta_\rho^2 = .01$, number of years smoked, $F(1, 28) = 0.10$, $p = .757$, $\eta_\rho^2 = .00$, Fagerström Test for Cigarette Dependence score, $F(1, 28) = 0.93$, $p = .343$, $\eta_\rho^2 = .03$, number of previous quit attempts, $F(1, 20) = 0.81$, $p = .380$, $\eta_\rho^2 = .04$, and seriousness of quit attempt, $F(1, 28) = 1.16$, $p = .290$, $\eta_\rho^2 = .04$. In addition, the number of

participants who had previously used NRT was not significantly different between groups, $\chi^2$ (1, *n* = 30) = 2.54, *p* = .111*, phi* = .36.

There was no significant group difference in CO levels collected at Visit 2, *F*(1, 28) = 1.79, *p* = .192, $\eta_\rho^2$ = .06. No significant group differences were found for baseline (pre-treatment) craving, *F*(1, 28) = 0.29, *p* = .595, $\eta_\rho^2$ = .01, irritability, *F*(1, 28) = 0.89, *p* = .353, $\eta_\rho^2$ = .03, restlessness, *F*(1, 28) = 0.12, *p* = .734, $\eta_\rho^2$ = .00, or poor concentration, *F*(1, 28) = 0.03, *p* = .871, $\eta_\rho^2$ = .00, assessed at Visit 2.

Table 3

*Demographic and Smoking Behaviour Variables*

| | Exercise Condition | | | Control Condition | | |
|---|---|---|---|---|---|---|
| Variable | *M* | *SD* | % | *M* | *SD* | % |
| Demographic: | | | | | | |
| Age | 38.64 | 8.25 | | 41.73 | 12.10 | |
| Gender (male) | | | 20 | | | 46 |
| Weight (kg) | 85.86 | 7.83 | | 87.71 | 14.40 | |
| Height (cm) | 176.79 | 6.38 | | 173.87 | 7.95 | |
| BMI ($kg/m^2$) | 27.42 | 3.75 | | 28.86 | 3.59 | |
| Physical activity (IPAQ) | | | | | | |
| High | | | 33 | | | 27 |
| Moderate | | | 20 | | | 53 |
| Low | | | 47 | | | 20 |
| Smoking behaviour: | | | | | | |
| Visit 1 CO level | 16.27 | 6.24 | | 20.64 | 6.78 | |
| Visit 2 CO level | 4.87 | 1.81 | | 5.67 | 1.45 | |
| Number of cigarettes per day | 18.23 | 8.34 | | 17.07 | 6.04 | |
| Number of years smoking | 22.87 | 6.42 | | 24.00 | 12.50 | |
| FTCD | 4.13 | 2.50 | | 4.93 | 2.02 | |
| Number of quit attempts | 2.50 | 1.78 | | 3.17 | 1.70 | |
| Previously used NRT | | | 47 | | | 13 |
| Seriousness of quit attempt | 8.73 | 2.34 | | 9.43 | 0.90 | |

*Note.* BMI = Body Mass Index; IPAQ = International Physical Activity Questionnaire; CO = carbon monoxide; FTCD = Fagerström Test for Cigarette Dependence; NRT = Nicotine Replacement Therapy

## Main Analyses

**Craving (primary outcome).** A significant condition by time interaction effect was found for desire to smoke, $F(6, 23) = 2.70$, $p = .039$, Wilks' $\Lambda = .59$, $\eta_\rho^2 = .41$. Both groups demonstrated a decrease in craving over time; however, the exercise condition's was of a greater magnitude (Table 4 and Figure 3).

**Withdrawal symptoms (secondary outcomes).** No significant condition by time interaction effects were found for restlessness (Table 5 and Figure 4), $F(6, 23) = 1.97$, $p = .112$, Wilks' $\Lambda = .66$, $\eta_\rho^2 = .34$, irritability (Table 6 and Figure 5), $F(6, 23) = 0.70$, $p = .653$, Wilks' $\Lambda = .85$, $\eta_\rho^2 = .15$, or poor concentration (Table 7 and Figure 6), $F(6, 23) = 0.91$, $p = .508$, Wilks' $\Lambda = .81$, $\eta_\rho^2 = .19$. However, significant time effects were found for restlessness, $F(6, 23) = 2.61$, $p = .044$, Wilks' $\Lambda = .60$, $\eta_\rho^2 = .41$, and irritability, $F(6, 23) = 3.29$, $p = .017$, Wilks' $\Lambda = .54$, $\eta_\rho^2 = .46$, with both conditions demonstrating reductions in scores from baseline. While ratings of poor concentration decreased from baseline in both conditions, no significant time effect occurred, $F(6, 23) = 2.47$, $p = .055$, Wilks' $\Lambda = .61$, $\eta_\rho^2 = .39$.

**Correlations.** Of the craving and withdrawal constructs, residual change scores in restlessness, irritability, and poor concentration were found to be significantly and positively correlated with one another (Table 8).

Table 4

*Means, Standard Deviations, and 95% Confidence Intervals for Craving Before, During, and After Treatment*

| | Exercise Condition | | | Control Condition | | |
|---|---|---|---|---|---|---|
| Time | *M* | *SD* | 95% CI | *M* | *SD* | 95% CI |
| Baseline | 5.67 | 1.11 | [5.13, 6.21] | 5.87 | 0.92 | [5.33, 6.41] |
| 10-min of treatment | 3.87 | 1.51 | [3.13, 4.61] | 4.93 | 1.28 | [4.19, 5.67] |
| 20-min of treatment | 2.93 | 1.44 | [2.11, 3.76] | 3.67 | 1.68 | [2.84, 4.49] |
| 10-min post | 2.67 | 1.35 | [1.85, 3.49] | 3.47 | 1.73 | [2.65, 4.29] |
| 20-min post | 2.80 | 1.08 | [2.02, 3.58] | 3.27 | 1.79 | [2.48, 4.05] |
| 30-min post | 2.60 | 1.24 | [1.84, 3.36] | 3.20 | 1.61 | [2.44, 3.96] |
| 40-min post | 2.47 | 1.06 | [1.70, 3.24] | 3.13 | 1.77 | [2.36, 3.90] |

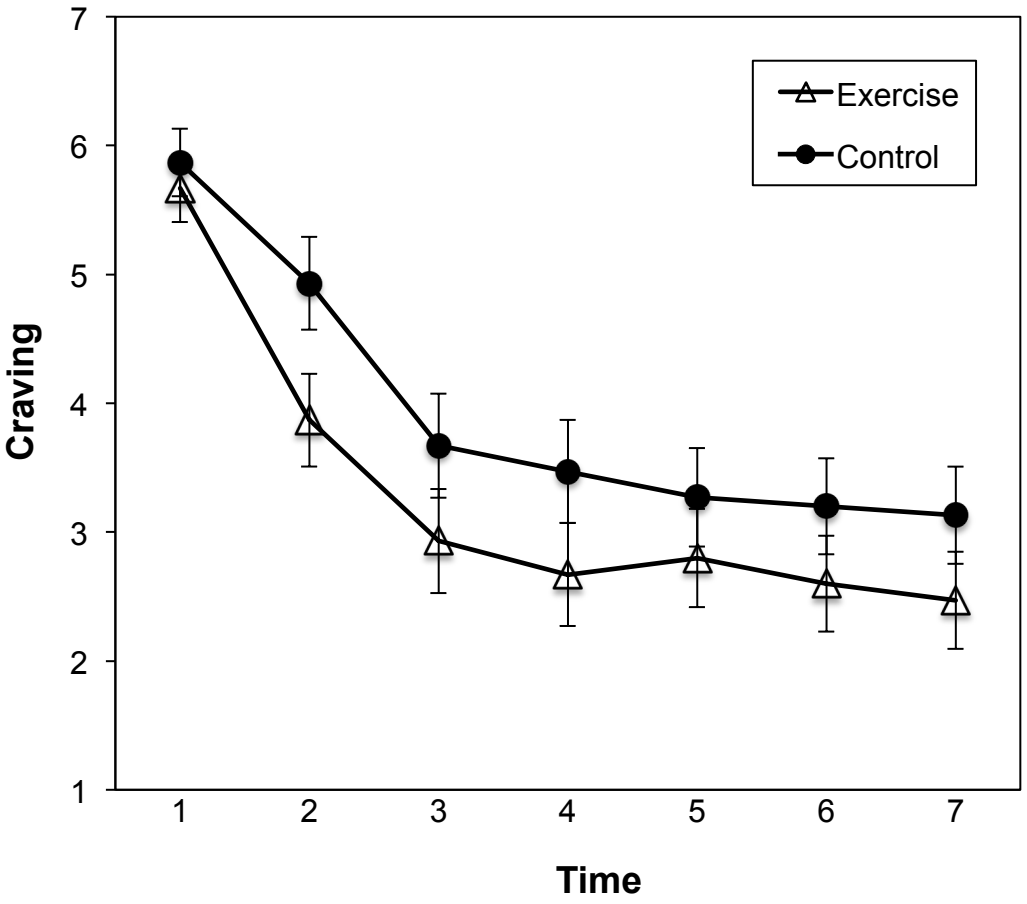


*Figure 3.* Craving relative to time (1 = baseline, 2 = 10-min of treatment, 3 = 20-min of treatment, 4 = 10-min post-treatment, 5 = 20-min post-treatment, 6 = 30-min post-treatment, 7 = 40-min post-treatment). Error bars represent standard errors.

Table 5

*Means, Standard Deviations, and 95% Confidence Intervals for Restlessness Before, During, and After Treatment*

| | Exercise Condition | | | Control Condition | | |
|---|---|---|---|---|---|---|
| Time | *M* | *SD* | 95% CI | *M* | *SD* | 95% CI |
| Baseline | 2.33 | 1.05 | [1.77, 2.90] | 2.20 | 1.08 | [1.64, 2.76] |
| 10-min of treatment | 1.27 | 0.59 | [0.91, 1.62] | 1.87 | 0.74 | [1.51, 2.22] |
| 20-min of treatment | 1.33 | 0.62 | [0.96, 1.70] | 1.80 | 0.77 | [1.43, 2.17] |
| 10-min post | 1.20 | 0.41 | [0.85, 1.56] | 1.97 | 0.86 | [1.61, 2.32] |
| 20-min post | 1.40 | 0.51 | [1.07, 1.73] | 1.90 | 0.71 | [1.57, 2.23] |
| 30-min post | 1.53 | 0.64 | [1.14, 1.93] | 1.87 | 0.83 | [1.47, 2.26] |
| 40-min post | 1.60 | 0.83 | [1.18, 2.02] | 1.83 | 0.75 | [1.42, 2.25] |

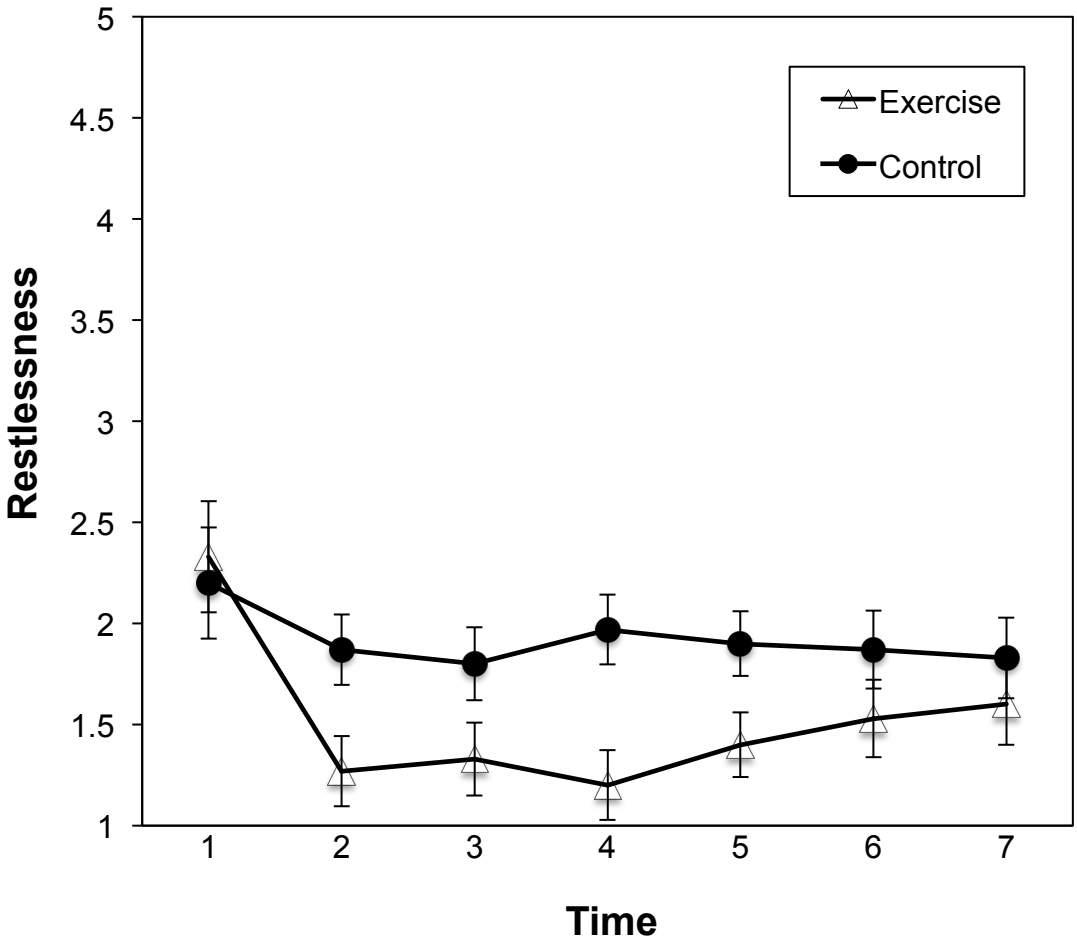


*Figure 4.* Restlessness relative to time (1 = baseline, 2 = 10-min of treatment, 3 = 20-min of treatment, 4 = 10-min post-treatment, 5 = 20-min post-treatment, 6 = 30-min post-treatment, 7 = 40-min post-treatment). Error bars represent standard errors.

Table 6

*Means, Standard Deviations, and 95% Confidence Intervals for Irritability Before, During, and After Treatment*

| | Exercise Condition | | | Control Condition | | |
|---|---|---|---|---|---|---|
| Time | *M* | *SD* | 95% CI | *M* | *SD* | 95% CI |
| Baseline | 1.80 | 0.78 | [1.29, 2.31] | 2.13 | 1.13 | [1.62, 2.64] |
| 10-min of treatment | 1.27 | 0.59 | [0.94, 1.59] | 1.60 | 0.63 | [1.28, 1.92] |
| 20-min of treatment | 1.07 | 0.26 | [0.74, 1.39] | 1.60 | 0.83 | [1.28, 1.92] |
| 10-min post | 1.20 | 0.56 | [0.88, 1.52] | 1.53 | 0.64 | [1.22, 1.85] |
| 20-min post | 1.27 | 0.46 | [0.88, 1.65] | 1.53 | 0.92 | [1.15, 1.92] |
| 30-min post | 1.23 | 0.42 | [0.86, 1.61] | 1.53 | 0.92 | [1.16, 1.91] |
| 40-min post | 1.20 | 0.41 | [0.83, 1.57] | 1.60 | 0.91 | [1.23, 1.97] |

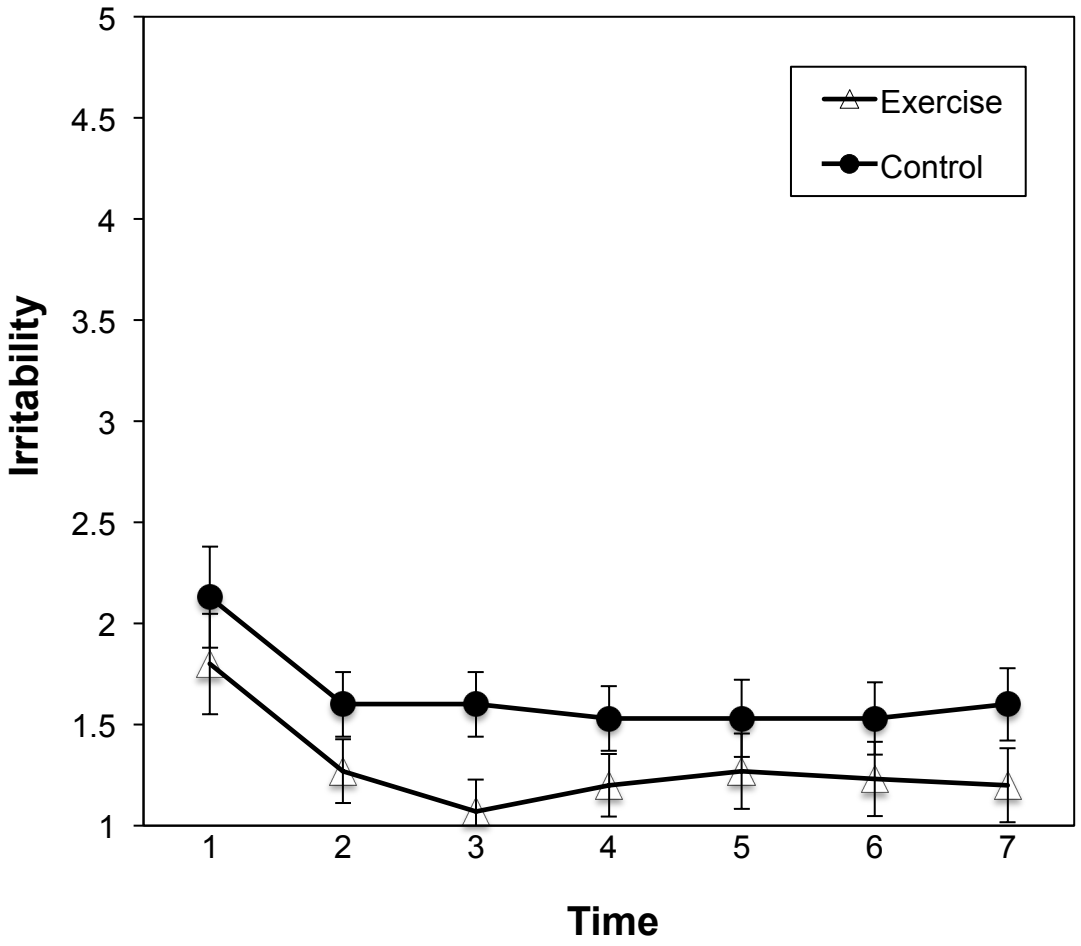


*Figure 5.* Irritability relative to time (1 = baseline, 2 = 10-min of treatment, 3 = 20-min of treatment, 4 = 10-min post-treatment, 5 = 20-min post-treatment, 6 = 30-min post-treatment, 7 = 40-min post-treatment). Error bars represent standard errors.

Table 7

*Means, Standard Deviations, and 95% Confidence Intervals for Poor Concentration Before, During, and After Treatment*

| | Exercise Condition | | | Control Condition | | |
|---|---|---|---|---|---|---|
| Time | *M* | *SD* | 95% CI | *M* | *SD* | 95% CI |
| Baseline | 2.00 | 1.13 | [1.41, 2.59] | 2.07 | 1.10 | [1.48, 2.66] |
| 10-min of treatment | 1.60 | 0.83 | [1.15, 2.05] | 1.73 | 0.88 | [1.28, 2.19] |
| 20-min of treatment | 1.60 | 0.83 | [1.16, 2.04] | 1.47 | 0.83 | [1.03, 1.91] |
| 10-min post | 1.33 | 0.49 | [0.95, 1.72] | 1.67 | 0.90 | [1.28, 2.05] |
| 20-min post | 1.20 | 0.41 | [0.85, 1.55] | 1.53 | 0.83 | [1.19, 1.88] |
| 30-min post | 1.20 | 0.41 | [0.92, 1.48] | 1.33 | 0.62 | [1.06, 1.61] |
| 40-min post | 1.27 | 0.59 | [0.91, 1.62] | 1.47 | 0.74 | [1.11, 1.82] |

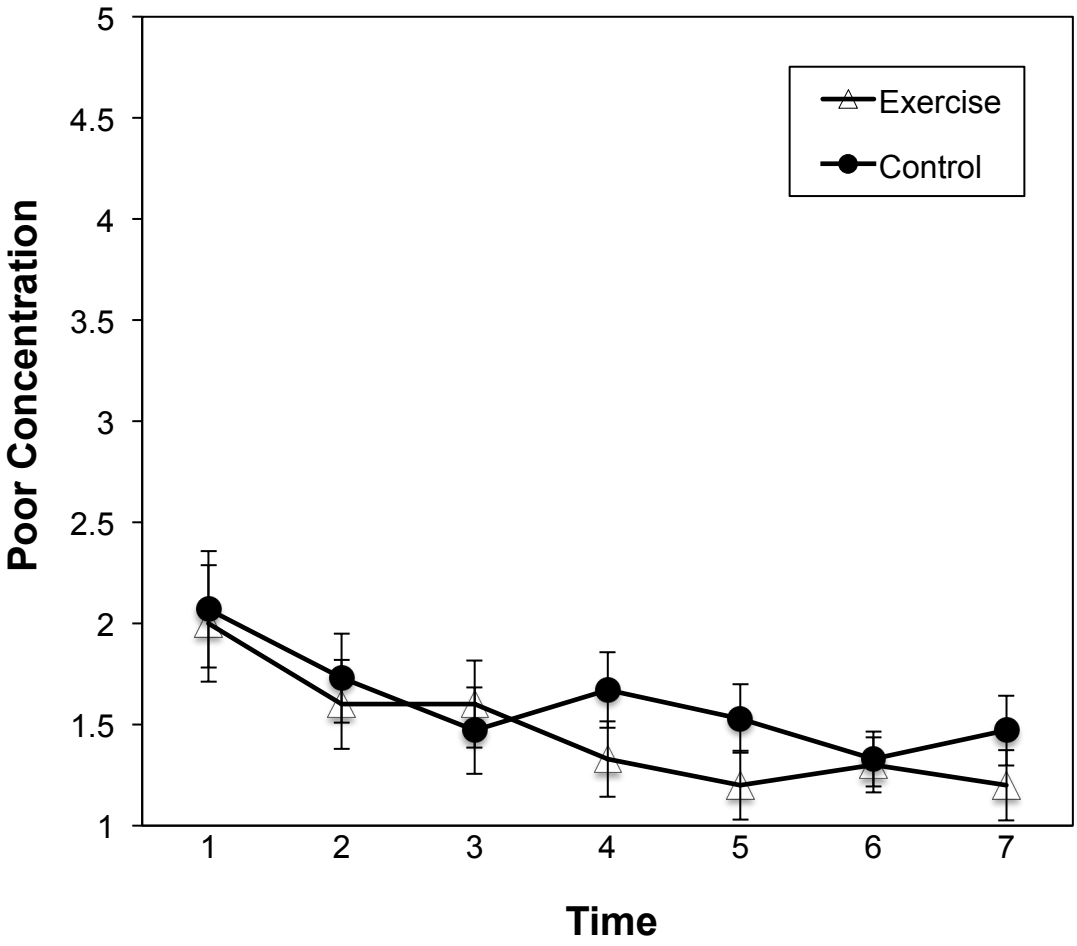


*Figure 6.* Poor concentration relative to time (1 = baseline, 2 = 10-min of treatment, 3 = 20-min of treatment, 4 = 10-min post-treatment, 5 = 20-min post-treatment, 6 = 30-min post-treatment, 7 = 40-min post-treatment). Error bars represent standard errors.

Table 8

*Correlations Between Residuals for Craving and Withdrawal Symptoms*

| Measure | *1* | *2* | *3* | *4* |
|---|---|---|---|---|
| 1. Residual craving | — | .21 | -.10 | -.12 |
| 2. Residual restlessness | | — | .51* | .47* |
| 3. Residual irritability | | | — | .68* |
| 4. Residual poor concentration | | | | — |

* $p < .05$

# Chapter Three: Discussion

The present study examined whether an acute bout of moderate-intensity exercise produced additional cigarette craving (primary outcome) and withdrawal (secondary outcome) relief to the nicotine lozenge in the initial 15 hours of abstinence for smokers undergoing a real-life quit attempt. This randomized controlled trial involved two conditions, both of which consumed a nicotine lozenge and engaged in either an acute bout of moderate intensity exercise or sat passively. Craving and withdrawal symptoms (i.e., restlessness, irritability, and poor concentration) were assessed before (baseline), during (10 and 20 minutes), and after (10, 20, 30, and 40 minutes) treatment at 10-minute intervals.

## Craving

Findings from the present study indicate that exercising at a moderate intensity reduces cigarette cravings to a greater degree than sitting passively in recently quit smokers who are consuming a nicotine lozenge. Both groups showed decreases in craving from baseline, however, the experimental condition (acute exercise and nicotine lozenge) had lower scores at each assessment point compared to the control condition (nicotine lozenge alone).

The largest reduction in craving occurred during the 20-minute treatment period for both conditions (i.e., steepest slopes in Figure 3). From baseline to 10 and 20 minutes of treatment, the experimental condition had decreases of 31.7% and 48.3%, respectively, and the control condition dropped by 16.0% and 37.5%,

respectively. Thus, the experimental condition had a 10.8% larger reduction in craving than the control at the end of treatment.

Craving scores for both conditions continued to decrease following treatment. However, these reductions were smaller in magnitude than those reported during treatment. From baseline to post-treatment assessment points (i.e., 10, 20, 30, and 40 minutes), the experimental condition had respective declines of 52.9%, 50.6%, 52.9%, and 56.4%, whereas the control condition had reductions of 40.9%, 44.3%, 45.5%, and 46.7%, respectively. Thus, the difference at 40-minutes post-treatment favoured the experimental condition by 10.3%. This is comparable to the 10.8% difference that was found immediately after treatment. Therefore, the benefit of supplementing the nicotine lozenge with exercise was preserved even after treatment stopped.

The results of the present study substantiate the work of Harper and colleagues (2012) who found that acute exercise alleviated cigarette cravings in smokers on the nicotine patch. Specifically, participants reported 20.8%, 16.7%, and 22.7% reductions in cravings following exercise while having quit and been on the patch for 1, 7, and 9 weeks, respectively. The reduction in craving scores reported in the present study is twice as large (48.3%) as those found by Harper et al. This may be because the two studies differed in their durations of abstinence and NRT products used. It has been suggested that cravings are most intense during the initial days of abstinence. Hence, recently quit smokers (i.e., 15 hours of abstinence in the present study) should report higher baseline cravings, and in turn, greater change scores, than those who have been smoke-free for days or weeks (i.e., Harper et al.'s study). The steady-release of nicotine

from the transdermal patch alleviates background cravings, while the instantaneous effect of both the nicotine lozenge and exercise target episodic cravings. Therefore, a larger reduction in episodic craving would be expected in the present study because two acute cessation aids were used that provide immediate relief. Nonetheless, both studies provide strong evidence that an acute bout of exercise can supplement, and is not redundant to, the craving relief experienced with NRT products.

An interesting inference can be drawn by the difference in groups' change scores reported in the present study. On the 7-point craving scale, the experimental and control groups had respective decreases of 2.74 and 2.20 points from before to immediately after treatment. This equates to a 0.52-point difference in favour of the exercise condition. In other words, exercising while consuming a nicotine lozenge produced an additional half of a point reduction in craving compared to the lozenge alone. Using the same measure of craving, Muramoto and colleagues (2003) found the nicotine lozenge resulted in a 1.43-point decrease and, as previously mentioned, Roberts et al. (2012) and Hassova et al. (2013) found respective 1.90 and 2.04 point differences in change scores that favoured the exercise groups (vs. passive controls). Based on these findings, if the effects of exercise and the nicotine lozenge were 100% additive, a 2.0-point difference in change scores between the experimental (exercise and nicotine lozenge = 3.43) and control groups (nicotine lozenge alone = 1.43) would have been expected. While this would have been optimal, the difference found in the present study was approximately one-quarter in size (0.52). Nevertheless, the effect produced when exercise was added to the nicotine lozenge was significant.

These findings suggest that acute exercise and the nicotine lozenge are functioning, to some extent, through distinct mechanisms. The manner by which the nicotine lozenge exerts its effect on cigarette craving is better understood than that of exercise. As previously mentioned, NRT products effectively suppress cravings by binding to nicotine-deprived nAChRs in the brain that were once stimulated by nicotine in cigarettes. In regards to explaining the exercise-craving relationship, it is unlikely that the aforementioned affect and cognitive (i.e., distraction and expectancy) hypotheses hold any merit. However, the biological mechanisms (i.e., attention-shifts, cortisol, dopamine, catecholamines, heart rate variability, and nicotine metabolism) that have been proposed seem plausible, but have not yet been rigorously investigated. Therefore, future research should aim to test these hypotheses to gather a better understanding of the acute effects of exercise.

While the benefit of combining the two modalities has been demonstrated in a laboratory setting, the ecological validity of this finding must be further examined. For example, perceived environmental and psychological barriers may discourage smokers from using this combined treatment approach in a naturalistic setting. Therefore, using ecological momentary assessment (i.e., smart-phone application), researchers could gather information pertaining to the challenges smokers encounter to incorporating exercise with the nicotine lozenge during a real-life craving episode. From there, tailor-made feedback statements could be developed that help mitigate specific obstacles. These statements could then be delivered through the smart-phone application when individuals are at-risk of relapse and experiencing intense cravings.

**Withdrawal Symptoms**

The present study demonstrates that symptoms of restlessness, irritability, and poor concentration, which are heightened in nicotine-deprived smokers, can be effectively ameliorated by a single dose of a nicotine lozenge. Although no significant group by time interaction effects were found, those who exercised while consuming the nicotine lozenge appeared to have greater reductions in restlessness and irritability compared to those who sat passively.

**Restlessness.** Whether individuals consumed the lozenge while exercising or sitting passively, decreases in restlessness were found. Hence, a single nicotine lozenge can alleviate feelings of restlessness in recently quit smokers. While the conditions were not significantly different, the patterns of restlessness scores exhibited in Figure 4 are behaving as expected and thus worth describing. As hypothesized, the experimental condition had larger decreases in restlessness scores compared to the control condition. During treatment (baseline to 10 and 20 minutes), the experimental condition's restlessness score decreased by 45.5% and 42.9%, respectively, whereas the control condition reported reductions of 15.0% and 18.2%. Therefore, the experimental condition had a 24.7% larger decline in restlessness from baseline to the end of treatment. This percent difference is larger than that found for craving. However, it must be remembered that the absolute reduction in restlessness was 1 point for the exercise condition and 0.33 of a point for the control condition at the end of treatment. Both of these absolute point reductions are much smaller than what was reported for cravings. With the variability scores (SD) reported in Table 6, these modest point reductions are likely responsible for

the statistical analysis being underpowered (.59) and not reaching significance ($p$ = .112).

Following treatment, restlessness scores of the experimental group increased slightly while those of the control condition remained relatively stable. At 10, 20, 30, and 40 minutes post-treatment, the experimental condition reported respective decreases of 48.5%, 38.6%, 34.3%, and 31.4%, and the control condition had declines of 10.5%, 13.6%, 15.1%, and 16.7%, respectively. As shown, the difference between the conditions diminished to 14.7%. Nevertheless, the experimental conditioned continued to report lower scores than the control condition at each post-treatment time point. Therefore, it appears that the effects of exercise augment the reductions in restlessness that occurs with the nicotine lozenge. However, the additive effect of exercise begins to subside once terminated.

Unfortunately, these findings cannot be directly compared to the work of Harper and colleagues (2012) because the Shiffman-Jarvik scale (Shiffman & Jarvik, 1976) that they used assessed different withdrawal symptoms from the MPSS, which was used in the present study. However, Ussher and colleagues (2009) did employ the MPSS to examine the effect of 10 minutes of isometric exercise on restlessness. They found that the exercise condition had a significantly (28%) larger decrease in restlessness score compared to the passive control. This finding supports the notion that exercise can effectively reduce feelings of restlessness in recently quit smokers, although no NRT product was involved.

**Irritability.** Both conditions showed decreases in irritability scores from baseline. Thus, a nicotine lozenge can temporarily alleviate feelings of irritability that accompany smoking abstinence. Although no significant interaction effect was found, greater reductions in irritability scores occurred with those who exercised while consuming the lozenge as opposed to sitting. Relative to baseline values, the experimental condition had decreases of 29.4% and 40.6% at 10 and 20 minutes of treatment, respectively, while the control condition dropped by 25% at both assessment points. Therefore, those who exercised had a 15.6% greater reduction at the end of treatment. At 10, 20, 30, and 40 minutes post-treatment, the experimental condition had declines of 33.3%, 29.4%, 31.5%, and 33.3%, respectively, and the control group remained relatively stable at 28.1%, 28.1%, 28.1%, and 25.0%. As exhibited with restlessness, the difference in reductions diminished (to 8.3%) but continued to favour the experimental condition. Overall, supplementing the nicotine lozenge with concurrent exercise provides some additional, albeit small and temporary, relief from feelings of irritability.

While no other research has yet to verify this effect, Ussher and colleagues (2009) found that the isometric exercise condition reported greater reductions in irritability scores compared to the controls in both a natural (16.0%) and laboratory setting (38.8%). Although no NRT was utilized, they did demonstrate that feelings of irritability resulting from nicotine withdrawal could be significantly alleviated by acute exercise. Until more consistent results emerge for restlessness and irritability outcomes, identifying the mechanistic pathways of how exercise influences these withdrawal symptoms will have to wait.

**Poor concentration.** Ratings of poor concentration were shown to significantly decrease in both conditions upon implementing the nicotine lozenge. No significant interaction effect was found or appeared to be emerging. Therefore, it does not seem that an acute bout of exercise augments the effect of the lozenge to a notable degree. Relative to baseline values, the experimental condition had declines of 20.0%, 20.0%, 33.4%, 40.0%, 40.0% and 36.7% at each 10-minute interval and the control condition had declines of 16.2%; 29.0%, 19.4%, 25.8, 33.4%, and 29.0%. Contrary to expectations, the control condition had a larger decline (9.0%) in poor concentration than the exercise condition at the end of treatment. This outcome did not endure following treatment, where the difference in change scores favoured the experimental group by 7.7%. These group differences should be interpreted with caution as the means fluctuated at each assessment point and the surrounding error bars were large (Figure 6). Unlike restlessness and irritability symptoms, no consistent pattern was found to conclude that ratings of poor concentration are reduced to a greater degree when exercise is added to the nicotine lozenge.

It has been hypothesized that exercise might work to improve concentration during periods of nicotine withdrawal by shifting one's attention away from cravings, and in turn, increasing one's attentional capacity towards the task at hand. Ultimately, this would reduce the withdrawal symptom of poor concentration (Janse Van Rensburg & Taylor, 2008). Findings pertaining to the effect of acute exercise on concentration abilities have been mixed. Daniel and colleagues (2009) used the MPSS to assess perceived concentration difficulties and found significantly larger reductions among those who exercised versus

those who sat passively. Conversely, Janse Van Rensburg and Taylor (2008) objectively measured the cognitive performance using a Stroop (1935) colour-word interference task and found that exercise did not enhance cognitive functioning relative to the passive control condition. Nevertheless, the effect of combining exercise with NRT on concentration should not be dismissed until a more robust and objective measure of cognitive performance is used.

**Strengths and Limitations**

There are a number of strengths to the present study. For instance, the subjective assessments were validated, objective measures (i.e., heart rate data, CO reader) were used when appropriate, the randomization minimized contamination of extraneous variables, and the post-treatment period was sufficient in duration (40 minutes) to examine the residual effects of treatment. Furthermore, incorporating a pilot sample was advantageous because it exposed the optimal timing of administering the two treatment modalities. Lastly, using a sample of smokers undergoing a real-life quitting attempt enhanced the ecological validity of the present study. The majority of previous studies involve temporarily abstaining smokers who are likely to return to smoking. As a result, their reported symptoms may not be entirely representative of those experienced by real-life quitters.

Despite the aforementioned strengths, there are limitations of this study that must be acknowledged. For example, the researcher and participants were not blinded to their allocated treatment. In addition, the generalizability of these findings is limited to smokers who have quit only 15 hours prior. Furthermore, the

present trial was conducted in a laboratory setting, and therefore, may not translate to the actual environment and situations that quitters will encounter during peak episodic cravings. While previous research (i.e., Harper et al., 2012) suggests that exercise can still alleviate cravings in those who have been smoke-free and on the patch for weeks, this cannot be said for certain in the present study.

## Conclusions

Findings from the present study demonstrate that an acute bout of exercise provides additional craving relief to the nicotine lozenge in recently quit smokers. Therefore, individuals should employ both cessation aids simultaneously to maximize reductions in cravings. More research is required to untangle the underlying mechanisms through which exercise exerts its effect. Furthermore, the feasibility of engaging in a bout of exercise when experiencing heightened cigarette cravings in a natural environment must be examined.

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# Appendix A

**Recruitment Poster**

# QUIT-SMOKING RESEARCH STUDY!

# PARTICIPANTS NEEDED

The Exercise and Health Psychology Lab at Western University is conducting a study to determine the effects of exercise and NICORETTE® Lozenges on craving and withdrawal symptoms.

Participants will be asked to come into our laboratory twice, before and after quitting, to exercise and complete questionnaires.

To be eligible you must:
• Be between 18-64 years of age
• Smoke at least 5 cigarettes per day
• Not have any other substance dependency issues (e.g. alcohol)
• Not have any physical limitations that prevent walking
• Not pregnant, considering becoming pregnant or breast-feeding

All **men and women** will be provided with a quit-smoking package, including:

✓ NICORETTE® Lozenges

✓ Daily access to our exercise facility for 2 weeks

✓ Forever Free™: A Guide To Remaining Smoke Free

*Participants will be compensated financially for their time*

If you are interested in participating or would like to hear more about this study, please contact Amelia and take a tab below.

## Recruitment E-mail

Subject Line: Invitation to Participate in a Quit-Smoking Program

You are being invited to participate in a quit-smoking program that involves quit-smoking aids, including: NICORETTE® Lozenges, Forever Free™: Guide To Remaining Smoke Free, and access to our exercise facility for 2 weeks.
The study requires participants to come into the Exercise and Health Psychology Lab (Room 408, Labatt Health Sciences Building) at Western University twice, before and after quitting, to exercise and complete questionnaires. If you would like more information on this study or would like to receive a letter of information about this study please contact the Amelia at the contact information given below.

Thank you,

**Amelia Tritter**
[redacted]

# Ethics Approval

Western Research

Research Ethics

**Use of Human Participants - Ethics Approval Notice**

**Principal Investigator:**Prof. Harry Prapavessis
**File Number:**103508
**Review Level:**Full Board
**Approved Local Adult Participants:**60
**Approved Local Minor Participants:**0
**Protocol Title:**The effects of acute exercise on craving and withdrawal symptoms while using a nicotine replacement therapy lozenge
**Department & Institution:**Health Sciences\Kinesiology,Western University
**Sponsor:**
**Ethics Approval Date:**April 16, 2013
**Ethics Expiry Date:**March 31, 2014

**Documents Reviewed & Approved & Documents Received for Information:**

| Document Name | Comments | Version Date |
|---|---|---|
| Instruments | Study Measures and Handouts | |
| Letter of Information & Consent | | 2013/03/19 |
| Recruitment Items | | 2013/03/19 |
| Western University Protocol | | 2013/03/19 |

This is to notify you that the University of Western Ontario Health Sciences Research Ethics Board (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this HSREB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request form.

Member of the HSREB that are named as investigators in research studies, or declare a conflict of interest, do not participate in discussions related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

[redacted]

**Signature**

**Ethics Officer to Contact for Further Information**

[redacted]

*This is an official document. Please retain the original in your files.*

**Western University, Research,** Support Services Bldg., Rm. 5150
London, ON, Canada N6A 3K7 t. 519.661.3036 f. 519.850.2466 www.uwo.ca/research/services/ethics

## Letter of Information

### LETTER OF INFORMATION

**Study Title: The effect of exercise on cigarette craving and withdrawal symptoms while using a nicotine lozenge.**

**Principal Study Investigator:**
Harry Prapavessis, Ph.D. (School of Kinesiology, The University of Western Ontario)

**Co-Investigator:**
Amelia Tritter, B.A. (School of Kinesiology, Western University)

You are being invited to participate in a research study looking at the effects of exercise and nicotine lozenges on craving and withdrawal symptoms in smokers who have recently quit. This is a randomized control trial (a type of research study), which includes eligible volunteers who choose to take part. Please take your time to make a decision, and discuss this proposal with your personal doctor, family members and friends, as you feel inclined. The purpose of this letter is to provide you with the information you require to make an informed decision on participating in this research. This letter contains information to help you decide whether or not to participate in this research study. It is important for you to know why the study is being conducted and what it will involve. Please take the time to read this carefully and feel free to ask questions if anything is unclear or there are words or phrases you do not understand. We are asking you to take part because you are an adult between 18 and 64 years of age who smokes.

**Purpose of the study**
Exercise and nicotine lozenges have shown to reduce cigarette cravings and withdrawal symptoms that are experienced when trying to quit smoking.

The objective of this study is to examine the effects of an acute bout of moderate intensity exercise and a nicotine lozenge on smoking cravings and withdrawal symptoms in smokers who have recently quit.

**Participants**
Sixty participants will be asked to take part in this research. To be eligible to participate, you must meet the following criteria: 18 and 64 years of age, smoke a minimum of 5 cigarettes per day, have not been engaged in a serious quit attempt in the last six months, must not be suffering from an illness (e.g. cold) that would affect your typical smoking behaviour, do not have a medical condition that prevents you from exercising, not be pregnant, intending on becoming pregnant or breast-feeding. As recommended in the NICORETTE® Lozenge label, you are not able to participate if you have had, or are aware of having, a heart disease, a recent heart attack, an irregular heartbeat, high blood pressure not controlled with medication, a stomach ulcer, or diabetes, and/or are using a non-nicotine stop smoking drug or prescription medication for depression or asthma. You

must also be able to read and write in English and have a telephone or e-mail account that the investigators can contact you at.

**Research Procedure**
If you choose to take part in this study, you will be asked to complete three study components:
A) first laboratory session, B) quit smoking, C) second laboratory session.
The laboratory sessions will be held at the Exercise and Health Psychology Laboratory (EHPL) at Western University. The EHPL is located in Room 408 of the Labatt Health Sciences Building. The first laboratory session will take approximately 30 minutes, and the second visit will be approximately 90 minutes.

**A) First laboratory session**
During your first laboratory session, you will complete a questionnaire package (see Item 1) and the following information will be collected: weight, height, and breath carbon monoxide levels (see Item 2). At the end of your first laboratory session, we will schedule your second laboratory session within seven days of your first laboratory session. It is within your rights to refuse to answer any questionnaire items and we will honour your rights.

**B) Quit smoking**
You will be asked to quit smoking 17 hours before your second laboratory visit (see Item 7). We will confirm that you have not smoked in the last 17 hours by asking you to provide a breath carbon monoxide level (see Item 2). In addition, we will ask you to refrain from using nicotine products during these initial 17 hours of quitting.

**C) Second laboratory session**
When you arrive for the second lab visit, you will be asked to provide a breath carbon monoxide level to confirm abstinence (Item 2). If the carbon monoxide value shows that you are not smoke-free at this time, we will reschedule your appointment. If at that time you again are unable to abstain, you will be ineligible to continue with the study. You will then complete a questionnaire package containing items pertaining to your current cigarette cravings and withdrawal symptoms (see Item 3). After completing the questionnaire package, you will be given instructions on how to consume the 2mg NICORETTE® Lozenge (Item 4). The researcher will answer any questions you have about the product and you will be asked to provide verbal and written confirmation of your understanding. After placing the lozenge in your mouth, you will be randomly assigned to either sit in a quiet room and read or participate in an exercise session (i.e. walk on a treadmill at a moderate intensity) for 30 minutes. Individuals will be randomized into study arms using a computer-generated numbers table. You will not be able to choose which group you are assigned to and that group allocation will be random, therefore, you have an equal chance of getting into either group. At the 10-minute and 20-minute marks of having the lozenge in your mouth, you will complete the craving questionnaire (Item 5). Immediately after exercising or reading, you will complete craving and withdrawal questionnaires (Item 6).

In addition, you will be asked to complete this questionnaire package two more times (10 and 20 minutes post-treatment). During this time, the researcher will give you a tour of the exercise facility and you will be given your quit-smoking package, which includes: 27 2mg NICORETTE® Lozenges (with instructions), the Forever Free™: A Guide To Remaining Smoke Free set of 8 booklets, direct assess to the Smokers Help Line (1-877-513-5333), and the hours in which the exercise facility will be open for use over the next two weeks.

**Experimental description (items 1-6)**

Item 1: Pre-treatment questionnaire package (1st lab visit)
Time Involvement: 30 minutes
The questionnaire package will include: demographics information sheet, smoking history questionnaire, physical activity questionnaire, nicotine dependence questionnaire, cigarette cravings questionnaire and withdrawal symptoms questionnaire.

Item 2: Carbon monoxide assessments (1st and 2nd lab visits)
Time Involvement: 15 seconds
We will ask you to breathe into a machine called the Bedfont Smokerlyzer. This machine measures the amount of carbon monoxide (CO) as you breathe out. It does not cause any harm or discomfort to you. This Smokerlyzer measures how much you have smoked in the past several hours. A CO value of less than 6 parts per million will confirm that you have temporarily stopped smoking.

Item 3: Baseline & Post-treatment questionnaire package (2nd lab visit)
Time Involvement: 20 minutes
The questionnaire package will include: cigarette cravings questionnaire and withdrawal symptoms questionnaire

Item 4: Nicotine lozenge (2nd lab visit)
Time Involvement: 20-30 minutes to dissolve
We will ask you to place the lozenge in your mouth and occasionally move the lozenge from one side of your mouth to the other until completely dissolved. You will be instructed to not chew or swallow lozenge; and not eat or drink 15 minutes before using or while the lozenge is in your mouth.

Item 5: During-lozenge questionnaire (2nd lab visit)
Time Involvement: 20 seconds
We will ask that you complete the craving questionnaire 10 and 20 minutes after placing the lozenge in your mouth.

Item 6: Quit smoking
We ask that you quit smoking at least 17 hours before your second lab visit (17-24 hours).

**Risks**

While in the study, you may experience side effects. Known side effects are listed below, but other effects may occur that we cannot predict. If you are or become pregnant you must notify the investigator because smoking and NRT products propose a risk to you and

the foetus; therefore, you will be removed from the study.

Exercise: There are some inherent risks of injury associated with exercise participation, particularly among people who are not used to exercising. You may, for example, feel mild muscle "tightness" or soreness that lasts for a couple of days. The possible benefits associated with exercise may outweigh the potential minor discomfort of beginning a supervised, laboratory-based exercise program. To minimize the physical risks of exercise, proper warm-up/cool-down and stretching protocols will be performed by a trained exercise counsellor. Additionally, the exercise program delivered will be tailored to your individual fitness level, and modified according to your comfort level. Furthermore, you will only be allowed to participate in this exercise program if you complete the PAR-Q (Physical Activity Readiness Questionnaire) forms to ensure that it is safe for you to begin an exercise program. The exercise facilitator will be both CPR and First Aid trained, and experienced in working with previously inactive populations.If any physical or mental risks arise during treatment, The Student Emergency Response Team (SERT) will be available to provide immediate assistance. SERT will assist the exercise supervisor until the 911 emergency services arrive. Should you have a minor injury, for instance sore knees, or cramped muscles (e.g. a "Charlie horse"), while exercising you will receive first aid onsite as required. A first aid kit and ice packs will be available for minor injuries.

Quitting smoking**:** You may experience withdrawal symptoms during the time you are abstaining from cigarettes. Such symptoms may include feeling edgy and nervous, dizzy, sweaty, having trouble concentrating, headaches, insomnia, increased appetite and weight gain, muscular pain, constipation, fatigue, or having an upset stomach. All of these symptoms are common for those who have quit smoking so you should not be alarmed. Moderate intensity exercise has been shown to reduce smoking withdrawal symptoms, so it could be that those in the moderate intensity exercise treatment condition experience relief from some of these symptoms. Another common side effect of quitting smoking is that your "smoker's cough" gets worse for the first few days after you quit. This is your body's way of attempting to rid the lungs of congestion. Your smoker's cough will improve largely if you have become smoke-free for a number of days.

Nicotine Lozenge: The primary side effects of the lozenge include: sore throat, heartburn, nausea/indigestion, and hiccups. People who experience irregular heartbeat, severe throat irritation, or mouth problems should consult their doctor. Failing to follow instructions can put you in danger of a nicotine overdose. If you are on nicotine lozenges for a long period of time, this may increase your risk of experiencing withdrawal symptoms after ending treatment.

**Benefits**

Your participation may help you and us gain knowledge to shape the development of future exercise and smoking cessation programs.

**Participation**

Participation in this study is voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with no effect on your academic or

employment status. If you decide to take part you will be given this Letter of Information to keep and be asked to sign the consent form. If you withdraw from the study, you maintain the right to request that any data collected from you not be used in the study. If you make such a request, all of the data collected from you will be destroyed. Please contact the study coordinator, Amelia Tritter, if you wish to withdraw from the study. If you are participating in another study at this time, please inform the study researchers right away to determine if it is appropriate for you to participate in this study.

**New Findings**
If, during the course of this study, new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the investigator (for instance, if a new quit-smoking aid becomes available).

**Confidentiality**
We will be collecting information from 60 participants for this study. All the information you provide to the researcher will be kept in the strictest confidence. You will be assigned an identification number and all data collected from you will be recorded and stored under this number only. All data will be stored in coded form on computers accessible only to research staff in a secure office. A master list matching your personal identification (i.e. first and last name) to your participant number will be generated and stored in a locked cabinet. The master list will be stored separately from the stored data. You will not be identified in any documents relating to the research. No information obtained during the study will be discussed with anyone outside of the research team. If the results of the study are published, your name will not be used.

Representatives of the Western University Health Sciences Research Ethics Board and regulatory bodies (Health Canada) may contact you or require access to your study-related records to monitor the conduct of the research. If we find information we are required by law to disclose, we cannot guarantee confidentiality. We will strive to ensure the confidentiality of your research-related records. Absolute confidentiality cannot be guaranteed, as we may have to disclose certain information under certain laws.

**Compensation**
Free parking will be provided for your visits to the laboratory. You will be reimbursed $5.50 upon arrival at each visit to compensate you for transportation (i.e. bus fare or gas). Upon terminating the study, you will be given an additional $39.00. We provide you with the majority of compensation at the end of the study because this is where the majority of your time will be needed. This fund can be used for future transportation to the laboratory if interested in using our exercise facility. In addition, this fund can be used to purchase additional nicotine replacement therapy products.

If you have private medical or life insurance, you should check with your insurance company before you agree to take part in the study to confirm your participation in this study will not affect your insurance coverage and/or access to benefits.

This study is covered by Western University's insurance policy and if during the course of the study, any injury should occur to you, not due to your fault or negligence, all

medical expenses necessary to treat such injury will be paid provided: a) you comply at all times with the study researcher's instructions b) you promptly report any such injury to the study researchers conducting the study, and c) the expenses are not otherwise covered by your provincial health care. Financial compensation for such things as lost wages, disability or discomfort due to this type of injury is not routinely available. You do not waive any legal rights by signing the consent form.

**Alternative treatments**
If you decide not to participate or if you withdraw from the study before it is completed, the alternative course of treatment could be to see your family physician for advice on how to quit smoking. Another alternative to the procedures described above is not to participate in the study and continue on just as you do now.

**Contact person(s)**
If you have any questions about your rights as a research participant or the conduct of the study you may contact Dr. David Hill, Scientific Director, Lawson Health Research Institute.

This letter is for you to keep. You will be given a copy of this letter of information and consent form once it has been signed. If you have any concerns, please feel free to contact one of the researchers below. You may request the general findings of this research study from the researchers after the study is complete. You do not waive any legal rights by singing the consent form.

**INFORMED CONSENT**

**Study Title: The effect of exercise on cigarette craving and withdrawal symptoms while using a nicotine lozenge.**

I have read the Letter of Information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

Please send me the overall conclusions from this trial: Yes □ No □

I would like to be contacted for other research studies: Yes □ No □

**Consenting Signature:**

Participant: _____
Please Print Name

Participant: _____
Please Sign Name

Date: _____

**Researcher Signature:**

Person obtaining informed consent: _____
Please Print Name

Person obtaining informed consent: _____
Please Sign Name

Date: _____

# Appendix B

## Craving

INSTRUCTIONS: Please read the following statement and CIRCLE the number that most accurately reflects how you feel in the table underneath.

1. I have a desire to smoke.

| Strongly disagree | | | Neither agree nor disagree | | | Strongly agree |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |

## Withdrawal Symptoms

Please CIRCLE one number for each of the items below for how you feel RIGHT IN THIS MOMENT.

| | Not at all | Slightly | Somewhat | Very | Extremely |
|---|---|---|---|---|---|
| 1. Irritable | 1 | 2 | 3 | 4 | 5 |
| 2. Restless | 1 | 2 | 3 | 4 | 5 |
| 3. Poor concentration | 1 | 2 | 3 | 4 | 5 |

## Demographic and Smoking Behaviour Questionnaire

First Name:_____ Last Name:_____

Address:_____
STREET ADDRESS, CITY, POSTAL CODE

Home Phone: _____- _____-_____

Email Address: _____@_____

Date of Birth: _____/_____/_____ Age: _____

Gender: ☐ Male ☐Female If female, day of menstrual cycle: _____

Height: _____ Weight: _____ BMI: _____

Please indicate the number of years you have smoked: _____

On average, how many cigarettes do you smoke per day? : _____

How many times have you tried to quit smoking?: _____

Have you tried quitting smoking using Nicotine Replacement Therapy? ☐ Yes ☐ No

If yes, please specify the product (e.g. patch, inhaler, lozenge, gum): _____

Do you currently smoke any other substance besides cigarettes? ☐ Yes ☐ No

If yes, please specify (e.g. marijuana, cigar, pipe, cigarello, hookah): _____

Have you ever smoked any other substance besides cigarettes? ☐ Yes ☐ No

If yes, please specify (e.g. marijuana, cigar, pipe, cigarello, hookah): _____

Does anyone in your household currently smoke? ☐ Yes ☐ No

Do you drink Alcohol? ☐ Yes ☐ No If yes, number of drinks per week? _____

What is the approximate date and time of the last cigarette you have smoked?

Date: _____ Time: _____

On a scale from 1 to 10, *How serious are you about this quit-attempt?* _____

## International Physical Activity Questionnaire (Short-form)

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

### *PART 1: JOB-RELATED PHYSICAL ACTIVITY*

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

   ☐ Yes

   ☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

   _____ **hours per day** _____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

   _____ **days per week**

   ☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day** _____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day** _____ **minutes per day**

***PART 2: TRANSPORTATION PHYSICAL ACTIVITY***

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day** _____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day** _____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

**_____ days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

**_____ hours per day** **_____ minutes per day**

***PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

**_____ days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

**_____ hours per day** **_____ minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

**_____ days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

**_____ hours per day** **_____ minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day** _____ **minutes per day**

***PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY***

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day** _____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day** _____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

**_____ days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?

**_____ hours per day** **_____ minutes per day**

***PART 5: TIME SPENT SITTING***

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

**_____ hours per day** **_____ minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

**_____ hours per day** **_____ minutes per day**

## Fagerström Test for Cigarette Dependence

| Please answer the following: | | **Your Answer:** |
|---|---|---|
| (F1) How many cigarettes per day do you usually smoke? *(write the number on the line and circle the number [between 0 and 3] that best represents your cigarette consumption)* | | CIG/DAY: |
| | 10 or less | 0 |
| | 11 to 20 | 1 |
| | 21 to 30 | 2 |
| | 31 or more | 3 |
| (F2) How soon after you wake up do you smoke your first cigarette? *(circle one response)* | Within 5 minutes | 3 |
| | 6-30 minutes | 2 |
| | 31 or more | 0 |
| (F3) Do you find it difficult to refrain from smoking in places where it is forbidden (e.g. in church, at the library, in the cinema?) *(circle one response)* | No | 0 |
| | Yes | 1 |
| (F4) Which cigarette would you most hate to give up? *(circle one response)* | The first of the morning | 1 |
| | Other | 0 |
| (F5) Do you smoke more frequently in the first hours after waking than during the rest of the day *(circle one)* | No | 0 |
| | Yes | 1 |
| (F6) Do you smoke if you are so ill that you are in bed most of the day? *(circle one response)* | No | 0 |
| | Yes | 1 |

## Physical Activity Readiness Questionnaire

1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?
a. [ ] Yes
b. [ ] No

2. Do you feel pain in your chest when you do physical activity?
a. [ ] Yes
b. [ ] No

3. In the past month, have you had chest pain when you were not doing physical activity?
a. [ ] Yes
b. [ ] No

4. Do you lose your balance because of dizziness or do you ever lose consciousness?
a. [ ] Yes
b. [ ] No

5. Do you have a bone or joint problem that could be made worse by a change in your physical activity?
a. [ ] Yes
b. [ ] No

6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart?
a. [ ] Yes
b. [ ] No

7. Do you know of any other reason why you should not do physical activity?
a. [ ] Yes
b. [ ] No

_____
Date

# Curriculum Vitae for Amelia Tritter

## POST-SECONDARY EDUCATION AND DEGREES

*Western University*
London, Ontario, Canada
**Bachelor of Arts**, Honours Kinesiology
May 2012

*Western University*
London, Ontario, Canada
**Master of Arts (Thesis)**, Kinesiology, Exercise and Health Psychology
August 2014

*Western University*
London, Ontario, Canada
**Juris Doctor**
Expected May 2017

## HONOURS AND AWARDS

Western University
Dean of Law Entrance Scholarship
2014-2015

Ontario Graduate Scholarship
Master's Award
2013-2014

CIHR Strategic Training Program in Cancer Research and Technology Transfer
Master's Award
2013-2014

Ashley Studentships for Research in Tobacco Control – Ontario Tobacco Research Unit
Master's Award
2013-2014

School of Kinesiology Teaching and Research Award
Master's Award
2012-2014

Western Graduate Research Scholarship
Master's Award
2012-2014

Canadian Institutes of Health Research – *accepted funding*
Frederick Banting and Charles Best Canada Graduate Scholarship
2012-2013

CIHR Strategic Training Program in Cancer Research and Technology Transfer
Master's Award
2012-2014

Ontario Graduate Scholarship
Master's Award
2012-2013

CIHR Strategic Training Program in Cancer Research and Technology Transfer
Undergraduate Summer Studentship
May – August 2011

Delcan Engineering Awards Scholarship
Undergraduate Award
2007-2010

Western Scholarship of Distinction
Undergraduate Entrance Award
2007-2008

## REFEREED PUBLICATIONS

**Tritter, A.,** Fitzgeorge, L., De Jesus, S., Harper, T., & Prapavessis, H. (2014, May). Credibility beliefs towards nicotine replacement therapy and exercise as cessation aids in women attempting to quit smoking. *International Journal of Psychological Studies, 6*(2), 11-18.

**Tritter, A.,** Fitzgeorge, L., Cramp, A., Valiulus, P., & Prapavessis, H. (2013, November). Self-efficacy and affect responses in sprint interval training. *Psychology of Sport and Exercise, 14*(6), 886-890.

Harper, T., Fitzgeorge, L., **Tritter, A.,** & Prapavessis, H. (2013, June). Are treatment expectations related to reductions in craving and withdrawal symptoms following anacute bout of exercise? *Mental Health & Physical Activity*, *6*(2), 83-86.

Harper, T., Fitzgeorge, L., **Tritter, A.,** & Prapavessis, H. (2012, December). Acute exercise effects on craving and withdrawal symptoms among women attempting to quit smoking using nicotine replacement therapy. *Journal of Smoking Cessation*, *7*(2), 72-79.

## CONFERENCE POSTERS AND PRESENTATIONS

**Tritter, A.,** Fitzgeorge, L., & Prapavessis, H. (2013, March). *Credibility Beliefs Towards Nicotine Replacement Therapy and Exercise as Cessation Aids in Women Attempting to Quit Smoking*. Poster presented at the Society for Research on Nicotine and Tobacco Annual International Meeting, Boston, Massachusetts.

Fong, A., De Jesus, S., **Tritter, A.,** Fitzgeorge, L., & Prapavessis, H. (2013, March). *Implications of Weight Concern on Anthropometric Measures in Women Attempting to Quit Smoking*. Poster presented at the Society of Behavioral Medicine Meeting, San Francisco, California.

**Tritter, A.,** Fitzgeorge, L., Cramp, A., & Prapavessis, H. (2012, November). *Self-efficacy and Affect Responses in Sprint Interval Training.* Oral lecture presented at the Canadian Society for psychomotor Learning and Sport Psychology Conference, Halifax, Nova Scotia.

Harper, T., Fitzgeorge, L., **Tritter, A.,** & Prapavessis, H. (2012, April). *Higher Exercise Expectancy and Credibility Beliefs are Related to Greater Craving Reduction Following Exercise.* Poster presented at the Annual Meeting & Scientific Sessions of Society of Behavioral Medicine, New Orleans, Louisiana.

## UNDERGRADUATE THESIS

Tritter, A. Self-Efficacy and Affect Responses in Sprint Interval Training. Supervisor: Dr. Harry Prapavessis, Western University.

## TEACHING EXPERIENCE

**2014**

*Kinesiology 3476G* (Exercise and Health Behaviour Change), School of Kinesiology at Western University. Teaching Assistant. Prepared and delivered several lectures.

**2013**

*Kinesiology 3474B* (Psychological Intervention for Sport, Exercise and Injury Rehabilitation), School of Kinesiology at Western University. Prepared and delivered lecture entitled “Exercise and Emotional Well-Being”

**2012**

*Kinesiology 2276A* (Exercise Psychology), School of Kinesiology at Western University November: Prepared and delivered lecture entitled “Self-efficacy and Affect Responses in Sprint Interval Training”

# ADDITIONAL RESEARCH EXPERIENCE

*Research Associate,* The Effect of Exercise on Mental Health among Three Unique Populations
School of Health Studies, Western University
Contact: Dr. Anita Cramp, Ph. D.
August 2012 – May 2013
Project Description: The purpose of this trial is to determine the effectiveness of a 12-week personalized health and fitness program, being offered by Just Sweat Fitness, on improving participants' anxiety, depression, and quality of life. Participants include clients of St. Leonard's, the Hutton House and the London Abuse Women's Centre.

*Research Associate,* Getting Physical on Cigarettes Trial
Exercise and Health Psychology Laboratory
School of Kinesiology, Western University
Contact: Dr. Harry Prapavessis, Ph. D.
September 2009 – March 2014
Project Description: This trial aims to investigate the effectiveness of a home-based lifestyle exercise maintenance program in preventing smoking relapse and maintaining exercise and weight following the termination of a structured and supervised exercise and nicotine replacement therapy (NRT) smoking cessation intervention. Four hundred and twenty female smokers will be randomized into one of four research arms: Exercise Maintenance; Exercise Maintenance + Relapse Prevention Booklets; Relapse Prevention Booklets + Contact; Contact Control.

*Research Associate,* Smoking Imagery and Acute Exercise Study
Exercise and Health Psychology Laboratory
School of Kinesiology, Western University
Contact: Lisa Cooke, Ph. D. candidate
January – May 2012
Project Description: The purpose of this acute study was to examine the effect of exercise imagery and acute exercise on cigarette craving and withdrawal symptoms in temporarily abstinent smokers. Sixty male and female participants were randomized to one of three conditions: exercise, exercise imagery, or control.

*Research Associate,* Exercise Motivation Study
Exercise and Health Psychology Laboratory
School of Kinesiology, Western University
Contact: Lisa Cooke, Ph. D. candidate
January – June 2011
Project Description: The purpose of the study was to examine if a mental imagery intervention could increase integrated regulation among exercise initiates, and in turn, subsequently increase exercise behaviour. One hundred and sixty overweight, female exercise initiates were randomized to either the imagery or control (health information) conditions and underwent an 8-week cardiovascular exercise program. Once completing the 8-week program, five follow-up assessments occurred at 8-week intervals (extending 40 weeks beyond the end of the exercise program).

## ADDITIONAL QUALIFICATIONS

*Trained to operate a Metabolic Cart, interpret data, and create exercise prescriptions*
Able to conduct Spirometry and Peak $VO_2$ assessments

*Trained to operate Dual-emission X-ray absorptiometry and interpret accompanying data*
Able to operate iDXA body composition scans

*Standard First Aid CPR/AED Level C*
Canadian Red Cross

## RECENT EMPLOYMENT HISTORY

**May 2013 - Present**
*Exercise supervisor,* Health and Psychological Outcomes of Physical Activity at Western University
Supervise individual exercise sessions and conduct fitness assessments

**September 2013 – Present**
*Exercise instructor and fitness assessor,* Colon Health and Life-Long Exercise Change at Western University
Conduct weekly exercise sessions and physical assessments with cancer survivors

**September 2012 – March 2014**
*Fitness assessor,* Getting Physical on Cigarettes at Western University
Conduct $VO_2$ maximal fitness tests and lung health assessments

**January 2012 – Present**
*Note-Taker,* Services for Students with Disabilities (SSD) at Western University
Attend lectures and take notes for hearing impaired students

**May – August 2011 & 2012**
*Summer studentship,* Researcher for Getting Physical on Cigarettes at Western University
Recruited participants, conducted baseline and follow-up assessments, and input data

## VOLUNTEER EXPERIENCE

**2014-Present**
Research Ethics Board, Western University
Health Sciences committee representative

**2014-Present**
*Public Issues Team,* Canadian Cancer Society
Committee member responsible for promoting tobacco control legislation

**2013-Present**
*Kinesiology Graduate Board,* Western University
Vice President – responsible for academics and international students

**2013-Present**
*Society of Graduate Students*, Western University
Kinesiology representative

**2013-Present**
*Research Information Outreach Team,* Canadian Cancer Society
Committee member responsible for translating cancer research to the public

**2012-2013**
*Exercise and Mental Health Study*, Western University
Assisted with writing ethics proposal, organized and facilitated meetings with community partners, and collected and inputted data (questionnaires, fitness assessments)

**2012**
*Smoking Imagery and Acute Exercise Study,* Western University
Recruited participants, collected and inputted data (smoking log, carbon monoxide, heart rate, questionnaires), conducted exercise session, and contacted participants for follow-up

**2011**
*Exercise Motivation Study*, Western University
Administered imagery intervention, collected data (questionnaire), and conducted individual exercise sessions

**2009-2011**
*Getting Physical on Cigarettes Trial,* Western University
Collected and inputted data (questionnaires, heart rate, carbon monoxide), conducted group exercise sessions, and participated in group-mediated behaviour cognitive sessions

**2009-2010**
*Teaching Assistant for Anatomy,* Western University
Assisted during model-based replica component of 2$^{nd}$ year Anatomy course

**2009-2010**
*Fowler Kennedy Sports Medicine Clinic,* Western University
Conducted ultrasounds and supervised patients' performing exercises