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CIGARETTE CRAVINGS, TOBACCO WITHDRAWAL, AND SMOKING CESSATION: THE ROLE OF EXERCISE

Vaughan Roberts

A thesis submitted in fulfillment of the requirements for the degree of Doctor of Philosophy

University of Auckland, 2013
ABSTRACT

Introduction: Tobacco smoking is the leading preventable cause of death globally, with nearly six million tobacco-attributable deaths each year. Approximately 17% of the New Zealand (NZ) population smoke tobacco daily. Smoking cessation in NZ is therefore an important public health challenge. Despite the proven efficacy of the various cessation approaches, long-term cessation rates are still below 25%, and new approaches are needed to increase these. Exercise has been proposed as one potential aid to smoking cessation that, if effective, could be relatively inexpensive, acceptable and easy to introduce on a wide scale.

Objectives: To investigate if exercise has potential to assist with smoking cessation and the underlying psychological and physiological mechanisms explaining the relationship.

Design and results: Five complementary studies were undertaken. A systematic review of studies of the acute effects of exercise on cigarette cravings, tobacco withdrawal symptoms, affect, and smoking behaviour was conducted, to explore possible psychological and physiological mechanisms in the relationship between exercise and cigarette cravings. Fifteen studies published between 2006 and 2012 were identified. Meta-analyses of the effects of exercise and passive control conditions on cigarette cravings post–cessation treatment found that exercise significantly reduced cravings on average by 2 points on a 7-point scale. The review of possible mechanisms highlighted the need for further laboratory-based research on appetite suppression, affect, and neurobiological mechanisms including cortisol, noradrenaline, adrenaline, and heart rate variability.

The first empirical study was a small randomised crossover trial (n=40) that aimed to examine the effect of three different intensities of exercise on cigarette cravings, tobacco withdrawal symptoms, peripheral markers of neurobiological changes, and heart rate variability during temporary smoking abstinence. Statistically significant treatment effects
were observed for cigarette cravings [desire to smoke ($F_{[2, 91]} = 7.94, p = .0007$), strength of desire to smoke ($F_{[2,98]} = 5.51, p = .005$)], and some tobacco withdrawal symptoms [restlessness ($F_{[2,123]} = 3.27, p = .04$), hunger ($F_{[2,103]} = 6.38, p = .002$), and composite mood and physical symptoms score ($F_{[2,117]} = 3.62, p = .03$)]. There was a statistically significant interaction effect for noradrenaline ($F_{[8, 72]} = 2.23, p = .03$), with significant differences in least square means observed between light and vigorous conditions (Least squares mean difference [SE] = 2850 [592], $p <.0001$). However, no statistically significant interaction or main effects for plasma cortisol, salivary cortisol, adrenaline, glucose or insulin were observed. There were statistically significant interaction effects for time and frequency domain measures of heart rate variability.

A systematic review of studies of exercise interventions for smoking cessation was conducted. The review identified 20 studies published between 1985 and 2012. Meta-analyses of the effects of exercise and control conditions on point-prevalence and continuous abstinence at end of treatment, 6 months, and 12 months, revealed statistically significant differences in point-prevalence abstinence at end of treatment and 6 months, but no differences at 12 months or for continuous abstinence at any time point. Only one study found a statistically significant difference between exercise and control groups on smoking abstinence at 12 months’ follow-up. The review concluded that larger trials were needed, with sufficiently intense exercise interventions.

The second empirical study was a large ($n=906$), pragmatic randomised controlled trial (Fit2Quit), of the effectiveness and cost-effectiveness on smoking abstinence rates at six months of a telephone counselling exercise intervention when added to usual smoking cessation support delivered by the New Zealand Quitline, compared with usual smoking cessation support alone. No statistically significant differences were found between groups for smoking abstinence. However, a treatment effect for leisure time physical activity in favour of the intervention group (difference = 219.11 minutes per week; 95% CI 52.65, 385.58) was detected. The number of intervention calls delivered significantly
decreased the probability of smoking (OR 0.89, 95% CI 0.81, 0.97, p-value 0.011) in the intervention group. Overall, the intervention was not cost-effective in the short-term, but was cost-effective for those that adhered to the intervention. There were no differences between groups for any of the psychological or anthropometric outcomes measured in the face-to-face sub-study. A subsample (n=219) of Fit2Quit participants completed additional face-to-face measures.

Qualitative exit interviews (n=20) were also conducted with intervention group participants to explore their perspectives on the acceptability of the intervention. The intervention was well-received by most participants interviewed in the qualitative sub-sample, with the provision of support and encouragement from the participant support person considered the most beneficial aspect. Modifying future interventions to include greater tailoring of the call schedule, greater face-to-face contact, and an exercise support group may enhance effectiveness.

Conclusions: A short bout of vigorous intensity exercise reduces cigarette cravings during temporary smoking abstinence. This effect may be explained by autonomic nervous system responses and post-exercise increases in noradrenaline. However, further research with a larger sample is required to determine this. A six-month telephone-delivered exercise intervention combined with usual cessation support does not improve quit rates compared with usual cessation care alone, but appears to be an acceptable intervention approach. Findings suggest that the effectiveness of this approach may be enhanced if only those motivated to change their exercise behaviour are recruited and poor adherence rates can be addressed Recommendations for future research include exploring changes in heart rate variability, noradrenaline, and cortisol after vigorous exercise, increasing translation of the acute-effects of exercise observed in the laboratory to the real-world setting, and increasing adherence to existing intervention strategies. Exercise does appear to have a role to play as a smoking cessation aid, but only for those willing, motivated and ready to make a change to their
exercise behaviour. Thus, offering exercise to motivated individuals as one of a range of treatment options for smoking cessation could be a helpful approach.
ACKNOWLEDGEMENTS

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CONTRIBUTION OF STUDY INVESTIGATORS AND OTHERS

Associate Professor Ralph Maddison, Caroline Simpson, Associate Professor Chris Bullen, and Professor Harry Prapavessis contributed to the publication of the systematic review of acute studies in the journal Psychopharmacology. Miss Simpson and the candidate conducted the systematic review. Avinesh Pillai provided statistical support to conduct the meta-analyses.

The candidate led the design of the crossover trial, in consultation with Associate Professor Ralph Maddison Dr Nicholas Gant, and Dr John Sollers. Associate Professor Chris Bullen, Dr Hayden McRobbie, and Professor Harry Prapavessis advised on study procedures. The candidate conducted all aspects of the crossover trial including seeking funding, the ethics application, recruitment and data collection procedures, data processing, assays of blood and saliva samples, data analysis, and interpretation. Caroline Simpson assisted with recruitment and data collection. Dr Gant was on call during all assessments in the exercise metabolism laboratory, and together with Briar Rudsits, as trained phlebotomists were responsible for the collection of blood samples. Dr Gant and Stefan Wette provided training and oversaw the completion of the adrenaline, noradrenaline, plasma cortisol, and salivary cortisol assays. Dr Eric Thorstensen provided training and oversaw the completion of the insulin and glucose assays, which were conducted in his laboratory at the Liggins Institute, University of Auckland. Madeline Barbarich assisted with the insulin and glucose assays. Dr Sollers provided training to the candidate on heart rate variability collection, data processing, and analysis, and contributed to the processing, analysis, and interpretation of these data. Jonathan Rawstorn provided technical expertise and advice on data processing and presentation of the study results. Dr Yannan Jiang conducted some of the statistical analyses in consultation with the candidate and Associate Professor Maddison.
Associate Professor Maddison, Associate Professor Bullen, Dr Gant, and Dr Sollers were consulted during the process of interpretation of study findings.

The Fit2Quit trial was designed by Associate Professor Maddison, with advice and input from the other investigators. Funding for the trial was obtained prior to the candidate enrolling in a PhD. The candidate obtained ethical consent for the study, and together with Associate Professor Maddison designed the exercise intervention for the study. The candidate was involved in recruitment of participants, data collection, data entry and interpretation of study findings. Associate Professor Bullen, Dr Hayden McRobbie, Dr Marewa Glover, Sue Taylor, and Professor Prapavessis, gave expert advice on aspects of study design, execution and interpretation of results. Dr McRobbie provided technical expertise on smoking cessation. Dr Yannan Jiang prepared the statistical analysis plan and together with Joy Jiang conducted the statistical analyses. Professor Paul Brown and William Leung conducted all aspects of the cost-effectiveness analyses. All the above contributed to the main publication of results, as well as the earlier publication of the design and conduct of this trial. Dr Soren Brage provided expert advice on the Step test, and conducted the majority of the data processing required for these data. Midi Tsai managed all aspects of the study, and Sue Brewster and Zoe Blair managed the external study sites of Sport Auckland and Sport Waikato, respectively. Jacinta Harris and Ashley Gauld assisted Sue with the management of the project at Sport Auckland. Brooke Mitchell at Sport Waikato, and Amie O’Brien, Abbie Bigge, Ruksanna Paracha, and Wilbur Jetha at Sport Auckland provided the participant support to the exercise intervention group and assisted with data collection. Michelle Grigg and Marilyn Stephens managed the referral process from Quitline. With assistance from the participant support staff, the candidate, Jordan McIntyre, Midi Tsai, Leila Pfaeffli, and Michelle Lee conducted the recruitment and data collection phone calls. Face-to-face data collection was completed by the candidate, Midi Tsai, Brooke Mitchell, and the Sport Auckland participant support team. The candidate conducted the interviews and
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PUBLICATIONS AND CONFERENCE PRESENTATIONS

Peer reviewed publications


Publications submitted

Conference presentations and posters


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<tr>
<td>µl</td>
<td>microliter(s)</td>
</tr>
<tr>
<td>µU/mL</td>
<td>micro units per millilitre</td>
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<tr>
<td>AChE</td>
<td>Acetyl Cholinesterase</td>
</tr>
<tr>
<td>ACTH</td>
<td>Adrenocorticotropic hormone</td>
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<tr>
<td>ADACL</td>
<td>Activation-Deactivation Adjective Checklist</td>
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<tr>
<td>BE</td>
<td>Barrier efficacy</td>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>CBT</td>
<td>Cognitive Behavioural Therapy</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CO</td>
<td>Carbon monoxide</td>
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<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
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<td>CreSS</td>
<td>Clinical Research Support System</td>
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<tr>
<td>CV</td>
<td>Co-efficient variation</td>
</tr>
<tr>
<td>DTS</td>
<td>Desire to smoke</td>
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<tr>
<td>ECQ</td>
<td>Expectancy and credibility questionnaire</td>
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<tr>
<td>EIA</td>
<td>Enzyme-linked immunoassay</td>
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<tr>
<td>ES</td>
<td>Effect size</td>
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<tr>
<td>EQ-5D</td>
<td>European Quality of Life – 5 Dimensions</td>
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<tr>
<td>F</td>
<td>F statistic</td>
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<table>
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<tr>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>FCQ-S</td>
<td>State version of Food Cravings Questionnaire</td>
</tr>
<tr>
<td>fMRI</td>
<td>Functional magnetic resonance imaging</td>
</tr>
<tr>
<td>FTND</td>
<td>Fagerström Test of Nicotine Dependence</td>
</tr>
<tr>
<td>g</td>
<td>gram(s)</td>
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<tr>
<td>GPS</td>
<td>Global Positioning System</td>
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<tr>
<td>GRx</td>
<td>Green Prescription</td>
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<tr>
<td>HF</td>
<td>High frequency</td>
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<td>HR</td>
<td>Heart rate</td>
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<td>HRaR</td>
<td>Heart rate above rest</td>
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<td>HRR</td>
<td>Heart rate reserve</td>
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<tr>
<td>HRV</td>
<td>Heart rate variability</td>
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<td>HSE</td>
<td>Health Survey for England</td>
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<tr>
<td>Hz</td>
<td>Hertz</td>
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<tr>
<td>$I^2$</td>
<td>Chi-squared statistic</td>
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<tr>
<td>ICERS</td>
<td>Incremental cost-effectiveness ratios</td>
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<td>IPAQ</td>
<td>International Physical Activity Questionnaire</td>
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<td>IPD</td>
<td>Individual participant data</td>
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<td>IQR</td>
<td>Inter-quartile range</td>
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<td>ITT</td>
<td>Intention to treat</td>
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<td>Kg</td>
<td>Kilogram(s)</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>LCE</td>
<td>Locus of Causality for Exercise scale</td>
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<td>LF</td>
<td>Low frequency</td>
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<tr>
<td>LoA</td>
<td>Limits of agreement</td>
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<td>LSI</td>
<td>Leisure Score Index</td>
</tr>
<tr>
<td>MD</td>
<td>Mean difference</td>
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<tr>
<td>MET</td>
<td>Metabolic equivalent</td>
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<td>METmin/wk</td>
<td>Metabolic equivalent minutes per week</td>
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<tr>
<td>ml</td>
<td>milliliter(s)</td>
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<tr>
<td>mmHg</td>
<td>Millimetres of Mercury</td>
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<td>mmol/L</td>
<td>millimoles per litre</td>
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<tr>
<td>MPSS</td>
<td>Mood and Physical Symptoms Scale</td>
</tr>
<tr>
<td>ms</td>
<td>millisecond(s)</td>
</tr>
<tr>
<td>nAChR</td>
<td>Nicotine Acetylcholine Receptor</td>
</tr>
<tr>
<td>ng/ml</td>
<td>nanograms per milliliter</td>
</tr>
<tr>
<td>nm</td>
<td>nanometer(s)</td>
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<tr>
<td>NN</td>
<td>N to N interval on a recording of heart rate</td>
</tr>
<tr>
<td>NRT</td>
<td>Nicotine replacement therapy</td>
</tr>
<tr>
<td>NZ</td>
<td>New Zealand</td>
</tr>
<tr>
<td>°C</td>
<td>degrees Celsius</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>p</td>
<td>significance value</td>
</tr>
<tr>
<td>PA</td>
<td>Physical activity</td>
</tr>
<tr>
<td>PAI</td>
<td>Physiological activity intensity</td>
</tr>
<tr>
<td>pg/ml</td>
<td>pictograms per millilitre</td>
</tr>
<tr>
<td>pNN50 %</td>
<td>Percentage of the number of adjacent NN intervals that differed by more than 50ms</td>
</tr>
<tr>
<td>ppm</td>
<td>Parts per million</td>
</tr>
<tr>
<td>PSP</td>
<td>Participant support person</td>
</tr>
<tr>
<td>QALYS</td>
<td>Quality Adjusted Life Years</td>
</tr>
<tr>
<td>QRS</td>
<td>The complex of Q-wave, R-wave, S-wave on a recording of heart rate</td>
</tr>
<tr>
<td>QSU-brief</td>
<td>Questionnaire of smoking urges – brief</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>RMSSD</td>
<td>Square root of the mean squared differences between adjacent R-R intervals</td>
</tr>
<tr>
<td>RPE</td>
<td>Rating of perceived exertion</td>
</tr>
<tr>
<td>RR</td>
<td>Relative Risk</td>
</tr>
<tr>
<td>R-R</td>
<td>R to R interval on a recording of heart rate</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SE</td>
<td>Standard error</td>
</tr>
<tr>
<td>SoD</td>
<td>Strength of desire to smoke</td>
</tr>
<tr>
<td>SRNT</td>
<td>Society for Research on Nicotine and Tobacco</td>
</tr>
</tbody>
</table>
TMB Tetramethylbenzidine

TWS Tobacco withdrawal syndrome

UK United Kingdom

US or USA United States of America

VO_{2\text{max}} Maximum volume of oxygen consumption

Further abbreviations are listed beneath Tables 2 and 12
DEFINITION OF TERMS

Cravings and tobacco withdrawal symptoms:

The term “cravings” or “cigarette cravings” is often categorised as a withdrawal symptom. However, within this thesis, it is considered a distinct construct. In this thesis “cigarette cravings” is used to describe desire to smoke, strength of desire to smoke, or urge to smoke. The term “tobacco withdrawal symptoms/syndrome” refers to a well-recognised group of subjective experiences other than cravings, also experienced during smoking abstinence, including depression, anxiety, hunger, poor concentration, restlessness, irritability, stress, and tension.

Exercise and physical activity:

The terms exercise and physical activity are often used interchangeably to refer to informal lifestyle physical activities and more formal structured activities. In general, within this thesis, the terms reflect the following definitions by Caspersen et al.3 “Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure… and can be categorized into occupational, sports, conditioning, household, or other activities” (p. 126). “Exercise is a subset of physical activity that is planned, structured, and repetitive and has, as a final or an intermediate objective, the improvement or maintenance of physical fitness” (p. 126).

Smoking topography:

Smoking topography refers to how a person smokes a cigarette and includes measures of the number of puffs and puff volume, duration, and velocity.4 5

Smoking abstinence, quitting and smoking cessation:

The terms smoking abstinence, quitting smoking and smoking cessation are often used interchangeably. Within this thesis, smoking cessation refers to the act of stopping smoking,
as does quitting smoking; whereas smoking abstinence refers to not smoking for a defined period of time. There are two primary measures of smoking abstinence: point prevalence abstinence and continuous abstinence, which are defined in detail in Chapter 4.

*Peripheral markers of neurobiology/ neurobiological changes:*

These terms refer to potential mechanisms underlying the relationship between cigarette cravings and exercise that relate to the biology of the nervous system.
1.1 BACKGROUND

The aim of this thesis is to tackle tobacco smoking, one of the greatest threats to public health, by investigating the relationship between smoking cessation and exercise.

Currently, over one fifth of the world’s population smoke tobacco. Tobacco smoking is the leading preventable cause of death, with nearly six million tobacco-attributable deaths each year globally. Half of all people who smoke will die from a smoking related disease, and half of these people will die in middle age. If the current situation remains unchanged, it is estimated that one billion people will die from a smoking related disease in the 21st century. Tobacco use is also a leading risk factor for lost healthy years of life, ranking first on the list of risk factors in high-income countries, and sixth globally.

In New Zealand (NZ), approximately 17% of the population smoke tobacco daily. Prevalence rates are higher amongst Māori (indigenous New Zealanders, 44%) and Pacific peoples (31%) than the overall population. Smoking is directly responsible for an estimated 4500 deaths each year in NZ including 22% of all Māori deaths. Tobacco smoking is the most important single contributing factor to lost healthy years of life and to inequalities in Māori/non-Māori life expectancy.

The effects on health from tobacco smoking are many, and include a wide range of cancers, cardiovascular disease, chronic obstructive pulmonary disease (COPD), pregnancy complications, and other chronic diseases. Moreover, there are a multitude of consequences attributable to exposure to second-hand tobacco smoke, which is considered more toxic than the smoke cigarette users inhale, and affects
other non-smoking adults and children. In NZ, approximately 350 people die each year from second-hand smoke exposure. Policies and interventions to reduce the prevalence of smoking have been in place globally and in NZ since the early 1960’s. The NZ Government’s aim is for smoking rates to be less than 5% by 2025. To achieve this, the Ministry of Health has established “better help for smokers to quit” as one of its six priority health targets. The majority of NZ’s smokers are supportive of this direction. Four out of five NZ smokers express regret at ever having started smoking and 40% try to quit every year. However, studies have shown that fewer than 5% of those who try to quit without support remain abstinent for six months or more. Dependence on nicotine, the primary psychoactive ingredient found in tobacco, underpins much of the struggle that smokers face when they try to quit, and it is well established that the addiction to nicotine sustains tobacco use. The biochemical effects of nicotine are powerful and immediate, reaching nicotinic acetylcholine receptors (nAChR) in the brain in seven seconds of cigarette inhalation. Moreover, in addition to the chemical effects, long-term smoking becomes associated with certain habitual behaviours and sensory cues through conditioning, which compound the challenge smokers face when quitting. Smoking cessation is an important public health challenge as it has intermediate and long-term health benefits, a fact recognized in all NZ’s health strategies. A recent study of 1.3 million United Kingdom (UK) women found that more than 90% of the excess mortality caused by smoking was avoided by stopping smoking before 40 years of age. Treatments to aid smoking cessation that are widely available, accessible, and cost-effective would therefore have great potential for public health benefit.
The most effective smoking cessation treatments typically combine behavioural support with pharmacotherapy.\textsuperscript{29} Behavioural support can be delivered in various formats (e.g., via the telephone or internet, via SMS messaging, or face-to-face in a group or individual setting) and can improve the chances of quitting by an estimated 2-7\%.\textsuperscript{30-34} Pharmacotherapies such as nicotine replacement therapies (NRT), bupropion (Zyban\textsuperscript{®}), and varenicline (Champix\textsuperscript{®}) are also effective and may double or even triple the chances of long-term abstinence.\textsuperscript{35 36}

Telephone-based counselling is another effective approach. In NZ, the national toll-free Quitline is a national smoking cessation service provided by The Quit Group, a government-funded organisation. Quitline offers a range of services including telephone-delivered behavioural support (three sessions) and, if callers choose, an 8-week supply of subsidised nicotine patches, gum or lozenges via a voucher redeemable at community pharmacies (cost NZ$3 per item per four weeks supply). For users of Quitline, abstinence rates are estimated to be 21\% at six months\textsuperscript{37} and 15\% or more at 12 months.\textsuperscript{38}

Despite the proven efficacy of the various cessation approaches, long-term cessation rates are still below 25\%.\textsuperscript{38} If the current rate of decline in smoking prevalence continues on the same trajectory, it will take 100 years before adult smoking prevalence in NZ reaches the NZ Government target of 5\%. New approaches to smoking cessation are needed and, ideally, such approaches should provide additional benefits to existing proven strategies. This thesis examines the role of exercise as an aid to augment existing cessation strategies.

Due to the nicotine dependence that is central to tobacco use,\textsuperscript{39} smoking cessation is associated with a well-defined withdrawal syndrome, which includes symptoms such as sleep disturbance, irritability, anxiety, depression, and craving. Symptoms are particularly strong during the first two weeks of a quit attempt, and severity of desire
to smoke is predictive of relapse. In the longer term, cessation of smoking is also commonly associated with an average weight gain of 5kg within the first year.

There is a growing body of evidence to indicate that regular exercise may ameliorate most of the negative effects of nicotine withdrawal, such as the symptoms of depression, anxiety, and psychosocial stress, as well as weight gain. Sleep patterns as well as cognitive functioning may also be improved by exercise.

Underlying these assumptions are the similar effects of nicotine and exercise on the central nervous system and neurobiological processes in the brain, and as such, exercise may provide an alternative reinforcer to smoking. Neurotransmitters, growth factors, and second messengers regulated by both nicotine and exercise include dopamine, noradrenaline, adrenaline, glutamate, brain-derived neurotrophic factor (BDNF) and extracellular-signal-regulated kinases (ERKs). The release of dopamine, in particular, signals a pleasurable experience which reinforces the effects of nicotine or exercise. It is plausible therefore that exercise may help offset some of the negative effects of nicotine withdrawal experienced during smoking cessation.

In addition to similar effects on neurobiological processes in the brain, exercise has also been proposed as an alternative behaviour to smoking because it acts as a distraction from smoking-related thoughts, increases self-esteem and enhances coping ability and confidence, which may help protect against smoking relapse. In the longer term exercise may help mitigate post-cessation weight gain, which is important given that weight gain concerns are predictive of reluctance to quit smoking and smoking relapse. Moreover, being physical active has a number of benefits to health beyond its potential as a smoking cessation aid, and has been proposed as a useful tobacco harm reduction strategy for those unable to stop smoking completely.
Chapter 1: Introduction

However, despite these underlying assumptions, the mechanisms underlying the relationship between exercise and smoking cessation are still unclear, and further research is required to investigate the role of exercise as an aid to smoking cessation. There are two distinct, but linked, streams of research within the literature on the relationship between exercise and smoking cessation. One stream has explored the acute effects of exercise on tobacco withdrawal symptoms (TWS) and cravings, whilst the other examines the chronic effects of exercise on smoking cessation. A number of reviews of the scientific evidence within these two research streams have been conducted, and suggest that whilst an acute bout of exercise mitigates the magnitude and duration of TWS and cravings during periods of temporary smoking abstinence, its long-term benefit for smoking abstinence is less clear. Moreover, there is still much to be understood about the type, frequency, duration and intensity of exercise most effective at reducing cravings, and increasing smoking abstinence rates. The underlying psychobiological or physiological mechanisms involved in the exercise-cravings relationship also remain unclear. If the mechanisms involved can be accurately determined then future interventions can be tailored to target those mechanisms and ultimately increase long-term abstinence rates.

1.2 AIM OF THE THESIS

The aim of this thesis was to investigate the relationship between exercise and smoking cessation, and to explore potential mechanisms to explain the relationship. This aim has been achieved by undertaking two systematic reviews of the literature, one for each stream of research in the area, and by conducting two empirical studies. The first systematic review explored studies of the acute effects of exercise on TWS and cigarette cravings. The first empirical study examined the impact of different intensities of exercise on TWS and cravings during temporary smoking abstinence in a randomised crossover trial. The second systematic review examined studies of
exercise interventions for smoking cessation. The second empirical study was a large pragmatic randomised controlled trial (RCT) of the impact of an exercise intervention on smoking cessation rates, which included a face-to-face sub-study (participants who completed face-to-face assessments) and a qualitative sub-study of participant perceptions of the trial intervention. The intention was to provide a complete account of the two research streams within the exercise and smoking literature, link the two streams together, and provide direction for future research.

1.3 STRUCTURE OF THE THESIS

The thesis is organised into seven chapters and appendices. This chapter (Chapter 1) introduces the topic and the rationale for the thesis. The subsequent chapters are outlined below:

Chapter 2 presents a systematic review of studies examining the acute effects of brief bouts of exercise on cigarette cravings, TWS, affect, and smoking behaviour. This is an update to a previous review, and includes a meta-analysis of the effects of exercise on cigarette cravings, and was published in Psychopharmacology in 2012. Although another review and meta-analysis exploring the effects of exercise on cigarette cravings has recently been published, there are differences in methodology between the two reviews that are discussed below. Moreover, the present review of additional outcomes (not reviewed by Haasova et al.) makes a substantial contribution to the literature.

Chapter 3 describes in detail the methods and results of a RCT (n=40) to determine the effects of three different exercise intensities on cigarette cravings and TWS, and to explore potential psychological and physiological mediators of this relationship. Findings are discussed and related to previous research.

Chapter 4 presents a systematic review of trials of exercise interventions for smoking cessation, and includes meta-analyses of the effects of exercise on smoking...
Chapter 1: Introduction

abstinence. Although a Cochrane review on this topic was recently updated in 2012, the addition of the meta-analyses and inclusion of studies of less than 6 months’ duration is a novel contribution to the literature. The merits and limitations of these methodological differences are discussed.

Chapter 5 consists of a detailed account of the methods and results of a large pragmatic RCT (n=906) of an exercise intervention for smoking cessation (Fit2Quit: Exercise to enhance smoking cessation outcomes trial). Although the main trial results are presented, the focus of this thesis was on the tertiary outcomes (body mass index [BMI], weight, physical fitness, leisure exercise, self-efficacy, barrier-efficacy, and motivation) measured in the sub-sample of participants who were assessed face-to-face (face-to-face sub-sample, n=219). Findings are discussed and related to previous research.

Chapter 6 presents the methods and results of a qualitative sub-study undertaken with a sample of Fit2Quit intervention group participants (n=20) to determine their perceptions of the intervention and suggested improvements for future research.

Chapter 7 comprises a discussion of the findings of all of the research presented in this thesis and draws conclusions. Implications for future research and practice are also discussed.

The appendices contain all relevant study materials and other related documents.

It is important to note that much of this research was conducted concurrently and not always in chronological sequence. However, for the purpose of structuring this thesis in an accessible way for the reader, the studies were organised as if in sequence, as described above. For example, the Fit2Quit trial presented in Chapter 5 was designed prior to the commencement of this PhD, based on the recommendations of the Cochrane review of exercise interventions for smoking cessation. Therefore, although the Fit2Quit trial is not presented until Chapter 5, it was the first study to
Chapter 1: Introduction

commence, and the findings from the study in Chapter 3 were therefore unable to be used to inform the Fit2Quit intervention design. The sequencing of the 5 studies presented in chapters 2-6 is presented graphically below. Although the two systematic reviews (presented in Chapters 2 and 4) were planned in 2009, the timelines for these chapters in the below chart extend from the date of the first literature search to the final search for each in June 2012. The time lines for Chapters 3, 5, and 6 represent the time from the beginning of study set-up to the end of data analysis. The final drafts of all chapters were completed in December 2012.

<table>
<thead>
<tr>
<th>Study chapter</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
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<tbody>
<tr>
<td>Chapter 2</td>
<td>Q3</td>
<td>Q4</td>
<td>Q1</td>
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<td>Chapter 5</td>
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</tr>
<tr>
<td>Chapter 6</td>
<td></td>
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</tbody>
</table>
CHAPTER 2  THE ACUTE EFFECTS OF EXERCISE ON CIGARETTE CRAVINGS, WITHDRAWAL SYMPTOMS, AFFECT AND SMOKING BEHAVIOUR: SYSTEMATIC REVIEW UPDATE AND META-ANALYSIS

2.1  INTRODUCTION
This chapter describes the method and findings of an updated systematic review and meta-analysis of studies examining the acute effects of exercise on cigarette cravings, TWS, affect and smoking behaviour.

2.1.1  BACKGROUND
Smoking cessation is associated with TWS such as sleep disturbance, irritability, poor concentration, and depressed mood, as well as intense craving for a cigarette.\(^{70}\) Craving, the presence of withdrawal symptoms, and weight gain are all associated with an increased risk of smoking relapse and impact negatively on attempts to quit.\(^ {40}\) Therefore, identifying ways to reduce these negative effects of smoking abstinence may be important in increasing the success of quit attempts.

Participation in regular exercise appears to ameliorate the intensity and frequency of many of the TWS and cravings associated with smoking cessation.\(^ {64}\) However, findings from intervention studies designed to investigate if exercise assists individuals to quit smoking have shown mixed results.\(^ {68}\) A clearer understanding of the relationships between exercise, TWS and cravings during temporary smoking abstinence may improve the design and effectiveness of future exercise-based smoking cessation interventions.

Taylor et al., conducted a systematic review of studies examining the acute effects of exercise on cigarette cravings, TWS, affect, and smoking behaviour, which was published in 2007.\(^ {64}\) The following is a summary of the findings of that review.
2.1.2 SUMMARY OF PREVIOUS REVIEW

Taylor et al.,\(^{64}\) identified 14 studies published between 1983 and 2006 that examined the effect of exercise on TWS. Of the 12 studies that compared exercise with a control condition, all showed at least one positive effect on withdrawal.\(^{64}\) This was the case for both brief (5 to 10 minute) bouts of moderate intensity exercise among smokers who were abstinent overnight,\(^{66,72}\) and for 30 to 40 minute bouts of vigorous intensity among smokers trying to quit.\(^{73}\) Withdrawal symptoms found to be affected by brief bouts of exercise included anxiety, stress, poor concentration, tension, restlessness, and irritability. Nine\(^{66,72-81}\) of the 10 studies that compared the effects of an exercise condition with a passive condition on cravings found a significant reduction in cravings following exercise. Studies that assessed strength of urges to smoke showed that an average reduction of 1.1 points on a 7-point scale could be achieved. Three of the studies\(^{73,78,79}\) found that exercise had a positive effect on mood and affect during smoking abstinence, increasing activation and energy, and decreasing negative affect and tension. One study suggested tension was a mediating factor for reductions in desire to smoke.\(^{78}\) The review included four studies that measured time to \textit{ad libitum} smoking, all of which found increases ranging from 8 to 57 minutes following exercise.\(^{75,76,79,82}\) Except for one study,\(^{73}\) which measured cravings throughout a 12-week smoking cessation programme, all of the studies measured cravings during temporary abstinence only (i.e. participants were asked to abstain from smoking for a short period of time [\(\leq 15\) hours] prior to the measurement of cravings), and all were conducted in the laboratory setting.

Taylor et al.;\(^{64}\) highlighted some key issues to be addressed in future research. These included the need to: a) increase the ecologic validity of subsequent findings either by conducting studies in natural, free-living conditions rather than the laboratory setting, or by attempting to create a more familiar environment within the laboratory by exposing participants to smoking cues, and b) elucidate the
mechanisms underpinning the beneficial effects of exercise on TWS and cravings. In regard to the second issue, Taylor et al.\textsuperscript{64} surmised that distraction is unlikely to be a mediating factor and proposed that other potential mechanisms such as stress reduction and activation, psychobiological mechanisms, and appetite suppression may be important. The authors suggested that exercise may mimic the effects of smoking by both relaxing and activating the individual. Additional research to examine the role of β-endorphins and opioids as well as dopaminergic activity in the context of exercise and cigarette cravings and TWS was also proposed. Taylor et al.\textsuperscript{64} concluded that a brief bout of exercise can reduce cravings for a cigarette at levels comparable to those of glucose and oral nicotine replacement therapy (NRT), and should therefore be recommended.

Since this review, a large number of studies examining the effects of exercise on cravings and TWS have been published.\textsuperscript{64} It was therefore considered appropriate and timely to conduct a review of these studies published since the Taylor et al.\textsuperscript{64} review, and to conduct a meta-analysis of all studies examining the effects of exercise on cigarette cravings.

The first draft of this systematic review was completed in February 2012 and published in the journal of Psychopharmacology in May 2012. A final search for additional studies for this review was conducted in June 2012.

2.1.3 OBJECTIVES

The purpose of this chapter is twofold. First, the chapter comprises an update of the 2007 Taylor et al. review of the acute effects of exercise on TWS, cravings, affect, and smoking behaviour during temporary smoking abstinence, including an exploration of potential mediators of the exercise-cravings relationship, using methods consistent with the original review.\textsuperscript{64} Second, it presents a meta-analysis of
all published studies to date, to determine more robust estimates of the strength of the effect of exercise on cigarette cravings.

2.2 METHOD

2.2.1 SELECTION CRITERIA

2.2.1.1 Study design

All study designs were eligible for inclusion if they examined the acute effects of exercise on cigarette cravings.

2.2.1.2 Study participants

Trials involving male and female smokers (≥18 years) of all ethnicities were eligible for inclusion.

2.2.1.3 Treatment conditions

Eligible trials were those involving a period of smoking abstinence where at least one group of participants (or treatment condition) completed a bout of exercise, compared with a passive control, another intensity of exercise, or another exercise modality. Trials which examined exercise credibility and expectancy, and assessed changes between pre- and post-exercise measures were also included. Treatment conditions of all durations were included.

2.2.1.4 Outcomes

For inclusion in the review, eligible trials reported at least one of the following outcomes: (1) a measure of cigarette cravings, (2) a measure of TWS, (3) a measure of affect, or (4) a measure of smoking topography or behaviour. For inclusion in the meta-analyses, eligible trials measured and reported one or both of the following cigarette cravings outcomes: (1) desire to smoke, or (2) strength of desire to smoke. Further secondary outcomes narratively reviewed were: (1) other measures
of cravings and TWS, including Shiffman-Jarvik withdrawal scale,\textsuperscript{85} Questionnaire of smoking urges – brief (QSU-brief),\textsuperscript{86} and the Mood and Physical Symptoms Scale (MPSS),\textsuperscript{84} (2) affect, (3) distraction, (4) expectation, (5) intervention credibility, (6) cortisol, (7) regional brain activation, (8) cue-based reactivity, (9) Stroop task reaction time, (10) attentional bias, and (11) smoking topography.

2.2.1.5 **Exclusion Criteria**

The search was limited to all studies of human adult participants (≥18 years) published between January 2006 and June 2012. There were no specific criteria for study design.

2.2.2 **DATA SOURCES AND SEARCH STRATEGY**

2.2.2.1 **Databases searched**

A systematic search of the literature was conducted using online searches of the following electronic data bases: Sports Discus, MEDLINE, PubMed, Web of Science, EMBASE, PsycINFO, Cochrane Tobacco Addiction Group specialised register, the ETD Digital Library-Networked Digital Library of Theses and Dissertations, and Proquest Digital Dissertations. The reference lists of relevant articles, and abstracts from the Society for Research on Nicotine and Tobacco (SRNT) annual meetings from 2006 to 2010 were also hand-searched.

2.2.2.2 **Search terms**

The keywords used were exercise, physical activity, smoking, tobacco, nicotine, smoking cessation, withdrawal, craving, and affect.

2.2.2.3 **Study selection**

The search of electronic databases identified 142 studies. Two reviewers independently examined the abstracts of all studies for inclusion. Where a decision to include or exclude a study could not be attained from the abstract, the full article was reviewed. Prominent researchers in the field were contacted and asked for any studies currently under review or in press. Four further studies were identified. For
Chapter 2: Systematic Review of Acute Studies

the SRNT abstracts, decisions to exclude a study were made based on the title of the abstract, and the remaining abstracts were reviewed for inclusion.

### 2.2.2.4 Description of included studies

In accordance with the previous review, all journal articles, conference abstracts, theses, and dissertations that studied the effects of a brief bout of exercise on TWS, cravings, or affect during temporary abstinence were included. Fifteen studies met the inclusion criteria for review, as at June 30, 2012. Full details of each study are presented in Table 2. Three studies were from unpublished doctoral dissertations.\(^7\)\(^8\)

### 2.2.3 DATA EXTRACTION AND SYNTHESIS

The following data were extracted from each included study: setting, study design, study objectives, method of recruitment, method of randomisation, participant characteristics (age, sex, ethnicity, smoking behaviour, Fagerström Test of Nicotine Dependence [FTND] score,\(^8\) exercise level at baseline), inclusion and exclusion criteria, sample size, treatment condition descriptions (including exercise intensity and duration), definition and measure of smoking abstinence, method of validation, quality information, loss to follow-up, results, and limitations. Where data from a publication were not adequately described, additional information was sought from the authors.

Results of studies that were sufficiently alike in terms of comparison groups and outcomes were combined in the meta-analyses. Two senior researchers and a biostatistician were consulted to determine which studies were suitable for combining. Meta-analyses were conducted where there were a sufficient number of studies (n=4) for a particular outcome, and the published data were in a suitable format. A narrative review of other outcomes of interest was also conducted.
2.2.4 ASSESSMENT OF STUDY QUALITY

Assessment of study quality and risk of bias was based on the recommendations by the Cochrane Collaboration. The Cochrane Collaboration recommends that standard scales and checklists to assess study quality should not be used, arguing that calculating a summary score of study quality involves assigning weights to different items in the scale, and it is difficult to justify the weights assigned. In a review of tools used to assess the quality of randomised trials, Moher et al. found that many of the standard scales used to assess quality or risk of bias focus more on incomplete reporting rather than actual conduct. Therefore, the Cochrane Collaboration suggests using their domain-based evaluation, in which critical assessments are made separately for different domains. There are six domains: 1) sequence generation, 2) allocation concealment, 3) blinding of participants, personnel and outcome assessors, 4) incomplete outcome data, 5) selective outcome reporting, and 6) other sources of bias. A summary description of each of the above domains is required for each study. Criteria for judging risk of bias are detailed in the Cochrane Collaboration Handbook for Systematic Reviews. Studies are judged as either ‘Yes’ meets the criteria (low risk of bias), ‘No’ does not meet the criteria (high risk of bias), or ‘Unclear’ (uncertain risk of bias), based on the information available for each domain. An overall summary of risk of bias for each study is then produced, and the overall judgement of risk of bias is incorporated in the meta-analysis. The following table, adapted from the Cochrane Handbook for Systematic Reviews of Interventions, was used as a guide to summarise overall risk of bias for each study.
Chapter 2: Systematic Review of Acute Studies

### Table 1: Guide to Assigning Summary Risk Bias Scores*

<table>
<thead>
<tr>
<th>Risk of bias</th>
<th>Interpretation</th>
<th>Within a study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Plausible bias unlikely to seriously alter the results</td>
<td>Low risk of bias for all key domains</td>
</tr>
<tr>
<td>Unclear</td>
<td>Plausible bias that raises some doubt about the results</td>
<td>Unclear risk of bias for one or more key domains</td>
</tr>
<tr>
<td>High</td>
<td>Plausible bias that seriously weakens the confidence in the results</td>
<td>High risk of bias for one or more key domains</td>
</tr>
</tbody>
</table>

*adapted from the Cochrane handbook

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2.3 RESULTS

2.3.1 CHARACTERISTICS OF INCLUDED STUDIES

A total of fifteen new studies including 583 participants were included in the review. Twelve were published in peer-reviewed journals, and three were from two PhD dissertations. While one of the identified studies was published within the time frame, it was included in the previous review, so was not included in this review. Eight studies were from the UK, four were from Canada, and three were from the United States (US).

2.3.2 CHARACTERISTICS OF INCLUDED PARTICIPANTS, INTERVENTIONS AND OUTCOMES

The study populations varied greatly in age, ranging from 16 to 70+ years. However, study participants were generally homogeneous with regard to ethnic background (predominantly Caucasian) and health status (potential participants receiving treatment for any physical or psychological condition, and/or with contraindications to performing exercise, were excluded in 14 studies). Eleven studies recruited both male and female participants, three studies only female participants, and one study only male participants.

The outcome variables identified included measures of cigarette cravings, TWS, affect, and biomarkers for stress and craving. Some studies also measured and...
compared Stroop task reaction time,\textsuperscript{100} awareness,\textsuperscript{103} perceived credibility and expectancy of the usefulness of the intervention,\textsuperscript{87,94} and smoking topography.\textsuperscript{97}

With regard to study design, the majority of studies followed a similar research paradigm. All studies included participants who smoked at least 10 cigarettes per day. Three studies \textsuperscript{87,104} examined the acute effects of exercise on cravings and withdrawal symptoms at certain time points in participants undergoing a quit attempt. All other studies asked participants to temporarily abstain from smoking prior to attending the treatment session. The exercise intensities tested ranged from low intensity isometric exercise to vigorous running and cycling at up to 85\% heart rate reserve (HRR). In five studies a between-group parallel arm design was used,\textsuperscript{94-96,103} \textsuperscript{104} a within-subject crossover design was employed in eight,\textsuperscript{88,93,97-102} and a within-subject over time design was used in two studies.\textsuperscript{87} See Table 2 for a detailed summary of study participant characteristics, treatment conditions, study design, measures, and outcomes.
### Table 2: Summary of Included Studies

<table>
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<tr>
<th>Study</th>
<th>Subjects characteristics</th>
<th>Abstinence period</th>
<th>Exercise characteristics</th>
<th>Measures</th>
<th>Design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daniel et al.</td>
<td>22 m &amp; 23 f. Age = 16-65 yrs. Mean = 24. Mean cigs = 14.4 per day. Mean FTND = 4.2 Mean baseline SoD = 4.4 Exercise: VPA &lt;3 times per week for &gt;20min, or MPA &lt;5 times per week for &gt;30min.</td>
<td>Mean = 13 hrs</td>
<td>Read a (a) positive (b) negative (c) ambiguous paragraph about the relationship between TWS and exercise prior to 10mins cycling between 40-60% of HRR.</td>
<td>Cravings measure - Desire to smoke (Tiffany) Expectations - Credibility Scale Response - MPSS &amp;</td>
<td>Between-subject (randomly assigned). Assessments – Expectations: 1month pre &amp; 20mins pre. Response: 10-, 5- &amp; 0-min pre, mid, &amp; IP, 5- &amp; 10-min post. Compared response to expectations.</td>
<td>Expectation manipulation was successful. No sig. differences in MPSS or SoD between expectation groups. Significant reduction in symptoms and SoD during and after exercise for all groups (ES ranged from 0.4-0.8).</td>
</tr>
<tr>
<td>Everson et al.</td>
<td>25 m &amp; 20 f. Mean age = 21.8 Mean cigs = 13.6 per day. Mean FTND = 3.4 Mean baseline SoD = 4.6 Exercise: ≤3 times per week for &gt;30min</td>
<td>Mean = 17 hrs</td>
<td>10-mins (a) cycled 40-59% HRR (b) cycled 60-84%HRR (c) Sat quietly with no distractions</td>
<td>Cravings measure – SoD (West), Other measures - MPSS &amp; SEES</td>
<td>Between-subject (randomly assigned, stratified for gender). Assessments: pre, mid, &amp; 5- &amp; 30-mins post.</td>
<td>(a &amp; b) &lt; (c) Desire to smoke during and 5-min post. (ES during = .82 (a), 1.15 (b); ES 5-min post = .79 (a), 1.03 (b) (a) reduced TWS and improved mood 5-min post. (b) increased PD &amp; MPSS, &amp; reduced happiness scores. No effects at 30-min post.</td>
</tr>
<tr>
<td>Janse Van Rensburg et al.</td>
<td>15 m &amp; 8 f. Mean age = 23.1 Mean cigs = 13.7 per day. Mean FTND = 3.4</td>
<td>15 hrs</td>
<td>15-mins (a) Brisk walk (treadmill) (Mean RPE = 10.8 (1.67) range 6-20 (b) Passive control</td>
<td>Cravings measures - Desire to smoke (Tiffany), 10-item QSU. Other measures - Stroop Task reaction time</td>
<td>Randomised cross-over design. Assessments pre, &amp; IP, 5-, 10- &amp; 15-min post for all measures. Additional assessment at mid for 'desire to smoke' &amp; QSU.</td>
<td>(a) &amp; (b) no sig. difference for Stroop. (a) reduced desire to smoke, QSU Factor 1 &amp; 2 and reduced cravings up to 15-mins post cf (b). ES ranged from .86 – 1.02</td>
</tr>
<tr>
<td>Study</td>
<td>Group Details</td>
<td>Intervention Duration</td>
<td>Intervention Details</td>
<td>Cravings Measures</td>
<td>Design Details</td>
<td>Findings</td>
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<tr>
<td>Janse Van Rensburg et al. 98</td>
<td>15 m &amp; 5 f. Mean age = 29.05 Mean cigs = 15.6 per day. Mean FTND = 4.0 Mean baseline desire to smoke = 5.3</td>
<td>15 hrs</td>
<td>15-mins &lt;br&gt; (a) Cycling (RPE = 11-13) &lt;br&gt; (b) Sitting passively with no distractions</td>
<td>Cravings measures - Attentional bias measurement, Desire to smoke (Tiffany)</td>
<td>Randomised cross-over design. Eye tracking protocol pre- &amp; post-treatment. Desire to smoke assessed pre-, mid- &amp; post-treatment, &amp; post-eye tracking protocol.</td>
<td>(a) Reduced desire to smoke mid (ES = 1.07) &amp; post (ES = 1.06) treatment cf (b). Dwell time &amp; initial fixation towards smoking images was reduced with (a) cf (b).</td>
</tr>
<tr>
<td>Janse Van Rensburg et al. 99</td>
<td>10 m &amp; f. Age = 18-50. Mean cigs = 13.7 per day. Mean FTND = 3.4 Mean baseline desire to smoke = 4.6</td>
<td>15 hrs</td>
<td>10-mins &lt;br&gt; (a) Cycling (RPE = 11-13) &lt;br&gt; (b) Sitting passively with no distractions</td>
<td>Cravings measures – fMRI brain activation, Desire to smoke (Tiffany)</td>
<td>Randomised cross-over design. 10-mins exercise then 15-mins fMRI scanner. Desire to smoke assessed pre-, mid- &amp; post-treatment.</td>
<td>Scanning found decreased activation in areas of the brain associated with reward, motivation &amp; visuo-spatial attention after (a) cf (b). (a) Reduced desire to smoke mid (ES = .88) &amp; post- (ES = 1.14) treatment cf (b).</td>
</tr>
<tr>
<td>Ussher et al. 100</td>
<td>31 m &amp; 17 f. Mean age = 27.8 Mean cigs = 15.5 per day. Mean FTND = 5.0</td>
<td>Mean = 16.7 hrs</td>
<td>10-mins &lt;br&gt; (a) Body scan &lt;br&gt; (b) Isometric exercise (jaw clenching, fist clenching, pushing the palms of the hands together, pushing down on the thighs, squeezing thighs together, pushing feet into the floor) &lt;br&gt; (c) Listening to a audio-recording of a natural history text</td>
<td>Cravings measure - SoD (West) Other measures – MAAS, modified MPSS, perceived credibility</td>
<td>Between subjects (randomly assigned). Assessment pre &amp; IP, 5-, 10- &amp; 30-mins post intervention in the laboratory. Then undertook intervention again during next 3 hours in their ‘normal’ environment assessed pre &amp; IP, 5- &amp; 30mins post intervention.</td>
<td>Desire to smoke and withdrawal symptoms reduced in (a &amp; b) cf (c) for up to 30-mins post in lab setting (ES ranged from .61 - .94), &amp; up to 5-mins post in ‘normal’ setting. No sig. diff between (a) &amp; (b).</td>
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<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Time</th>
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<th>Cravings measures</th>
<th>Other Measures</th>
<th>Study Design</th>
<th>Results</th>
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<tr>
<td>Ho et al. 1998</td>
<td>8 m.</td>
<td>24 hrs</td>
<td>(a) resistance exercises (6 exercises, 3 x 10 of each) (b) quiet rest (c) rest (and ad libitum smoking)</td>
<td>Cravings measure SoD (West) Other measures - (1) serum cotinine, (2) plasma ACTH, (3) plasmacortisol, (4) saliva cortisol, (5) HR, (6)SBP &amp; (7)DBP</td>
<td>(8) MPSS, (9) PASAT</td>
<td>Randomised, cross-over design. Abstained from 4PM, then treatment next morning, then mental challenge in the afternoon. Assessments pre-AM, IP-AM, 30-mins post-AM, &amp; pre-PM, IP-PM, 30-mins post-PM.</td>
<td>(a) elevated (2, 3, 5 &amp; 7) at IP-AM cf (b &amp; c), (2, 3, 4) at pre-PM no sig. difference between (a) &amp; (b). (a) Showed no sig. difference for SoD, MPSS of PASAT.</td>
</tr>
<tr>
<td>Scerbo et al. 1997</td>
<td>10 m &amp; 8 f.</td>
<td>3 hrs</td>
<td>15-mins (a) running (80-85% HRR) (b) walking (45-50% HRR) (c) sitting on a chair on a treadmill</td>
<td>Cravings measures Desire to smoke (Tiffany), SoD (West) Other measures - HR, salivary cortisol</td>
<td>(a) &amp; (b) reduced SoD cf (c) (sig ES ranged from −0.4 = 1.48). No sig. difference between (a) &amp; (b) for SoD but effects lasted longer with (a). (a) Only, attenuated the decline in cortisol concentrations.</td>
<td></td>
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<tr>
<td>Faulkner et al. 1997</td>
<td>11 m &amp; 8 f.</td>
<td>Mean = 8 hrs</td>
<td>10 mins (a) self-paced brisk walking (Mean RPE = 11.89(1.79), range 6-20) (b) passively sitting on a chair beside a treadmill</td>
<td>Cravings measure - Desire to smoke (Tiffany), Other measures - Smoking topography (Puff volume, puff duration, puff count, interpuff interval, time to first puff) HR,</td>
<td>Randomised cross-over design. Desire to smoke assessed pre, mid, IP, 10-, 20- &amp; 30-mins post treatment. Smoking topography assessed 20-mins post each treatment.</td>
<td>(a) Reduced desire to smoke cf (b) mid condition (ES = .98), but not post condition. (a) Sig longer time to first puff cf (b). Trends in favour of (a) for other topography outcomes.</td>
<td></td>
</tr>
<tr>
<td>Elibero et al. 1995</td>
<td>76 m &amp; f.</td>
<td>1 hr</td>
<td>30-mins (a) walking on a treadmill (65-75% HRR) (b) Hatha yoga (asanas included bridge, forward bend, table, cow, cobra) (c) view a video about exercise</td>
<td>Cravings measure(s) - QSU-brief, a picture-based cue reactivity assessment Other measures - a brief mood form</td>
<td>Between-subject (randomly assigned), Assessment pre &amp; IP, &amp; 20-min post.</td>
<td>(a &amp; b) reduced QSU-Factor 1 cf (c). (a) Showed decreased craving toward smoking pictures but increased toward neutral pictures. (b) Showed decreased craving toward both pictures. (c) Showed increased craving toward both types of cues.</td>
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<table>
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<th>Methods</th>
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<tr>
<td>Harper, Study 1&lt;sup&gt;1&lt;/sup&gt;</td>
<td>119 f. Mean age = 41 Mean cigs = 17 per day.</td>
<td>a) 1 week, b) 7 weeks, and c) 10 weeks post quit date</td>
<td>20-mins on choice of treadmill, rowing machine, stair climber, or stationary bike. (a) moderate intensity exercise (50-60% HRR) (b) vigorous intensity exercise (&gt;70% HRR) (c) vigorous intensity exercise (&gt;70% HRR).</td>
<td>Cravings measure - Shiffman-Jarvik withdrawal scale Sub-study of exercise + NRT smoking cessation intervention trial. Assessment pre &amp; IP Significant reductions in craving were observed following exercise at time points (a), (b), &amp; (c) and psychological withdrawal and sedation at (a) &amp; (b)</td>
</tr>
<tr>
<td>Harper, Study 2&lt;sup&gt;2&lt;/sup&gt;</td>
<td>58 f. Mean age = 43 Mean cigs = 18 per day.</td>
<td>1 week post quit date</td>
<td>20-mins on choice of treadmill, rowing machine, stair climber, or stationary bike. Moderate intensity exercise (50-60% HRR) Participants categorised into High EX-EXP and Low EX-EXP, and High EX-CRED and Low EX-CRED</td>
<td>Cravings measure - Shiffman-Jarvik withdrawal scale Other measures - ECQ Sub-study of exercise + NRT smoking cessation intervention trial. ECQ: pre. Withdrawal scale: pre &amp; IP High EX-EXP &gt; reduction in craving following exercise cf Low EX-EXP. High EX-CRED &gt; reduction in craving following exercise cf Low EX-CRED.</td>
</tr>
<tr>
<td>Arbour-Nicetopoulous&lt;sup&gt;3&lt;/sup&gt;</td>
<td>14 m &amp; f Mean age = 50 Mean cigs = 10 Mean FTND = 4.71</td>
<td>Mean = 7.84 hrs</td>
<td>a)10-mins brisk walking on a treadmill b) 10-mins sitting passively on a chair beside a treadmill</td>
<td>Cravings measure – Desire to smoke (Tiffany) Other measures – PAR-Q, MPSS, Feeling scale (Hardy &amp; Rejeski, 1989), Felt arousal scale (Svebak &amp; Murgatroyd, 1985) Randomised crossover design. Pilot study among individuals with SMI participating in a smoking cessation programme. All measures pre, mid, IP, 10-, &amp; 20- mins post No significant main effects were found for time or condition for cravings. Sig time x condition interaction for affective valence: a) felt more pleasant than b). a) &gt; activation than b). No sig effects on MPSS outcomes.</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Characteristics</th>
<th>Intervention</th>
<th>Baseline</th>
<th>Outcomes</th>
</tr>
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<tbody>
<tr>
<td>Williams</td>
<td>60 f</td>
<td>Mean age = 42</td>
<td>Each contact (3 x per week) throughout an 8-week smoking cessation programme</td>
<td>a) 50-mins brisk walking on a treadmill, 3 x per week; b) 30-mins watching videos on health and lifestyle issues, 3 x per week</td>
</tr>
<tr>
<td>Janse Van Rensburg et al.</td>
<td>20 m &amp; f</td>
<td>Age = 18-50, Mean cigs = 12.3 per day</td>
<td>10-mins</td>
<td>Cravings measures - fMRI brain activation, Desire to smoke (Tiffany), SoD (West)</td>
</tr>
</tbody>
</table>

m = male; f = female; RPE: Rating of Perceived Exertion; SoD: Strength of Desire to smoke; MPSS: Mood and Physical Symptoms Scale; SEES: Subjective Exercise Experience Scale (PD: Psychological Distress, PWB: Positive Well Being); IP: Immediately Post; ES: Effect Size; HRR: Heart Rate Reserve; TWS: Tobacco Withdrawal Symptoms; 10-QSU: 10-question Questionnaire on Smoking Urges; fMRI: functional Magnetic Resonance Imaging; MAAS: Mindful Attention Awareness Scale; ACTH: Adrenocorticotropic hormone; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; SV-POMS: Shortened Version of the Profile of Mood State Questionnaire; PASAT: Paced Auditory Serial Addition Task; HR: Heart Rate; ECQ: treatment expectancy and credibility questionnaire; High EX-EXP: High exercise expectancy group; Low EX-EXP: Low exercise expectancy group; High EX-CRED: High exercise credibility group; Low EX-CRED: Low exercise credibility group; PAR-Q: Physical activity readiness questionnaire; SMI: Serious mental illness; ADACL: The Activation-Deactivation-Adjective-Checklist;
2.3.3 RISK OF BIAS IN INCLUDED STUDIES

The assessment of risk of bias was based on the guidelines in the Cochrane handbook for Systematic reviews of interventions. As a whole, the studies were of adequate quality. Aspects of study design specific to this area of research make it difficult to assess study quality in accordance with the Cochrane guidelines. For example, blinding of participants to treatment is inherently difficult when the treatment is exercise. Acute studies are also unlikely to suffer from loss to follow-up. The following is a summary of the domain-based evaluation for risk of bias.

2.3.3.1 Allocation

Adequate random sequence generation was employed in 14 studies, with the exception of the study by Scerbo et al., which assigned participants sequentially to each condition based on recruitment order. It was unclear in all studies whether allocation to treatment groups was concealed up to the point of randomisation.

2.3.3.2 Blinding

As participants are assigned to particular types/intensities of exercise and/or passive control conditions, and may be aware of the expected psychological benefits of exercise, it is not possible to blind participants to treatment. This potential source of bias could increase the magnitude of the treatment effect in favour of exercise. However, the effect of participant expectation has been examined, and is discussed with reference to two studies below.

2.3.3.3 Incomplete outcome data

As the majority of studies examined outcomes within a short time frame (i.e. during periods of temporary smoking abstinence, in one assessment before and after treatment), the studies were unlikely to suffer from biases associated with incomplete outcome data. The two studies by Harper and the study by Williams et al. were conducted within the context of an exercise programme for smoking cessation. Williams et al., accounted for loss to follow-up throughout their trial using intention-to-treat (ITT)
analyses. Harper reported participant withdrawals between each assessment stage but as the two Harper studies focused on the acute effects of exercise on cravings outcomes at each time-point, the effects of exercise could only be examined in the participants that attended each assessment.

2.3.3.4 Other potential sources of bias

All 15 studies were considered free of other potential sources of bias. Groups were comparable at baseline in all studies, and all studies were deemed to be free of selective reporting bias. Four of the 11 studies that examined cravings during temporary abstinence reported conducting a sample size calculation a priori,\textsuperscript{96, 97, 100, 102} although only two studies\textsuperscript{88, 93} were insufficiently powered to detect a difference between conditions in cravings, suggesting that the target sample sizes in the other studies were based on previous research.

2.3.3.5 Summary of study quality

According to the Cochrane Handbook guidelines, due to the lack of blinding all of the reviewed studies would be categorised as having an ‘unclear’ risk of bias. However, taking the specific aspects of the study designs employed in the reviewed studies into consideration, and the fact that blinding participants to their treatment allocation is difficult to achieve, the studies were of adequate quality.

2.3.4 EFFECTS OF EXERCISE INTERVENTIONS

The following sections describe the effects of exercise on cigarette cravings, TWS, affect, and smoking behaviour. A narrative review of these outcomes is presented first, and focuses on the 15 included trials published (or in press) after January 2007. Meta-analyses of the effects of exercise on cigarette cravings from all published studies to date are then presented. The narrative review and meta-analyses results are then discussed with respect to variables that may mediate the relationship between exercise and cigarette cravings.
2.3.5 NARRATIVE REVIEW

2.3.5.1 Effects of exercise on cigarette cravings

All of the 15 studies measured cravings to smoke. Twelve of these found exercise had a positive effect on cigarette cravings (desire to smoke, strength of desire to smoke, or anticipated pleasure from smoking), with reported immediate effects lasting up to 30 minutes post-treatment.\(^{87,94-103}\) One study showed a positive effect of exercise on cigarette cravings during treatment, but not post-treatment.\(^{97}\) Three studies failed to show an effect,\(^{88,93,104}\) although two of these showed trends in favour of exercise.\(^{93,104}\)

The measure of cigarette cravings varied between studies (See Table 2). Self-report was the predominant method used to measure cravings but other approaches included picture-based cue reactivity,\(^{95}\) attention bias (increased attention to smoking-related stimuli),\(^{98}\) and brain activation using functional MRI (fMRI).\(^{99,101}\) Significant reductions in cravings were found following exercise for all of these measures of cravings, relative to control conditions and/or relative to baseline.

Ten studies measured either desire to smoke\(^{83}\) or strength of desire to smoke (SoD)\(^{84}\) and compared exercise with a control condition. Five studies\(^{88,96,101-103}\) measured SoD on either a 6-point\(^{88}\) or a 7-point\(^{96,101-103}\) scale. Calculated Cohen’s d effect sizes\(^{105}\) revealed moderate to large effects (0.4 to 1.48) of exercise on strength of desire to smoke for four of the studies.\(^{96,101-103}\) Six studies measured desire to smoke on a 7-point scale.\(^{97-102}\) Moderate to large effects (0.65\(^{102}\) to 1.98\(^{101}\)) were also observed. The magnitude of significant post-treatment effect sizes peaked either during or soon after exercise; however, significant effect sizes were found up to 30 minutes post exercise, including 30 minutes post 15 minutes walking [effect size (ES) = 0.4 (desire to smoke) and 0.92 (SoD)\(^{102}\)] and 30 minutes post isometric exercise [ES = 0.69 (SoD)\(^{103}\)].

A number of studies compared different intensities of exercise. Two studies\(^{96,102}\) compared the effect of moderate versus vigorous intensity exercise on cravings, and showed similar effects on desire to smoke. Scerbo et al.,\(^{102}\) compared passive (sitting
on a chair placed on a treadmill), walking (considered moderate-intensity exercise in this study, 45-50% HRR), and running (80-85% HRR) conditions using a within-participant crossover design, whereas Everson et al.\textsuperscript{96} compared passive waiting with moderate (40-59% HRR) and vigorous (60-84% HRR) intensity cycling. There were no significant differences between the effects of moderate and vigorous intensity exercise on cravings in either study, although both studies found significant differences between both exercise conditions and the passive controls.

Harper\textsuperscript{87} also assessed the effects of acute bouts of both moderate and vigorous intensity exercise on cravings, but did not conduct a direct comparison between the two intensities. In a sample of female smokers participating in a 14-week exercise aided NRT programme for smoking cessation, cravings (measured with the Shiffman-Jarvik withdrawal scale\textsuperscript{85}) were assessed before and after an exercise treatment session at week 5 (1 week post quit date and on 21-mg NRT patch), week 11 (7 weeks post quit date and on 14-mg NRT patch), and week 13 (9 weeks post quit date and on 7-mg NRT patch). Participants were asked to exercise for 20 minutes at a moderate intensity (50-60% HRR) at week 5, and a vigorous intensity (>70% HRR) at weeks 11 and 13, on their choice of cardio equipment (stationary exercise bike, stair climber, rowing machine, or treadmill). Significant reductions in cravings from pre- to post-exercise were found at all three time points (i.e., week 5 $\eta^2 = .294$; week 11 $\eta^2 = .252$; and week 13 $\eta^2 = .153$). Harper concluded that in an actual quit attempt involving NRT, craving relief following an acute bout of exercise can be achieved.

Two studies examined light-intensity yoga\textsuperscript{85} and isometric exercise\textsuperscript{103} and found statistically significant reductions in cravings to smoke. Elibero et al.\textsuperscript{95} compared three conditions, 30 minutes of yoga, 30 minutes of moderate intensity [70% of maximum heart rate (HR)] walking on a treadmill, and a passive control group, and showed that both exercise groups significantly decreased urges to smoke (measured with the QSU-brief)\textsuperscript{86} compared with the control group. Relative to the control group, who had
increased cravings when presented with both smoking and neutral images, cravings were reduced in both exercise groups in response to smoking-related images, and in the yoga group in response to neutral images. Ussher et al.,\textsuperscript{103} showed a significant reduction in cravings following 10 minutes isometric exercise, which included jaw clenching, fist clenching, and pushing the palms of the hands together.

One study examined the effect of resistance-based exercise (back squat, bench press, bent-over row, arm curl, Romanian deadlift, and sit ups) and reported no significant differences in cravings to smoke, compared with a passive control group;\textsuperscript{88} although there were small-to-moderate effect sizes (0.26-0.44) post-treatment, which were perhaps due to being statistically underpowered. This is the only study to date to have examined resistance exercise in this context, and further research is required to determine the impact of resistance exercise.

Two studies sought to determine whether reductions in cravings post-exercise were related to participant’s outcome expectancy.\textsuperscript{87, 94} Daniel et al.\textsuperscript{94} manipulated participants’ expectancy of an effect of exercise by randomly assigning participants to read either a positive, negative, or neutral statement on the effects of exercise on cravings; whereas Harper\textsuperscript{87} asked participants to complete the treatment expectancy and credibility questionnaire (ECQ)\textsuperscript{106} and based on ECQ responses, categorised participants as high or low exercise expectancy, and high or low exercise credibility. Credibility items in the ECQ relate to how believable and convincing the exercise seems; whereas expectancy items relate to the participant’s belief of how the exercise will affect withdrawal. Both studies demonstrated significant differences between pre- and post-exercise craving scores. However, whereas Daniel et al.\textsuperscript{94} found no differences between groups, Harper\textsuperscript{87} showed significantly greater reductions in cravings in those categorised as high in exercise expectancy compared to those categorised low in exercise expectancy. Significantly greater reductions were also observed for those classified as high versus low credibility.
2.3.5.2 Tobacco Withdrawal symptoms

Withdrawal symptoms known to be reduced by exercise include irritability, depression, tension, restlessness, difficulty concentrating, and stress. Five studies measured TWS using the MPSS, and two used the Shiffman-Jarvik withdrawal scale. Three of the five studies that measured TWS with the MPSS found a positive effect of exercise on at least one withdrawal symptom. Of these three studies, two compared exercise with a passive control condition, and both found a significant difference between conditions in favour of exercise (isometric exercise and moderate-intensity cycling). In contrast, increased composite MPSS scores were found during bouts of vigorous intensity exercise, suggesting an adverse effect on symptoms; however, these adverse effects were not evident after exercise.

Harper showed that 20-minute bouts of moderate intensity exercise at week 5 of an exercise-aided NRT smoking cessation programme and vigorous intensity exercise at week 11 of the programme significantly reduced psychological and sedation withdrawal symptoms from pre- to post-exercise. Differences between pre- and post-exercise scores for these withdrawal symptoms at week 13 of the programme also approached statistical significance (p = 0.083).

Two studies sought to determine whether reductions in TWS post-exercise were related to participant’s outcome expectancy. Both studies demonstrated significant differences between pre- and post-exercise TWS scores; however, there were no differences between groups for outcome expectancy. It is worth noting that in the study by Harper, those in the high exercise expectancy and high exercise credibility groups experienced greater reductions in withdrawal symptoms following exercise than those in the low expectancy and credibility groups, although these were not statistically significant.

Janse Van Rensburg and Taylor assessed the effects of exercise (15-minute self-paced walk) on impaired concentration by measuring cognitive function using the
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Stroop Task. While no significant group-by-time interaction or main effect of condition for Stroop Task reaction time was found, between condition t-tests at each time point revealed significantly lower mean reaction time scores at 10 and 15 minutes post-exercise compared to those in the passive control group. This study represented a methodological improvement compared to previous self-reported measures of concentration.

2.3.5.3 Affect

Four of the five studies that examined the effect of exercise on affect found a positive effect of exercise on at least one measure of affect. Elibero et al., showed that positive affect increased and negative affect decreased immediately after both 30 minutes of yoga and 30 minutes of moderate-intensity walking, and Everson et al., found that positive well-being was increased and psychological distress was decreased 5 minutes after 10 minutes of moderate-intensity cycling. These results are consistent with findings from the previous review. However, Everson et al., also found that positive well-being decreased and psychological distress increased during the vigorous exercise condition, mimicking the trend for composite MPSS score, described above. Using the Activation-Deactivation Adjective Checklist (ADACL), Williams et al., found significant time x treatment interaction effects for energy and tiredness, such that exercise (50 minutes brisk walking) participants reported higher mean energy and lower mean tiredness compared to control participants post-treatment, compared with no differences pre-treatment. Conversely, they found no such effects for tension or calmness. Finally, Arbour-Nicitopoulos et al. found a significant time x condition interaction effect for affective valence (pleasure-displeasure) using the 1-item Feeling Scale, but no interaction effect for activation (measured using the 1-item Felt Arousal Scale).
2.3.5.4  *Smoking topography or behaviour*

Only one study examined the effect of exercise on smoking topography. Using the Clinical Research Support System (CreSS) Pocket, a computer-based hand-held unit which automatically measures smoking behaviour parameters (Plowshare Technologies®, Borgwalt KC, Inc., Virginia), Faulkner et al. measured the time to first cigarette, the number of puffs per cigarette, the volume of carbon monoxide drawn in each puff, the duration of each puff, and the inter-puff interval, following either 10 minutes of brisk walking or 10 minutes of passive sitting, in a randomised crossover trial. The time to first puff was significantly longer following the brisk walking condition than following passive sitting, and there were trends towards significant effects in favour of walking for all of the other smoking topography outcomes. These preliminary findings suggest that participating in regular light-to-moderate exercise may help lengthen the time between each cigarette, and thus decrease the number of cigarettes smoked per day, which may assist in smoking cessation. However, more research is required with larger sample sizes, greater periods of abstinence, and less active smokers, as the authors suggest.

2.3.5.5  *Peripheral markers of neurobiology*

Based on previous recommendations, two studies have examined the effect of exercise on peripheral markers of neurobiology and their mechanistic role on the exercise-craving relationship. Scerbo et al. reported that the normal cortisol decrease during abstinence from cigarettes was attenuated by a 15-minute bout of vigorous intensity running, for up to 30 minutes post-exercise, and Ho found that plasma adrenocorticotropic hormone (ACTH), serum cortisol, heart rate, and systolic blood pressure were all elevated after resistance exercise compared with both a passive condition during abstinence and an *ad libitum* smoking condition. However, neither study found a relationship between these changes in biomarkers and changes in tobacco cravings or withdrawal.
2.3.6 META-ANALYSES

All studies published to date, including those reviewed by Taylor et al., were reviewed for inclusion in a meta-analysis of the effect of exercise on cigarette cravings during temporary abstinence. Due to the heterogeneity of craving outcomes across studies, it was not possible to combine all trial data in one meta-analysis to provide overall summary statistics for cigarette cravings. However, there were sufficient similar trials to conduct meta-analyses for two outcomes: (1) desire to smoke, and (2) SoD. Authors of studies which measured these outcomes but did not report means and standard deviations (SD) were contacted and asked to provide this information. Following exhaustive attempts to contact the authors, we were unable to obtain these essential descriptive data for two studies.

No studies reported change in mean (and SD) for desire to smoke or SoD from baseline to post-treatment. These data were therefore imputed according to the methods outlined by the Cochrane Heart Group for handling continuous variables. The change in mean from baseline to post-treatment for each condition was calculated by subtracting the mean at follow-up (zero or 5 minutes post-treatment, depending on when the outcome was measured in each study) from the mean at baseline. The SD of the difference (SD difference) was calculated with the following formula:

$$\	ext{SD difference} = \text{Standard error (SE) difference} \times \sqrt{n}$$

Where, $\text{SE difference} = \sqrt{[SD_1^2/n_1 + SD_2^2/n_2 \times (1-r)]}$

Where,

- $SD_1$ The standard deviation at baseline
- $n_1$ The number at baseline
- $SD_2$ The standard deviation at follow-up
- $n_2$ The number at follow-up
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$r$ The correlation coefficient

For the correlation coefficient, in the absence of large epidemiological studies in this area, a value of 0.5 was assumed. These data are presented in Table 3.
## TABLE 3: MEAN (SD) AT BASELINE AND FOLLOW-UP, AND THE DIFFERENCE IN MEANS (SD) FROM BASELINE TO FOLLOW-UP, FOR EXERCISE AND CONTROL CONDITIONS FOR DESIRE TO SMOKE AND STRENGTH OF DESIRE TO SMOKE

<table>
<thead>
<tr>
<th></th>
<th>Exercise Baseline</th>
<th>Exercise Follow-up</th>
<th>Difference (n)</th>
<th>Control Baseline</th>
<th>Control Follow-up</th>
<th>Difference (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Desire to smoke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taylor et al. 2006</td>
<td>6.10(1.60)</td>
<td>1.20(0.40)</td>
<td>-4.90(1.17) (15)</td>
<td>6.20(1.00)</td>
<td>5.50(1.60)</td>
<td>-0.70(1.33) (15)</td>
</tr>
<tr>
<td>Janse Van Rensburg et al. 2009a</td>
<td>5.10(1.75)</td>
<td>3.15(2.20)</td>
<td>-1.95(1.99) (20)</td>
<td>5.40(1.35)</td>
<td>5.05(1.50)</td>
<td>-0.35(1.43) (20)</td>
</tr>
<tr>
<td>Janse Van Rensburg et al. 2009b</td>
<td>4.80(0.47)</td>
<td>3.10(1.52)</td>
<td>-1.70(1.13) (10)</td>
<td>4.40(0.58)</td>
<td>4.80(1.69)</td>
<td>0.40(1.26) (10)</td>
</tr>
<tr>
<td>Scerbo et al. 2010</td>
<td>5.30(1.45)</td>
<td>3.10(1.66)</td>
<td>-2.20(1.56) (18)</td>
<td>5.40(1.58)</td>
<td>5.20(1.29)</td>
<td>-0.20(1.44) (18)</td>
</tr>
<tr>
<td>Faulkner et al. 2010</td>
<td>5.42(1.43)</td>
<td>5.58(1.26)</td>
<td>0.16(1.35) (19)</td>
<td>5.47(1.31)</td>
<td>3.79(1.62)</td>
<td>-1.68(1.47) (19)</td>
</tr>
<tr>
<td>Janse Van Rensburg et al., 2012</td>
<td>5.30(1.20)</td>
<td>3.40(1.50)</td>
<td>-1.90(1.36) (20)</td>
<td>5.30(1.20)</td>
<td>5.70(0.77)</td>
<td>0.40(1.01) (20)</td>
</tr>
<tr>
<td>Arbour-Nicitopoulou et al. 2011</td>
<td>2.29(1.68)</td>
<td>1.79(1.19)</td>
<td>-0.50(1.46) (14)</td>
<td>2.36(1.15)</td>
<td>2.50(1.74)</td>
<td>0.14(1.47) (14)</td>
</tr>
<tr>
<td>Janse Van Rensburg and Taylor 2008</td>
<td>4.90(1.20)</td>
<td>4.10(1.40)</td>
<td>-0.80(1.30) (23)</td>
<td>5.00(1.20)</td>
<td>5.30(0.97)</td>
<td>0.30(1.09) (23)</td>
</tr>
<tr>
<td>Taylor and Katomeri 2007</td>
<td>5.00(1.46)</td>
<td>2.81(1.96)</td>
<td>-2.19(1.73) (31)</td>
<td>5.10(1.37)</td>
<td>5.48(1.18)</td>
<td>0.38(1.28) (29)</td>
</tr>
<tr>
<td>Ussher et al. 2001</td>
<td>6.60(0.60)</td>
<td>2.31(1.33)</td>
<td>-4.29(1.03) (42)</td>
<td>6.10(0.80)</td>
<td>6.17(0.79)</td>
<td>0.07(0.80) (18)</td>
</tr>
<tr>
<td>Janse Van Rensburg and Taylor 2008</td>
<td>4.90(1.20)</td>
<td>4.10(1.40)</td>
<td>-0.80(1.30) (23)</td>
<td>5.00(1.20)</td>
<td>5.30(0.97)</td>
<td>0.30(1.09) (23)</td>
</tr>
<tr>
<td><strong>Strength of desire to smoke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taylor et al. 2005</td>
<td>5.80(1.40)</td>
<td>1.30(0.60)</td>
<td>-4.50(1.08) (15)</td>
<td>5.60(1.30)</td>
<td>5.70(1.20)</td>
<td>0.10(1.25) (15)</td>
</tr>
<tr>
<td>Scerbo et al. 2010</td>
<td>5.40(1.29)</td>
<td>3.00(1.88)</td>
<td>-2.40(1.61) (18)</td>
<td>5.80(1.17)</td>
<td>5.20(1.31)</td>
<td>-0.60(1.24) (18)</td>
</tr>
<tr>
<td>Janse Van Rensburg et al. 2012</td>
<td>5.00(1.30)</td>
<td>3.67(1.60)</td>
<td>-1.33(1.46) (20)</td>
<td>5.12(1.46)</td>
<td>5.38(1.00)</td>
<td>0.26(1.22) (20)</td>
</tr>
<tr>
<td>Ussher et al. 2001</td>
<td>6.60(1.00)</td>
<td>2.10(1.19)</td>
<td>-4.50(1.10) (42)</td>
<td>6.20(1.40)</td>
<td>6.39(0.98)</td>
<td>0.19(1.21) (18)</td>
</tr>
<tr>
<td>Everson et al. 2006</td>
<td>5.44(1.15)</td>
<td>4.56(2.41)</td>
<td>-0.88(1.89) (18)</td>
<td>4.32(2.21)</td>
<td>4.84(1.22)</td>
<td>0.52(1.79) (19)</td>
</tr>
<tr>
<td>Taylor and Katomeri 2007</td>
<td>4.06(1.26)</td>
<td>2.87(1.77)</td>
<td>-1.19(1.54) (31)</td>
<td>4.66(1.39)</td>
<td>5.24(1.41)</td>
<td>0.58(1.40) (29)</td>
</tr>
<tr>
<td>Ussher et al. 2006</td>
<td>5.15(1.81)</td>
<td>4.40(1.60)</td>
<td>-0.75(1.71) (20)</td>
<td>4.9(1.83)</td>
<td>4.90(1.83)</td>
<td>0.00(1.83) (20)</td>
</tr>
<tr>
<td>Everson et al. 2008</td>
<td>5.20(7.20)</td>
<td>3.28(1.63)</td>
<td>-1.92(5.22) (15)</td>
<td>4.01(1.63)</td>
<td>4.52(1.63)</td>
<td>0.51(1.63) (15)</td>
</tr>
<tr>
<td>Ussher et al. 2009</td>
<td>5.50(1.45)</td>
<td>3.50(1.26)</td>
<td>-2.00(1.36) (14)</td>
<td>4.81(1.83)</td>
<td>4.88(1.71)</td>
<td>0.07(1.77) (16)</td>
</tr>
</tbody>
</table>
To incorporate within-subject design studies into a meta-analysis with parallel group trials, the mean difference of the treatments and the corresponding SE are required. Using the imputations above, the mean difference in change from baseline to follow-up between groups was calculated using the following formula:

\[ M(\text{diff}) = M_E - M_C \]

Where,

- \( M(\text{diff}) \) The mean difference between groups
- \( M_E \) Exercise group mean (baseline) - exercise group mean (follow-up)
- \( M_C \) Control group mean (baseline) - control group mean (follow-up)

For within-subject design studies, the treatment effect was defined as the mean within-subject difference between conditions in change from baseline to follow-up, assuming no carry-over effect. As the studies did not report the mean difference in change from baseline between conditions, the SE for the within-subject differences could not be extracted. Therefore, the SE for the within-subject trials was imputed according to the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions, which state that when the SD of the difference between groups is not reported, the SE for the within-person differences (SE [MD]) can be imputed using the following formula:

\[ \text{SE [MD]} = \frac{SD_{\text{diff}}}{\sqrt{n}} \]

Where, \( SD_{\text{diff}} = \sqrt{SD_E^2 + SD_C^2 - (2 \times r \times SD_E \times SD_C)} \)

Where,

- \( SD_{\text{diff}} \) The standard deviation of the within-person differences between conditions
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$SD_E$  The standard deviation of the difference between baseline and follow-up in the experimental (exercise) group

$SD_C$  The standard deviation of the differences between baseline and follow-up in the control group

$r$  The correlation coefficient

The correlation between treatment outcomes was approximated using a conservative estimate of the correlation coefficient ($r = 0.62$) based on the difference between treatment group means, $p$ values, and $t$ statistics, at 0 or 5 minutes post-treatment, from trials included in the meta-analyses that reported this information. Several different correlation coefficients were imputed as part of sensitivity analyses. The corresponding SE was then calculated, as described in the *Cochrane Handbook for Systematic Reviews of Interventions*. The generic inverse variance method, with a random effects model applied, was used to combine both between- and within-subject design studies in the meta-analyses. Data synthesis and statistical analyses were conducted using the Cochrane Collaboration Review Manager (RevMan, version 5.1; The Cochrane Collaboration, Copenhagen, Denmark). When multiple comparisons were conducted within one study, the moderate-intensity condition was included in the meta-analyses, as moderate-intensity exercise was the predominant exercise intensity examined by the other included studies.

A total of 10 trials compared the difference between exercise and a passive control condition for desire to smoke. The weighted mean difference in self-reported desire to smoke between exercise and control conditions was -1.90 points on a 7-point scale in favour of exercise (95% confidence interval (CI), -3.06, -0.75; $p = 0.001$; Figure 1). A random effects model was used as significant heterogeneity was indicated ($I^2=98\%$, $p <0.00001$). Sensitivity analyses revealed that, based on
effect size, five studies were responsible for the heterogeneity.\textsuperscript{66, 78, 93, 97, 100} When excluding all five studies from the analysis, the $I^2$ statistic was reduced from 98% to 5% ($p = 0.38$). The pooled reduction in desire to smoke changed only slightly with the five studies excluded (-2.13, 95% CI -2.41, -1.84; $p < 0.00001$).

A total of nine trials ($n=295$)\textsuperscript{66, 76, 77, 80, 96, 101-103, 116} compared the difference between exercise and a passive control condition for SoD. The weighted mean difference in self-reported SoD between exercise and control conditions was -2.41 points on a 7-point scale in favour of exercise (95% CI, -3.45, -1.37; $p < 0.00001$; Figure 2). A random effects model was used as significant heterogeneity was indicated ($I^2=94\%$, $p < 0.00001$). Sensitivity analyses revealed that, based on effect size, two studies were responsible for the heterogeneity,\textsuperscript{66, 77} both of which reported large reductions in SoD. When excluding these two studies from the analysis, the $I^2$ statistic was reduced from 94% to 0% ($p = 0.63$). The pooled change in SoD with the two studies excluded was reduced to -1.74 (95% CI, -2.05, -1.44; $p < 0.00001$). One study,\textsuperscript{88} which measured SoD, was not included as a 6-point scale was used.
### FIGURE 1: META-ANALYSIS OF TRIALS COMPARING EXERCISE AND CONTROL CONDITIONS WITH CHANGE IN DESIRE TO SMOKE FROM BASELINE TO BETWEEN 0 AND 5 MINUTES POST TREATMENT AS THE OUTCOME MEASURED
### Figure 2: Meta-analysis of Trials Comparing Exercise and Control Condition with Strength of Desire to Smoke as the Outcome Measured Between 0 and 5 Minutes Post-Treatment

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Weight</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everson 2003 (a)</td>
<td>-2.43</td>
<td>1.41</td>
<td>19.7%</td>
<td>-2.43 [-6.30, 0.34]</td>
<td></td>
</tr>
<tr>
<td>Everson, 2006</td>
<td>-1.4</td>
<td>0.60</td>
<td>26.1%</td>
<td>-1.40 [-2.59, -0.21]</td>
<td></td>
</tr>
<tr>
<td>Janse Van Rensburg (2012)</td>
<td>-1.88</td>
<td>0.26</td>
<td>12.2%</td>
<td>-1.88 [-2.40, -1.36]</td>
<td></td>
</tr>
<tr>
<td>Escobo 2010 (a)</td>
<td>-1.6</td>
<td>0.30</td>
<td>12.1%</td>
<td>-1.60 [-2.30, -1.21]</td>
<td></td>
</tr>
<tr>
<td>Taylor 2005</td>
<td>-4.6</td>
<td>0.26</td>
<td>12.2%</td>
<td>-4.60 [-5.12, -4.08]</td>
<td></td>
</tr>
<tr>
<td>Taylor 2007</td>
<td>-1.77</td>
<td>0.37</td>
<td>11.9%</td>
<td>-1.77 [-2.51, -1.03]</td>
<td></td>
</tr>
<tr>
<td>Ussher 2001</td>
<td>-4.69</td>
<td>0.33</td>
<td>12.0%</td>
<td>-4.69 [-5.34, -4.04]</td>
<td></td>
</tr>
<tr>
<td>Ussher 2006</td>
<td>-0.75</td>
<td>0.55</td>
<td>11.1%</td>
<td>-0.75 [-1.65, 0.30]</td>
<td></td>
</tr>
<tr>
<td>Ussher 2009</td>
<td>-2.07</td>
<td>0.57</td>
<td>11.0%</td>
<td>-2.07 [-3.19, -0.95]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td>100.0%</td>
<td>-2.41</td>
<td>-2.41 [-3.45, -1.37]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 2.23; Ch² = 129.32, df = 6 (P < 0.00001), I² = 94%
Test for overall effect: Z = 4.54 (P < 0.00001)
2.4 DISCUSSION

The overall goal of this chapter was to update the evidence regarding the acute effects of exercise on TWS, cravings, and affect during temporary smoking abstinence, and to examine potential mediators of the exercise-TWS relationship. The evidence to date suggests that brief bouts of exercise decrease cravings for cigarettes at rates comparable to NRT. The duration of the effect of exercise on cravings ranged from 5 to 30 minutes post-exercise. This was the case for both moderate- and vigorous-intensity exercise, and very-light-intensity exercise.

However, the duration of the effect post-exercise needs further investigation, particularly in real-life situations. To date, only one study has examined bouts of exercise performed in the participants’ usual environment, rather than a controlled laboratory setting. In this study, duration of effect post-isometric exercise decreased from 30 minutes when performed in the laboratory to 5 minutes in the participants’ usual environment. Future studies should be conducted in more ecologically valid settings.

The magnitude of the effects of exercise on cravings is encouraging. The meta-analyses suggest that exercise is more effective than passive control conditions at reducing both desire to smoke and SoD, with weighted mean differences between exercise and control groups on a 7-point scale of -1.90 and -2.41, respectively.

Only two of nine studies that measured SoD on a 7-point scale failed to show a statistically significant difference between exercise and passive control conditions at 0 or 5 minutes post-condition. Ussher et al., however, did show a significantly greater reduction in the exercise group than the control group relative to baseline at these time points. The second study was conducted with a sample of 16-19-year-old adolescents, and the authors surmised that 10 minutes of moderate-intensity
exercise, previously found to be effective in adult populations,\textsuperscript{66, 72} may not be sufficient to produce reductions in cigarette cravings in younger smokers.

The meta-analyses findings are comparable to another recently published review,\textsuperscript{69} which also found statistically significant reductions in cravings following physical activity compared with passive control. The authors of the review used individual participant data (IPD) in their meta-analyses of “desire to smoke” and “strength of desire to smoke,” and outline a number of advantages of using an IPD meta-analysis approach over more traditional approaches, such as the approach used in this review. Their meta-analyses also included seven studies that were not included in our review.\textsuperscript{72, 74, 117-120} Three of these were conference abstracts,\textsuperscript{75, 118, 119} and one was a Masters dissertation,\textsuperscript{117} which were not detected during our search, one study has not been published yet,\textsuperscript{120} and we were unable to obtain the data required from the authors of the other two studies.\textsuperscript{72, 74} Nevertheless, despite these methodological differences, our findings are similar to the review by Haasova et al.,\textsuperscript{69} suggesting that the effects of acute exercise on cigarette cravings are robust.

Thus far, research has shown that light-, moderate-, and vigorous-intensity exercise all have a positive effect on cravings, although the duration and magnitude of these effects have been shown to vary across studies. Despite this, there has been increased interest in the potential role of light-intensity activities as a means to reduce cravings. The rationale is that if light-intensity activities are equally as effective at reducing cravings as higher intensity exercise, these activities may be more tolerable and sustainable for smokers. Moreover, light-intensity exercise-based smoking cessation programmes may result in greater uptake and adherence than moderate- or vigorous-intensity exercise programmes, particularly if they can be incorporated into the daily routine and performed in the workplace like those examined by Ussher et al.\textsuperscript{103} Various light-intensity exercise modalities have been examined including yoga\textsuperscript{95} and isometric exercise,\textsuperscript{103} both of which had positive
effects on cravings post-exercise. In addition, there has been increased focus on walking as a moderate-intensity activity. Although the magnitude of the effects reported suggests that moderate and vigorous exercise have much greater effects on tobacco cravings than light exercise, the duration of the effect is also important. It is noteworthy that all the significant differences in cravings between exercise and control conditions at 30 minutes post-treatment were for light- to moderate-intensity exercises (walking\textsuperscript{102} and isometric exercise\textsuperscript{103}). In summary, exercise is effective for reducing cigarette cravings, but given that the various intensities of exercise appear to influence the magnitude and duration of effects in different ways, the most meaningful and sustainable exercise approach for increasing quit rates remains unclear.

Increased consistency in measurement tools used would strengthen the body of research and improve comparability between studies. Many studies\textsuperscript{76 78 80 88 93 96 98-103} have used one or both of the Tiffany (‘I have a desire for a cigarette right now’ - predominantly rated on a 7-point scale from 1-strongly disagree to 7-strongly agree, and West questions (‘the strength of my desire to smoke right now is...’) predominantly rated on a 7-point scale from 1- very weak to 7- very strong,\textsuperscript{84} However, there were variations between studies in the number of points on the scale, and the anchors used for these items, with some studies employing 6-point scales and/or altering the scale response anchors to ‘1-not at all to 7-extremely’.

There were also differences between studies in the measurement of prescribed exercise intensity. While some studies\textsuperscript{87 94-96 102 103} reported percentage of HRR, others\textsuperscript{99 97-101} reported ratings of perceived exertion (RPE) while also reporting mean heart rate. These differences in approaches again make it difficult for comparison between studies.
2.4.1 POSSIBLE MECHANISMS

In their review, Taylor et al.,\textsuperscript{64} discussed potential mechanisms that may explain why exercise alleviates tobacco cravings. Proposed mechanisms included affect hypotheses such as stress reduction and activation, biological hypotheses such as β-endorphins, cortisol, or opioids, and cognitive hypotheses such as distraction. Since the Taylor et al. review, seven studies have explored potential mechanisms underlying the exercise-craving relationship. This section will discuss progress made and highlight opportunities for future research.

2.4.1.1 Affect hypotheses

Research has shown that exercise has a positive effect on affect,\textsuperscript{121} and it is possible that an increase in positive affect could result in decreased desire to smoke. Negative affect has been shown to be associated with increased withdrawal symptoms, desire to smoke, and relapse.\textsuperscript{122, 123} Two other studies found that when positive affect was higher, cravings were lower,\textsuperscript{95, 96} and of these, one tested changes in mood as a potential mediator but showed no effect on the exercise-craving relationship.\textsuperscript{95} Two other studies found positive effects of exercise on certain dimensions of affect immediately post-exercise, but found no effect of exercise on cravings.\textsuperscript{93, 104}

It is worth noting that exercise intensity has a differential effect on mood in abstaining smokers. For example, while Everson et al.\textsuperscript{96} showed similar effects for both moderate- and vigorous-intensity exercise on cravings, participants reported adverse effects on mood and happiness during the vigorous intensity exercise. Mood and happiness variables returned to baseline values once the exercise stopped, but this does raise the question that if moderate and vigorous exercise intensities have similar effects on cravings, then to avoid adverse effects on mood, perhaps moderate-intensity exercise, rather than vigorous-intensity exercise, should be prescribed.
In contrast to these findings, Bock et al.\textsuperscript{73} and Harper\textsuperscript{87} showed that a bout of vigorous exercise reduced negative affect and psychological withdrawal symptoms, respectively, in smokers undertaking an exercise-aided quit smoking programme. To explain the difference between these studies, Everson et al.\textsuperscript{96} proposed that the difference in affective response between the two studies may reflect the difference between temporary abstainers and those undertaking a quit attempt. Participants in their study were abstaining for a relatively short duration for research purposes only and were not motivated by an attempt to quit smoking. Therefore, they potentially showed less tolerance towards the adverse effects of vigorous-intensity exercise, than quitting smokers. Everson et al.\textsuperscript{96} suggested that there is potential to reframe the way smokers approach a bout of vigorous exercise, such that they focus on the benefit of reduced cravings after exercise, rather than their mood during exercise. This potentially exposes the pitfalls of these acute studies, whereby the effects do not necessarily translate to the real world situation, which smokers attempting to quit experience.

The primary focus of future research involving a measure of affect should be to examine the mediating effect of mood on the exercise-craving relationship. As Elibero et al.,\textsuperscript{95} did not find such a mediating effect, it would appear that the relationship between mood and cravings in the context of exercise may be more complex, with other unidentified factors involved.

2.4.1.2 Biological hypotheses

There are a number of biological changes that occur whilst smoking and when trying to quit. In their review, Taylor et al.,\textsuperscript{64} hypothesised psychobiological changes may mediate the changes in withdrawal symptoms associated with exercise. They suggested that more studies were needed to investigate changes in β-endorphins, opioids and cortisol; however, only a few subsequent studies have examined these proposed peripheral markers of neurobiology.
Recent work by Janse Van Rensberg and colleagues\textsuperscript{99, 101} has shed some light on some neurobiological processes. Two studies were conducted to measure activation in specific areas of the brain using fMRI after 10 minutes of moderate-intensity exercise on a cycle ergometer versus a passive control, following 15 hours’ smoking abstinence.\textsuperscript{99, 101} fMRI scans were conducted while participants were presented with a series of smoking-related images and neutral images. Subjective measures of cravings were also taken. Janse Van Rensberg et al.\textsuperscript{99, 101} showed that reductions in cravings post-exercise may be a result of the increased strain of exercise on the brain’s information-processing capacity, reducing activation in areas of the brain associated with reward processing and visuospatial attention, and concomitantly increasing activation in the medial rostral prefrontal cortex, an area of the brain associated with the ‘brain default mode’. This supports the hypothesis that exercise acts as a thought suppressant, shifting attention from cognitive to somatic thoughts.\textsuperscript{124}

Two studies\textsuperscript{88, 102} have showed that cortisol levels were higher post-exercise, but that differences in cortisol concentrations were not associated with changes in desire to smoke in either study. Design features in both studies suggest further examination of cortisol as a mechanism. First, Scerbo et al.\textsuperscript{102} used a shorter duration of smoking abstinence (3 hours prior to assessment) compared to most previous studies, which used 12-15 hours of overnight abstinence. The short abstinence period may have been insufficient to increase cigarette cravings, thereby attenuating the mechanistic effect of salivary cortisol. The second study,\textsuperscript{88} failed to find a significant effect of exercise on smoking withdrawal symptoms and urges to smoke, most likely due to the small sample and lack of statistical power, and mediation could not be tested.

To date, no other biological mediators of the exercise-craving relationship have been examined during temporary smoking abstinence. As Taylor et al.\textsuperscript{64} proposed, future research might consider the role of β-endorphins, opioids, and appetite suppression
on the relationship between cigarette cravings and exercise. Following this review it is also proposed that the role of catecholamines, heart rate variability (HRV), and rate of nicotine metabolism should also be examined. With respect to catecholamines, levels of adrenaline and noradrenaline have been shown to increase with smoking,\textsuperscript{125} and stopping smoking results in a decrease of both.\textsuperscript{126} During single bouts of exercise, the concentration of adrenaline and noradrenaline increases in proportion to the intensity and duration of exercise.\textsuperscript{127} This increase in adrenaline and noradrenaline post-exercise may explain the effect of exercise on cigarette cravings.

HRV is another potential mechanism which may explain the relationship between exercise and cigarette cravings. HRV refers to the variation in the interval between adjacent QRS complexes (the R to R [RR] interval),\textsuperscript{128} and it is a simple non-invasive method to evaluate the balance between parasympathetic and sympathetic effects at the sinoatrial level.\textsuperscript{128} The rate of firing at the sinus node is influenced by both parasympathetic (vagal) and sympathetic effects. Vagal tone is high at rest, but under conditions of stress, such as exercise or a cognitive task, sympathetic tone increases.\textsuperscript{129} Indices of HRV have been used to describe this sympathovagal balance. HRV is highest under vagal conditions, and is reduced during times of stress. Studies have shown that the prolonged stress of smoking over time causes reductions in HRV.\textsuperscript{130} 131 Four to six weeks after stopping smoking, HRV has been shown to increase again.\textsuperscript{132} More research is required to examine (a) whether short-term smoking abstinence has any immediate effect on HRV, (b) whether an acute bout of exercise has any immediate effect on HRV, (c) whether this effect mediates the relationship between TWS and exercise, and (d) whether exercise can increase the rate at which HRV increases post-cessation.

Finally, there is a dearth of research examining the effect of nicotine dependence on cravings and TWS. For instance, nicotine is metabolised to cotinine, and cotinine is metabolised to 3-hydroxycotinine by the liver enzyme cytochrome P450 2A6. The
rate of nicotine metabolism has been found to predict smoking behaviour. Future research is needed to examine whether the nicotine metabolite ratio influences cravings and TWS after an acute bout of exercise during a temporary or actual quit attempt.

2.4.1.3 Cognitive hypotheses

It was initially hypothesised that exercise may influence cognitive demand in such a manner that it acts as a distraction from smoking-related thoughts. However, two studies identified in the previous review found no effect of distraction on cigarette cravings, and it was therefore surmised the effects of exercise on cravings and withdrawal symptoms were not due to distraction. Since then, two studies have examined the effect of exercise expectation on TWS and cravings. Daniel et al., examined the effect of expectation by manipulating beliefs regarding the effect of exercise on TWS and cravings and found that, in comparison with baseline, significant reductions in TWS and cravings were observed, regardless of whether participants’ prior expectation of an effect was manipulated as positive, negative, or neutral. In accordance with Daniel et al., Harper also found no effect of expectation on TWS, but they did show that those classified as high in exercise expectancy or exercise credibility had significantly greater reductions in cravings post exercise relative to those classified as low in exercise expectancy or credibility.

Harper offers a number of explanations to explain this difference. First, the participants in the Daniel et al., study were only required to temporarily abstain from smoking, whereas Harper examined the effects of a single bout of exercise on cravings one week into a quit attempt. Participants undergoing a quit attempt are more invested in the outcome than those temporarily abstaining from smoking, and there is evidence to suggest that the more invested in the treatment outcome a person is, the greater the influence of credibility and expectancy on treatment effects. Second, outcome expectancy was manipulated by Daniel and colleagues...
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as positive, negative, or neutral, whereas Harper categorised participants based on their responses to the ECQ.\textsuperscript{106} Harper surmised that in order to experience an added reduction in craving, one has to naturally believe that exercise could result in such an effect, as opposed to being manipulated to believe in such an effect. Third, the duration of moderate intensity exercise was 20 minutes in the Harper study, rather than the 10 minute duration used by Daniel et al. Harper suggested that perhaps duration of exercise and exercise expectancy interact in such a way as to influence the effect of expectancy on cravings following exercise. Finally, it is important to note that although a difference between high exercise expectancy and low exercise expectancy groups in cravings post-exercise was observed in the Harper study, both groups reduced their cravings post exercise, and it is unclear whether the additional reduction in cravings in the high expectancy group is of clinical significance. However, given that the experience of cravings can have such a disruptive effect during a quit attempt, perhaps even a small additional reduction is clinically significant. Taken together, the findings from these studies suggest that expectancy and credibility do not play a major role, but these variables cannot be completely discounted, and more research into the effects of expectancy and credibility is warranted.

2.4.1.4 Other hypotheses

Contrary to the common belief that energy expended in exercise is automatically compensated for by subsequent energy intake, evidence suggests that bouts of vigorous exercise may suppress appetite.\textsuperscript{136} Hunger levels and subsequent food intake do not immediately rise after exercise, and there is only partial compensation for the energy expended.\textsuperscript{137} Nicotine acutely increases metabolic rate,\textsuperscript{138} and smoking cessation is commonly associated with increased caloric intake.\textsuperscript{139} An average weight gain of 4.5kg is often seen 6-12 months after quitting smoking.\textsuperscript{140-142} Taylor et al.\textsuperscript{64} also proposed that given that vigorous exercise, at least in the short
term, can suppress appetite, it is plausible that exercise could counter the decreased metabolic rate associated with smoking cessation, and ultimately attenuate weight gain. Considering that weight gain is a common predictor of relapse in quitting smokers, if exercise can suppress appetite in abstaining smokers, those attempting to quit may be less likely to gain weight, and consequently less likely to relapse. To date, no research has been conducted to examine this relationship, but given the potential impact on relapse, examination of appetite suppression as an exercise mechanism during smoking abstinence is warranted.

Plasma glucose concentrations increase briefly following exercise before decreasing slowly. Glucose has been shown to reduce urges to smoke, and increases short-term quit rates. Exercise associated increases in glucose may mediate the exercise-craving relationship. Alternatively, exercise-associated increases in catecholamines and cortisol may also mediate the effect of exercise on cravings, either by their relationship with glucose or via suppression of appetite.

2.4.2 SUMMARY

Overall, the 15 trials included in this review were of adequate methodological quality. Meta-analyses of all published studies showed that exercise is more effective than passive control conditions for reducing cravings for a cigarette during temporary smoking abstinence. However, given the multitude of measures used to assess other outcomes, similar conclusions cannot be drawn. Nevertheless, compared with passive control conditions, light-to-moderate exercise appears to have a positive effect on TWS, affect, and smoking behaviour outcomes.

In contrast, TWS and negative affect have been shown to increase during and after vigorous exercise, suggesting that vigorous exercise may be too intense for previously sedentary smokers. The most effective exercise intensity to reduce cravings remains unclear. Vigorous exercise appears to have the effect of greatest
magnitude, but reductions in cravings appear to last longer following light intensity exercise. More research is required to compare the different exercise intensities. Moreover, although much of the recent research in this area has studied different potential mechanisms, greater clarity of the effect of potential mechanisms on the exercise-cigarette cravings relationship is still needed.

2.5 CONCLUSION

The findings of this systematic review indicate that:

- Exercise is more effective than passive control conditions for reducing cravings for a cigarette during temporary smoking abstinence
- Light and moderate exercise appear to have a positive effect on tobacco withdrawal symptoms, affect, and smoking behaviour outcomes
- There are only small differences in the magnitude of cravings and TWS between light, moderate and vigorous exercise
- TWS and negative affect have been shown to increase during and after vigorous exercise, suggesting that vigorous exercise may be too intense for sedentary smokers
- The most effective intensity of exercise to reduce cravings, and the mechanisms associated with the effect of exercise, remain unclear
- Further research is required to a) examine potential mechanisms underlying the relationship between exercise and cravings, and b) establish the intensity and modality of exercise that provides the greatest magnitude and duration of reductions in cravings, but is also appropriate for mostly sedentary smokers trying to quit
This review advances knowledge on the role of exercise as a smoking cessation aid. The meta-analyses revealed that exercise has an acute effect on cigarette cravings, and the research on potential mechanisms suggests that whilst distraction may not play a major role, the argument for common effects of exercise and nicotine on neurobiological processes has merit. Much more research is needed to explore the acute effects of exercise on neurobiological processes among abstaining smokers to determine how exercise reduces cigarette cravings. This review also introduced HRV as a potential mechanism underlying the exercise-cravings, and research is needed to determine the effects of exercise on the autonomic nervous system in abstaining smokers. Finally, this review also highlights a dearth of research examining the effects of acute exercise on cigarette cravings in a real-world setting. More research is needed to determine whether the acute effect of exercise on cigarette cravings observed in the laboratory is a) translatable to the normal environment, and b) actually useful to aid a quit attempt.
CHAPTER 3  EFFECTS OF EXERCISE ON TOBACCO WITHDRAWAL SYMPTOMS AND PERIPHERAL MARKERS OF NEUROBIOLOGY DURING TEMPORARY SMOKING ABSTINENCE: A CROSSOVER TRIAL

3.1  INTRODUCTION

The systematic review in Chapter 2 highlighted that more research is required to determine the most effective intensity of exercise to reduce cravings and TWS, as well as the mechanisms underlying this relationship. The present study was designed to address these research gaps. Specifically, this study examined the effect of three different intensities of exercise (light, moderate, and vigorous) on cigarette cravings, TWS, affect and food cravings. Various peripheral markers of neurobiology proposed to mediate the exercise-cravings relationship (cortisol, adrenaline, noradrenaline, insulin, glucose) were also examined in a sub-sample of participants.

3.1.1  OBJECTIVES:

1. To examine the effects of brief bouts of light-, moderate-, and vigorous-intensity exercise on TWS, cravings and affect after overnight tobacco smoking abstinence.

2. To investigate the effect of brief bouts of light-, moderate- and vigorous-intensity exercise on food cravings after overnight tobacco smoking abstinence.

3. To determine the effect of brief bouts of light-, moderate-, and vigorous-intensity exercise on HRV.

4. To investigate the effect of brief bouts of light-, moderate-, and vigorous-intensity exercise on catecholamines (adrenaline and noradrenaline), cortisol, glucose, and insulin.
5. To determine the relationships between changes in catecholamines, cortisol, glucose, and insulin levels, with TWS, cravings and affect.

6. To determine the potential mediating effects of peripheral markers of neurobiology on the exercise-cravings relationship.

3.1.2 HYPOTHESES:

1. A brief bout of moderate-intensity exercise will significantly reduce TWS and cigarette cravings after exercise following overnight tobacco smoking abstinence, compared to a bout of light exercise.

2. A brief bout of vigorous-intensity exercise will significantly reduce TWS and cigarette cravings after exercise compared to a bout of light exercise.

3. A brief bout of moderate-intensity exercise will produce a similar reduction in TWS and cigarette cravings to a bout of vigorous-intensity exercise.

4. There will be a significant difference in HRV measures between conditions, with the greatest reductions in HRV observed during vigorous exercise.

5. There will be a reduction in food cravings following the bout of vigorous exercise, relative to moderate- and light-intensity exercise conditions.

6. There will be significant differences in plasma cortisol, salivary cortisol, adrenaline, noradrenaline, and glucose levels between conditions, with the greatest increases observed following the vigorous-intensity condition.

7. Changes in cortisol, adrenaline, noradrenaline, glucose, and insulin levels, and HRV will mediate the relationship between exercise and cravings.
3.2 METHOD

3.2.1 DESIGN AND PROCEDURE

3.2.1.1 Ethical approval

The study received ethical approval from the Northern Y Ethics Committee (NTY/10/10/079). Participation in the study was voluntary.

3.2.1.2 Participant recruitment

Participants were recruited via local media (print and radio), flyers posted at local community centres in Glen Innes, Auckland (medical centre, Marae, community centre, supermarket notice boards, advertising via social media [Facebook], and through www.getparticipants.com, a NZ website designed to help researchers recruit study participants). Interested participants were invited to contact the candidate at the National Institute for Health Innovation (NIHI).

3.2.1.3 Eligibility criteria

Participants were screened for eligibility over the telephone. Inclusion criteria were as follows: aged 18-70 years, currently smoke at least 10 cigarettes per day, currently smoke their first cigarette within 30 minutes of waking in the morning, self-reported capability to perform a 15-minute bout of vigorous exercise on a cycle ergometer, able to attend the study site for the duration of the study, willing to abstain from smoking and fast from all food and liquids (except water) overnight prior to three treatment sessions, and self-reported well health. Participants were excluded if they had experienced a stroke, heart attack or angina pectoris in the previous six months, had diabetes mellitus, a chemical dependence other than nicotine, a poorly controlled psychiatric disorder, hypertension (systolic blood pressure >150 mmHg and/or diastolic blood pressure >100 mmHg), history of severe depression, were pregnant or breast feeding, were currently using smoking cessation medications or wanted to stop smoking during the study period.
Chapter 3: Crossover Trial

Following telephone screening, all suitable participants were sent the study Participant Information Sheet (Appendix 2) and study Consent Form (Appendix 3) via post or email (according to their preference). Those interested in taking part in the biological sample collection component of the study (hereafter referred to as the peripheral markers sub-study) were sent a different Participant Information Sheet (Appendix 4) and Consent Form (Appendix 5). Participants were invited to attend a face-to-face screening session within one week of the telephone screening, during which they returned signed informed consent forms and completed demographic questions and measures of smoking and exercise history. Expired carbon monoxide, height and weight, blood pressure, and resting heart rate were then measured. Participants were then asked to complete a submaximal test on a stationary cycle ergometer to assess their physical fitness.

During each treatment session (described below), participants exercised at either light-, moderate-, or vigorous-exercise intensity. An incremental fitness testing protocol was used during the face-to-face screening session to determine the workload required to ensure participants exercised at the correct intensity during each treatment session. Participants exercised for a total of 16 minutes on a Monark stationary cycle ergometer (Monark 874E, Monark Sports and Medical, Sweden) whilst wearing a Polar Heart Rate Monitor (RS800CX, Polar Electro Inc. New York, USA). The test consisted of 4 x 4 minute stages, each involving an incremental increase in workload, which was determined by the amount of weight hanging on a basket connected to the Monark fly wheel. Testing started with the weight of the basket alone (1kg), with additional weights added at the end of each 4-minute stage. A subjective assessment of the participants current self-reported exercise regimen, health, age, body type and size, and their self-reported experience with cycling, determined the subsequent weight added at each stage, which was 0.3kg on
average. Participants were asked to maintain a cadence of 60 revolutions per minute throughout the test.

Following the face-to-face screening assessment, participant’s heart rate data were uploaded to a laptop computer and analysed using Polar ProTrainer 5™ software (Version 5.40.171). Mean heart rates were calculated for the last minute of rest (resting heart rate), and the last minute of each of the four stages of the fitness test. Heart rate values and the corresponding weight (g) for each stage were imported into a Microsoft Excel spreadsheet for analysis. Participant’s age was used to determine age predicted maximum heart rate (calculated as 220 – age). The slope and intercept of the resulting graph were used to calculate the workload and heart rate range required for the participant to exercise at the different intensities in the three treatment sessions. An example outlining this process is provided in Appendix 6.

### 3.2.1.4 Treatment sessions

Participants attended three assessments on three separate study days. For each assessment participants were asked not to smoke, eat or drink (except water) overnight for the 12 hours preceding assessment. Participants were asked to abstain from food to increase the salience of food cravings, while overnight abstinence ensured participants would experience tobacco withdrawal symptoms and cravings. On arrival, smoking abstinence was confirmed using expired carbon monoxide. A reading of <10ppm was required prior to any assessments. All assessment were conducted in a temperature controlled room at the University of Auckland’s Department of Sport and Exercise Science laboratory, which was equipped with the Monark cycle ergometer, a table and 2-3 chairs. To increase the ecological validity of the study, participants were provided with various forms of sensory stimuli (photos of people smoking, and food on the table) to increase urges to smoke as well as cravings for food. The presence of smoking related cues to elicit cravings has been widely used in experimental studies, and researchers have demonstrated
Chapter 3: Crossover Trial

reduction in cue-elicited cravings following exercise. In their review of studies examining the acute effects of exercise on cravings, Taylor et al., proposed that further research is needed to explore the effects of exercise in the presence of smoking related cues such as photographs of smoking images.

In total, participants completed three bouts of exercise, each of 15 minutes duration and at a different intensity: light 10%-20% heart rate reserve (HRR), moderate 40%-59% HRR, and vigorous 70%-85% HRR. HRR is the difference between maximal and resting heart rate (HR). HR was monitored throughout the session to ensure participants were exercising at the appropriate intensity. The order of the exercise intensity was allocated at random using an allocation sequence, which was computer generated by a senior biostatistician using a block randomisation approach with blocks size of six. A separate allocation sequence was produced for the sub-sample of participants who participated in the peripheral markers sub-study. Order sequences for each registration number were sealed in opaque envelopes by the biostatistician and given to the candidate to ensure allocation concealment. The order in which participants performed the differing intensities was randomly assigned using a 2x3x3 Latin-square method. Treatment orders therefore were:

- Light, Moderate, Vigorous
- Light, Vigorous, Moderate
- Moderate, Light, Vigorous
- Moderate, Vigorous, Light
- Vigorous, Light, Moderate
- Vigorous, Moderate, Light
An important consideration when designing this study was to balance the required number of treatment conditions against participant burden; therefore, a decision was made to exclude a passive control (no exercise) condition to reduce burden. Further justification for this decision was that previous studies have compared moderate- and vigorous-exercise intensities with no exercise and the favourable effect of exercise relative to passive control has been well established. Light-intensity exercise (10-20% HRR) was used as a pseudo control condition to keep all other variables constant but minimise physiological change. Previous researchers have argued both for and against the need for a pseudo control condition as opposed to a passive control condition. The use of a light-intensity pseudo control negates the argument that any effect found for moderate- or vigorous-intensity exercise was due to distraction. Although previous research has largely discounted the distraction hypothesis, the recent research by Harper on exercise credibility and expectancy which showed that those with high exercise expectancy and credibility had greater reductions in cravings, suggests that involvement of a cognitive mechanism cannot be completely discounted. Moreover, previous research has shown no effect between light intensity cardiovascular exercise and passive conditions.

3.2.1.5  Face-to-face screening appointment measures

Demographics, smoking history, and exercise history. Participants completed demographic information (age, sex, ethnicity, level of education, employment status, marital status, and income level), questions on smoking history (FTND\textsuperscript{146} cigarette consumption, previous quit attempts, age of smoking onset, and number of years they have smoked), and exercise history (Leisure Score Index) (Appendix 7).

The FTND\textsuperscript{146} was administered to measure perceived dependence on nicotine, and consists of 6 items, with a total score of 10 points. Scores are interpreted as follows: a score of 0 to 2 indicates very low addiction, a score of 3 to 4 low addiction, a score of 5 medium addiction, a score of 6 to 7 high addiction, and a score of 8 to 10 is
related to very high addiction. The FTND has shown high internal consistency and adequate retest reliability.\textsuperscript{147}

\textit{The Leisure Score Index} (LSI) of the Godin and Shephard Leisure Time Exercise Questionnaire\textsuperscript{148} is a 3-item questionnaire, which asks participants to indicate the frequency in which they participate in light, moderate, and vigorous activity for more than 15 minutes during leisure time in a 7-day period (e.g. “During a typical 7-day period [a week], how many times on the average do you do vigorous exercise for more than 15 minutes during your free time?”). This measure has been shown to have high retest reliability ($r = 0.81$)\textsuperscript{149} and moderate validity with $\text{VO}_2\text{max}$ ($r = 0.56$).\textsuperscript{150} Descriptions for the exercise intensities were provided. For example, vigorous intensity exercise was described as any exercise where the heart beats rapidly (e.g. running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance cycling). An overall LSI score is produced by multiplying the total vigorous activity bouts by nine, the moderate bouts by five, and the light intensity bouts by three, and then summing the products.

\textit{Blood pressure} was measured using an Omron T9p automated blood pressure monitor (Omron\textsuperscript{®} Healthcare, Kyoto, Japan). This device was calibrated prior to use. Participants were excluded from the study if their blood pressure was greater than 150 mmHg systolic and/or 100 mmHg diastolic, as per the above criteria.

\textit{Carbon Monoxide} (CO) in expired air was measured using a Bedfont Smokerlyser (Bedfont Scientific Ltd, Maidstone, England). Participants with a CO reading of greater than 10 ppm were considered smokers and deemed eligible for the study.\textsuperscript{151}

\textit{Resting heart rate} was measured with a Polar Heart Rate Monitor (RS800CX, Polar Electro Inc. New York, USA). Participants wore a chest strap and lay on a bed for at least 10 minutes to determine resting heart rate.
Height and weight. Height (cm) was measured to the nearest 0.1cm using a wall-mounted stadiometer, and weight (kg) was measured to the nearest 0.1kg, using a Wedderburn Tanita BWB-620 scale (Tanita Corporation, Japan).

All physiological measures during the screening appointment were recorded on a paper case record form (Appendix 8).

3.2.1.6 Treatment session measures

Tobacco cravings, TWS and affect were assessed 15 and 5 minutes prior to exercise and then 5, 10, 20, 30, 45 and 60 minutes post-exercise. Food cravings were measured at 15 minutes pre-exercise and 10, 30 and 60 minutes post-exercise.

Cigarette cravings. Desire to smoke was assessed using a 7-point scale (1-strongly disagree, 4-neither agree nor disagree, 7-strongly agree) for the statement: ‘I have a desire to smoke right now’. Strength of desire to smoke was assessed using a 7-point scale (1-very weak, 4-neither weak nor strong, 7-very strong) for the statement: ‘The strength of my desire to smoke right now is…’

Tobacco withdrawal symptoms. An adjusted version of the Mood and Physical Symptoms Scale (MPSS) was used to measure TWS. Participants were asked to rate their levels of irritability, depression, concentration, restlessness, tension, hunger, and stress, on 7-point scales (1-not at all, 4-somewhat, 7-extremely). An overall measure of TWS (composite withdrawal) was calculated by summing the scores from the seven individual scales. Scores for composite withdrawal could therefore range from 7 to 49.

Affect was assessed with the 11-point (from -5 to +5; low to high feeling of pleasure) Feeling Scale, and arousal was assessed with the 6-point (from 1 to 6; low to high feeling of activation/arousal) Felt Arousal Scale. These scales were measured and analysed separately, and both scales target basic affect at a generic level. The
generic nature of these measures has importance given the concurrent impact of food cravings, TWS, and exercise.

**Food cravings** were assessed with the state version of the Food Cravings Questionnaire (FCQ-S). The FCQ-S is a 15-item questionnaire. Each item asks participants to rate their level of craving on a 5-point scale (1-strongly disagree, 5-strongly agree). As an example, two of the items were 'I'm craving tasty food.' And 'Satisfying my appetite would make me feel less grouchy and irritable.'

Cravings, TWS, affect, arousal and food cravings were recorded on a paper case record form (Appendix 9).

**Perceived exertion.** Participants were asked ratings of perceived exertion (RPE) during exercise testing using the Borg Scale. A laminated card presenting the scale was displayed to each participant at 2-minute intervals during each exercise bout.

**Heart rate variability.** Polar heart rate monitors (RS800CX, Polar Electro Inc. New York, USA) were worn for the duration of each treatment session to record HRV pre, during, and post exercise. Heart rate data were uploaded via infra-red to the computer using Polar ProTrainer 5 heart rate monitor software (Version 5.40.171). Segments of each heart rate file were transferred to Kubios HRV Pro (Version 2.0, MATLAB ©, The MathWorks, Inc) for analysis. One 5-minute segment was taken from the baseline (pre-exercise) period, three 5-minute segments were taken from the 15-minute exercise period, and three 10-minute segments were taken from the 1-hour recovery period (at approximately 5-15 minutes, 25-35 minutes, and 45-55 minutes post-exercise). Error due to movement artifact was manually edited. Time and frequency domain measures were computed. In time domain measures, the heart rate at any point in time, or the intervals between successive normal QRS complexes, were determined. The time domain measures used for the statistical
analyses were the mean heart rate, the square root of the mean squared differences between adjacent R-R intervals (RMSSD), and the percentage of the number of adjacent R-R intervals that differed by more than 50ms (pNN50 %). Frequency domain measures provide the basic information of how power (i.e. variance) distributes as a function of frequency. The distribution of the power of low frequency (LF) and high frequency (HF) components vary in relation to changes in autonomic function. The frequency domain measure used for the analyses was the natural log (ln) of the HF power (power [ms²] in the high frequency range – 0.15 – 0.4 Hz).

All of the above measures were administered by the candidate, with assistance from a trained research assistant when required.

On completion, participants were thanked and allowed to smoke and eat as normal, although smoking cessation support was offered to those indicating a desire to quit.

3.2.2 PERIPHERAL MARKERS SUB-STUDY

3.2.2.1 Background

Chapter 2 discussed some potential biological mechanisms that might explain the relationship between exercise and cigarette cravings. This section provides more background into the peripheral markers of neurobiology included in this study: cortisol, catecholamines, glucose, and insulin.

Cortisol: Cortisol, the primary peripheral hypothalamic-pituitary-adrenocortical (HPA) hormone in humans, was examined in this study because of its potential mediating effect between exercise and cravings. Cortisol levels are elevated in everyday life among smokers compared with non-smokers, and have been shown to decline on the first day of abstinence during a quit attempt. Declines in cortisol have been shown to predict relapse and increase severity of withdrawal. Moreover, there is evidence to suggest that NRT is not sufficient to block the reduction in cortisol following smoking cessation. Exercise has been shown to elevate cortisol levels
in both trained and untrained subjects and is proportional to the exercise intensity.\textsuperscript{158} If exercise can attenuate declines in cortisol levels during the initial stages of a quit attempt, then perhaps it can reduce the likelihood of smoking relapse, and offer something above the effects of NRT.

\textit{Catecholamines}: As with cortisol, catecholamines (adrenaline and noradrenaline) were assessed to determine their mediating effects on cravings. Both adrenaline and noradrenaline underlie the fight-or-flight response, and are therefore high in times of stress. This stress response explains why levels of catecholamines are elevated in smokers.\textsuperscript{125} Catecholamine levels decrease rapidly in the first few hours of smoking abstinence.\textsuperscript{126} Acute bouts of exercise have been shown to increase concentrations of adrenaline and noradrenaline in proportion to the intensity and duration of exercise.\textsuperscript{127} Therefore, exercise may be able to attenuate reductions in catecholamines during smoking abstinence.

\textit{Glucose and insulin}: The rationale for measuring glucose and insulin in this context is that glucose has been shown to reduce cigarette cravings.\textsuperscript{38} Nicotine triggers hepatic glucose production. During short-term smoking abstinence, nicotine withdrawal symptoms associated with low blood glucose (headaches, dizziness, poor concentration, irritability, and hunger) can be relieved by intake of sugar, and subsequently, smoking cessation is commonly associated with increased caloric intake.\textsuperscript{139} Elevations in glucose and insulin occur immediately post-exercise and then decrease slowly thereafter.\textsuperscript{127} Exercise-induced increases in glucose may reduce cigarette cravings, and therefore may provide an alternative to snacking on high-carbohydrate foods.

3.2.2.2 \textit{Procedures}

The only additional inclusion and exclusion criteria for the peripheral markers sub-study were that participants were male, and willing to have blood and saliva samples taken. Women were excluded because hormonal fluctuations during the menstrual
cycle might have resulted in differences between conditions on different days, or required each experimental trial be conducted at the same phase of their cycle.

In addition to the above measures, blood and saliva samples were taken from sub-study participants. Blood samples were taken 30 minutes before exercise, and 5, 10, 20, 30, and 60 minutes post-exercise at each of the three treatment sessions.

Blood was drawn via an indwelling venous catheter inserted into a forearm vein. Six samples of 20ml of whole blood were drawn per day. Dr Nicholas Gant, a qualified phlebotomist, was responsible for all aspects of body fluid collections, assisted by suitably qualified technicians. At each time point, blood was collected in two separate EDTA vacutainers (BD Vacutainer®, BD New Zealand), one for plasma and one for serum. Plasma samples were placed in a centrifuge (Heraeus Labofuge 400R, Thermo Scientific, NZ), and spun for 10 minutes at 3000rpm. A pipette was then used to transfer the plasma from the vacutainer to the Eppendorf Safe Lock Tubes™. Samples were temporarily stored at -20°C until the end of each experimental trial, and then moved to -80°C until analysis. An identical process was followed for the serum samples, except they sat for 30 minutes prior to being placed and spun in the centrifuge.

Saliva samples were taken using salivettes® (Sarstedt, AG & Co, Germany) on arrival at each session (30 minutes before exercise), and 5, 10, 20, 30, and 60 minutes post-exercise during the session. Participants placed a cotton dental roll in their mouth for 2 minutes to absorb saliva. After 2 minutes the roll was returned to the salivette (a plastic tube). Samples were spun at 3000rpm for 5 minutes to recover the saliva.

Blood products and whole saliva were stored using an anonymous encoded labelling system. Blood and saliva remaining after analysis will be stored for 6 years in accordance with the University of Auckland guidelines for handling and storing.
human tissue, and disposed of according to local regulations for infectious substances six years after collection (December, 2017).

The samples were analysed to determine blood concentrations of cortisol, adrenaline, noradrenaline, glucose and insulin. Saliva samples were analysed to quantify the concentration of cortisol in saliva for comparison with plasma cortisol.

### 3.2.2.3 Assays of peripheral markers

**Enzyme Immunoassay of Plasma cortisol.** The Cayman Chemical’s ACE™ EIA kit (Cayman Chemical Company, Ann Arbor, MI, USA) was used for enzyme immunoassay of plasma cortisol. The assay is based on the competition between cortisol and cortisol-acetylcholinesterase (AChE) conjugate (cortisol tracer) for a limited number of cortisol-specific mouse monoclonal antibody binding sites. The plasma cortisol microtiter plate was coated with goat polyclonal anti-mouse IgG. Standards and samples (50µl), assayed in duplicate, were added to the respective wells of the microtiter plate, followed by 50µl of AChE tracer, and 50µl cortisol EIA monoclonal antibody. Because the concentration of the cortisol tracer was held constant while the concentration of cortisol varied, the amount of cortisol tracer that was able to bind to the Cortisol Monoclonal Antibody was inversely proportional to the concentration of cortisol in the well. The plate was then incubated overnight at 4°C, during which the antibody-cortisol complex bound to the goat polyclonal anti-mouse IgG attached to the well. The plate was washed to remove any unbound reagents and then Ellman’s Reagent (which contains the substrate AChE) was added to the well. The product of this enzymatic reaction had a distinct yellow colour. The absorbance of the solution in each well was read using a microplate reader at a wavelength of 405 nm. The intensity of the colour of the solution is proportional to the amount of cortisol tracer bound to the well, which is inversely proportional to the amount of free cortisol present in the well during the incubation. The protocol used for the EIA of plasma cortisol is located in Appendix 10. The coefficient variation (the
standard deviation divided by the mean) for each pair of duplicates was calculated. The average co-efficient variation across all plates was 0.11. Based on the intra-assay precision CV reported in the assay protocol manual, this was considered acceptable for this assay.

*Enzyme immunoassay of salivary cortisol.* The High Sensitivity Salivary Cortisol EIA Kit (Salimetrics, LLC, State College, PA, USA) was used for enzyme immunoassay of salivary cortisol. The cortisol microtiter plate was coated with monoclonal antibodies to cortisol. Standards and samples (25µl) were pipetted into the appropriate wells, and assayed in duplicate. The cortisol in the standards and samples competed with cortisol linked to horseradish peroxidase for the antibody binding sites. After incubation, unbound components were washed away. Bound cortisol peroxidase was measured by the reaction of the peroxidase enzyme on the TMB substrate. This reaction produced a blue colour. A yellow colour formed after stopping the reaction with sulphuric acid. The absorbance was read on a standard plate reader at 450 nm. The amount of cortisol peroxidase detected, as measured by the intensity of colour, is inversely proportional to the amount of cortisol present. The protocol used for the EIA of salivary cortisol is located in Appendix 11.

The standard curve and subsequent sample concentrations for both the salivary cortisol and plasma cortisol assays were calculated using the template provided online by the Cayman Chemical Company ([http://www.caymanchem.com/app/template/analysis%2CEIA.vm](http://www.caymanchem.com/app/template/analysis%2CEIA.vm), accessed on 22<sup>nd</sup> June 2012). The standard curve was obtained by plotting the absorbance readings measured for the standards (linear, y-axis) against the corresponding concentrations (logarithmic, x axis). The average co-efficient variation for each pair of duplicates across all plates was .09. Based on the intra-assay precision CV reported in the assay protocol manual, this was considered acceptable for this assay.
Enzyme Immunoassay of Adrenaline and Noradrenaline. The Adrenaline Research Elisa™ kit and the Noradrenaline Research Elisa™ kit (Labor Diagnostika Nord GMBH & Co. KG, Nordhorn, Germany) were used for the enzyme immunoassay of adrenaline and noradrenaline, respectively. Adrenaline and noradrenaline were assayed concurrently, such that one adrenaline kit assay and one noradrenaline kit assay were conducted on the same day. See Appendix 12 for the protocol for adrenaline and noradrenaline. Adrenaline and noradrenaline were extracted by using a cis-diolspecific affinity gel which was bound to the extraction plate. Each sample well of the extraction plate was filled with 200µl of sample and 300µl of distilled water. Standard and control wells were filled with 10µl standard/control and 490µl distilled water. Samples were assayed in duplicate. Following acylation, and the addition of hydrochloric acid to each well, 90µl of each well were pipetted into the respective wells of an empty microtiter plate, for enzymatic derivatisation. Following 2 hours incubation at 37°C, 100µl of each sample was pipetted into the respective wells of the Adrenaline (or Noradrenaline) microtiter plate. The antigen was bound to the solid phase of the microtiter plate. The derivatized standards, controls, and samples, and the solid phase bound analyte, competed for a fixed number of antiserum binding sites. After a 15- to 20-hour overnight incubation to reach equilibrium, the free antigen and free antigen-antiserum complexes were removed by washing with the Wash Buffer. The antibody bound to the solid phase was detected by an anti-rabbit IgG-peroxidase conjugate using tetramethylbenzidine (TMB) as a substrate. The absorbance of the solution in each well was read using a microplate reader at 450 nm. The concentration of unknown samples was calculated by comparing their absorbance with a reference curve prepared with known standard concentrations. The standard curve was obtained by plotting the absorbance readings measured for the standards (linear, y-axis) against the corresponding concentrations (logarithmic, x axis) using a 4-parameter model fit. The concentrations of the samples obtained from the standard curve were multiplied by a correction.
factor of 0.05. The average co-efficient variation for each pair of duplicates was 0.19 and 0.36 for noradrenaline and adrenaline, respectively. The noradrenaline CV was considered acceptable based on the intra-assay precision CV reported in the assay protocol manual, but the adrenaline CV was higher than the CV reported for intra-assay precision in the manual, and may have affected the results. The reason for this high variation is unclear, especially considering the candidate conducted both adrenaline and noradrenaline assays, as well as the assays for cortisol, and the coefficient variations for the other assays were all within acceptable ranges. The results of the adrenaline assay must be interpreted with this in mind.

*Enzymatic colorimetric assay of Glucose.* Glucose concentrations were measured on an Hitachi 902 autoanalyser (Hitachi High Technologies Corporation, Tokyo, Japan) by enzymatic colorimetric assay (Roche, Mannheim, Germany) using standard Roche reagents for Glucose. Glucose concentrations were produced by the autoanalyser immediately following the assay.

*Microparticle enzyme immunoassay of insulin.* Insulin concentrations were measured using an Abbott AxSYM system (Abbott Laboratories, Abbott Park, IL 60064, USA), by Microparticle Enzyme Immunoassay (MEIA) using standard AxSYM insulin reagents. Insulin concentrations were produced by the AxSYM system immediately following the assay.

### 3.2.3 CRITERIA FOR EVALUATION

**Primary efficacy criterion**

Comparison of exercise modality with respect to change in desire to smoke over 60 minutes

**Secondary criteria**

1. Plasma concentrations of cortisol, adrenaline, noradrenaline, glucose, and insulin, and their relationship to cigarette cravings
2. Changes in strength of desire to smoke over time
3. Changes in TWS over time
4. Changes in food cravings over time
5. Changes in HRV over time
6. Adverse effects
7. Subjective ratings of affect

3.2.4 STATISTICAL CONSIDERATIONS

3.2.4.1 Sample size
A sample of 48 participants would provide 90% power at a 5% significance level (two-sided) to detect a treatment difference between moderate and light intensity exercise of 1 point in desire to smoke on a 7-point scale at 20 minutes, assuming the within-subject SD is 1.5.

3.2.4.2 Data analysis
Statistical analyses were performed using the Statistical Programme for Social Sciences (SPSS) version 20 (IBM SPSS), and Statistical Analysis Software (SAS, version 9.2, SAS Institute Inc. Cary NC). All statistical tests were two-tailed and a 5% significance level maintained throughout the analyses.

Descriptives: All data are presented as means ± SD unless otherwise stated. Age, sex, ethnicity, socio-economic status, smoking information, physical activity, physical fitness, and the FTND were summarised using descriptive statistics. Figures for selected outcomes are presented showing the raw mean scores for each condition across time. Error bars on all figures are presented as normalised 95% confidence intervals as per the guidelines for confidence intervals in within-subject designs outlined by Morey.\textsuperscript{159} Although the error bars closely approximate the confidence intervals obtained from the mixed models, the figures present descriptive information
Regression analyses: Repeated measures linear mixed models were used to estimate and test the treatment effects by time and condition for each outcome measure. There were three treatment conditions (light, moderate, and vigorous) in the crossover design, and a maximum of six post-exercise measures for each variable. There were six time points at 5, 10, 20, 30, 45, and 60 minutes post-exercise, for desire to smoke, strength of desire to smoke, urge to smoke, individual and composite MPSS items, affect, and arousal; three time points at 10, 30, 60 minutes post exercise for food cravings; and five time points at 5, 10, 20, 30, 60 minutes post exercise for plasma cortisol, salivary cortisol, adrenaline, noradrenaline, insulin, and glucose. There were also six time points for the measures of HRV (three 5-minute periods during the exercise period and three 10-minute periods post exercise). For the heart rate and HRV measures, the mean for each participant from each time-segment was calculated, and then the overall sample mean was calculated for each time-segment.

All regression analyses were adjusted for baseline covariates (age, sex, ethnicity [Māori/non-Māori], visit number [chronological order of the three sessions], and outcome measure at baseline [the average of scores at 5 and 15 minutes before exercise]). If the time x treatment interaction was statistically significant, the differences in least square means at each time-point are presented. If the time x treatment interaction was not statistically significant, the repeated measures mixed model analysis was conducted without the interaction term to compare treatment

\[ \text{In order to adjust for baseline in the mixed model analyses, the baseline values for each condition were not included in the outcome, but as a covariate instead. It was, therefore, not possible to obtain a least squared mean and standard error for the baseline value. Therefore, in order to present figures with a baseline value, raw means were presented. The normalised confidence intervals for the raw means closely approximate the confidence intervals for the least squared means from the mixed model analyses. They provide an indication of significance, but statistical differences cannot be inferred from the figures alone.}\]
effects, and overall differences in least square means between each condition are presented. Tukey-Kramer adjustments for multiple comparisons were conducted to control for Type I error.

Bland-Altman plots\textsuperscript{160} were used to determine limits of agreement (LoA) between salivary and plasma cortisol to assess whether or not they are comparable measures. A Bland-Altman plot plots the difference between the two measures on the y-axis, and the mean of the two measures on the x-axis. LoA were calculated as the mean difference between measures ± two standard deviations.

\textbf{Mediation}: Regression analyses were conducted to determine whether change in affect, arousal, and peripheral markers of neurobiology (catecholamines, glucose, cortisol, insulin, HRV) mediated the relations between exercise and cravings. Treatment mediators identify possible mechanisms through which a treatment might achieve its effects. These mechanisms are causal links between treatment and outcome.\textsuperscript{161} According to Kraemer and colleagues,\textsuperscript{161} a mediator must measure a change occurring during treatment, must correlate with the treatment, possibly be a result of treatment, and have either an interactive or main effect on the dependent variable. The approach differs conceptually from that of Baron and Kenny.\textsuperscript{162} According to Kraemer et al.\textsuperscript{161} for mediation to occur, demonstration of precedence and correlation are required. A mediator occurs during treatment. They argue that if such criteria are not met, the interpretation of whether a variable is mediating or moderating is often arbitrary. The Kraemer et al.,\textsuperscript{161} model is exactly the same for moderators and mediators. The difference between a mediator and a moderator is defined in terms of time relation to treatment onset and correlation with treatment.\textsuperscript{161}
3.3 RESULTS

3.3.1 PARTICIPANTS

The flow of participants in the study is presented in Figure 3. In total, 43 participants were randomised. Three participants withdrew from the study after completing one session. Baseline characteristics and all statistical analyses are presented for the 40 participants that completed the trial. This modified ITT approach was used to ensure all participants in the analyses had provided sufficient data in all three conditions. There were no significant differences at baseline between the 40 participants that completed the trial and the three who withdrew.

3.3.2 BASELINE CHARACTERISTICS

Forty smokers who reported having their first cigarette of the day within 30 minutes of waking and smoked at least 10 cigarettes per day were recruited. Demographic information is presented in Table 4. Participants were predominantly male (63%) and NZ European (50%). There was a high proportion of Māori participants (38%). Participants had a mean FTND score of 5.3 (SD = 1.8), indicating a moderate level of nicotine dependence.
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FIGURE 3: FLOW DIAGRAM
## TABLE 4: BASELINE PARTICIPANT DEMOGRAPHIC DATA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>38 ± 12.1</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>25 (62.5%)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>15 (37.5%)</td>
</tr>
<tr>
<td>Ethnicity*</td>
<td></td>
</tr>
<tr>
<td>NZ European, n (%)</td>
<td>20 (50%)</td>
</tr>
<tr>
<td>Māori, n (%)</td>
<td>15 (37.5%)</td>
</tr>
<tr>
<td>Pacific, n (%)</td>
<td>4 (9%)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>11 (27.5%)</td>
</tr>
<tr>
<td>BMI, mean ± SD</td>
<td>27.2 ± 5.3</td>
</tr>
<tr>
<td>Number of cigarettes/day, mean ± SD</td>
<td>18.6 ± 6.4</td>
</tr>
<tr>
<td>Age of smoking onset, mean ± SD</td>
<td>14.3 ± 2.8</td>
</tr>
<tr>
<td>Years smoked, mean ± SD</td>
<td>21.8 ± 12.6</td>
</tr>
<tr>
<td>Fagerström Test of Nicotine Dependence score, mean ± SD</td>
<td>5.3 ± 1.8</td>
</tr>
<tr>
<td>Baseline expired carbon monoxide level (ppm), mean ± SD</td>
<td>19.3 ± 9.7</td>
</tr>
</tbody>
</table>

* Participants were asked to indicate all ethnic groups they belonged to in line with statistics NZ ethnicity protocols, so totals exceed 100%

Table 5 presents the means and standard deviations for all dependent variables (desire to smoke, strength of desire to smoke, and TWS, affect, arousal, and food cravings) at baseline (15 and 5 minutes before exercise) for each condition (light, moderate, vigorous).
### TABLE 5: MEAN (SD) FOR ALL DEPENDENT VARIABLES BY CONDITION, AT THE TWO BASELINE TIME POINTS (15 AND 5 MINUTES BEFORE EXERCISE)

<table>
<thead>
<tr>
<th></th>
<th>-15 minutes</th>
<th>-5 minutes</th>
<th></th>
<th>Light</th>
<th>Moderate</th>
<th>Vigorous</th>
<th>Light</th>
<th>Moderate</th>
<th>Vigorous</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Light</td>
<td>Moderate</td>
<td>Vigorous</td>
<td>Light</td>
<td>Moderate</td>
<td>Vigorous</td>
<td>Light</td>
<td>Moderate</td>
<td>Vigorous</td>
</tr>
<tr>
<td>Desire to smoke</td>
<td>4.75 (1.61)</td>
<td>4.48 (2.05)</td>
<td>4.65 (1.63)</td>
<td>4.63 (1.24)</td>
<td>4.05 (2.06)</td>
<td>4.00 (1.74)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength of desire to smoke</td>
<td>4.68 (1.91)</td>
<td>4.35 (1.99)</td>
<td>4.70 (1.67)</td>
<td>4.45 (1.81)</td>
<td>4.13 (1.98)</td>
<td>4.15 (1.67)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irritability</td>
<td>3.20 (1.73)</td>
<td>3.20 (1.84)</td>
<td>2.75 (1.58)</td>
<td>2.85 (1.67)</td>
<td>3.10 (1.63)</td>
<td>2.65 (1.44)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressed</td>
<td>1.93 (1.46)</td>
<td>1.98 (1.59)</td>
<td>1.83 (1.34)</td>
<td>1.73 (1.26)</td>
<td>2.05 (1.54)</td>
<td>1.78 (1.12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty concentrating</td>
<td>2.85 (1.97)</td>
<td>2.78 (1.67)</td>
<td>2.93 (1.73)</td>
<td>2.85 (1.92)</td>
<td>2.83 (1.62)</td>
<td>2.75 (1.46)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restless</td>
<td>3.25 (1.89)</td>
<td>3.30 (1.80)</td>
<td>2.93 (1.77)</td>
<td>3.28 (1.83)</td>
<td>3.08 (1.73)</td>
<td>2.73 (1.58)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tension</td>
<td>2.90 (1.78)</td>
<td>2.78 (1.86)</td>
<td>2.80 (1.60)</td>
<td>2.50 (1.78)</td>
<td>2.73 (1.75)</td>
<td>2.40 (1.53)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hungry</td>
<td>4.08 (1.87)</td>
<td>3.53 (2.10)</td>
<td>3.60 (1.72)</td>
<td>3.83 (1.74)</td>
<td>3.93 (2.06)</td>
<td>3.48 (1.74)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stressed</td>
<td>2.65 (1.85)</td>
<td>2.90 (1.88)</td>
<td>2.53 (1.47)</td>
<td>2.53 (1.69)</td>
<td>2.78 (1.72)</td>
<td>2.08 (1.29)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite MPSS*</td>
<td>19.40 (10.80)</td>
<td>19.02 (10.73)</td>
<td>18.00 (9.91)</td>
<td>18.19 (10.24)</td>
<td>19.05 (10.56)</td>
<td>16.60 (8.84)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arousal</td>
<td>2.63 (1.60)</td>
<td>2.35 (1.51)</td>
<td>2.53 (1.47)</td>
<td>2.33 (1.36)</td>
<td>2.37 (1.43)</td>
<td>2.59 (1.33)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affect</td>
<td>0.60 (2.06)</td>
<td>0.26 (2.19)</td>
<td>0.88 (1.85)</td>
<td>0.79 (2.11)</td>
<td>0.56 (2.02)</td>
<td>1.09 (1.84)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food cravings</td>
<td>37.49 (17.82)</td>
<td>36.63 (17.26)</td>
<td>32.98 (15.01)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*MPSS: Mood and physical symptoms scale overall score for tobacco withdrawal symptoms
3.3.3 DESIRE TO SMOKE

Figure 4 shows the raw mean scores for “desire to smoke” across time for the three treatment conditions. There was a reduction in desire to smoke from baseline to 5 minutes post exercise in all three conditions, with the greatest reduction observed following vigorous exercise. Desire to smoke gradually increased between 5 and 60 minutes post exercise in all three conditions.

FIGURE 4: RAW MEAN DESIRE TO SMOKE SCORES BY CONDITION ACROSS TIME.²

The repeated measures mixed model analysis for desire to smoke including the time x treatment interaction, after adjustment for baseline, found no statistically significant interaction effect between time points and treatment conditions ($p=0.23$). None of the

² Statistical differences cannot be inferred across time or between conditions from this figure. Desire to smoke is measured on a 7-point scale from 1-7.
baseline characteristics (age, ethnicity, or sex) were significant in the regression model.

The repeated measures mixed model without the time x treatment interaction revealed a statistically significant treatment effect for desire to smoke ($F_{[2, 91]} = 7.94, p = .0007$). There were significant differences between light and vigorous conditions ($p = .0006$), and moderate and vigorous conditions ($p = .019$). Table 6 presents differences in least square means between conditions in the treatment effect for all outcomes. The asterisks denote significance between treatments after Tukey-Kramer adjustment.

**TABLE 6: DIFFERENCES OF LEAST SQUARE MEANS BETWEEN CONDITIONS**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Estimate (Standard error)</th>
<th>L-M</th>
<th>L-V</th>
<th>M-V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desire to smoke</td>
<td>0.22 (0.20)</td>
<td>0.76 (0.20)**</td>
<td>0.54 (0.20)*</td>
<td></td>
</tr>
<tr>
<td>Strength of desire to smoke</td>
<td>0.09 (0.19)</td>
<td>0.57 (0.19)**</td>
<td>0.48 (0.19)*</td>
<td></td>
</tr>
<tr>
<td>Irritability</td>
<td>0.05 (0.17)</td>
<td>0.01 (0.17)</td>
<td>0.06 (0.17)</td>
<td></td>
</tr>
<tr>
<td>Depressed</td>
<td>0.18 (0.12)</td>
<td>0.11 (0.12)</td>
<td>0.29 (0.12)*</td>
<td></td>
</tr>
<tr>
<td>Difficulty concentrating</td>
<td>0.07 (0.15)</td>
<td>0.12 (0.15)</td>
<td>0.19 (0.15)</td>
<td></td>
</tr>
<tr>
<td>Restless</td>
<td>0.11 (0.13)</td>
<td>0.20 (0.12)</td>
<td>0.31 (0.12)*</td>
<td></td>
</tr>
<tr>
<td>Tension</td>
<td>0.05 (0.10)</td>
<td>0.11 (0.10)</td>
<td>0.16 (0.10)</td>
<td></td>
</tr>
<tr>
<td>Hungry</td>
<td>0.11 (0.17)</td>
<td>0.57 (0.17)**</td>
<td>0.46 (0.17)</td>
<td></td>
</tr>
<tr>
<td>Stressed</td>
<td>0.07 (0.13)</td>
<td>0.15 (0.13)</td>
<td>0.22 (0.13)</td>
<td></td>
</tr>
<tr>
<td>Urge to smoke</td>
<td>0.20 (0.20)</td>
<td>0.65 (0.20)**</td>
<td>0.44 (0.20)</td>
<td></td>
</tr>
<tr>
<td>Composite MPSS score</td>
<td>0.44 (0.67)</td>
<td>1.29 (0.67)</td>
<td>1.74 (0.67)*</td>
<td></td>
</tr>
<tr>
<td>Arousal</td>
<td>0.31 (0.13)</td>
<td>0.05 (0.13)</td>
<td>0.26 (0.13)</td>
<td></td>
</tr>
<tr>
<td>Affect</td>
<td>0.04 (0.22)</td>
<td>0.10 (0.22)</td>
<td>0.14 (0.22)</td>
<td></td>
</tr>
<tr>
<td>Food cravings</td>
<td>0.34 (1.71)</td>
<td>3.52 (1.71)</td>
<td>3.86 (1.71)</td>
<td></td>
</tr>
</tbody>
</table>

Significance after Tukey-Kramer adjustment

*p < .05

**p < .01

***p < .001
3.3.4 STRENGTH OF DESIRE TO SMOKE

Figure 5 shows the raw mean strength of desire to smoke scores across time for the three treatment conditions. Reductions immediately post-exercise were observed in all three conditions, with the greatest reduction after vigorous exercise, followed by gradual increases in all conditions thereafter.

The repeated measures mixed model without the time x treatment interaction, after baseline adjustment, found no statistically significant interaction effect between time points and treatment conditions ($p=0.28$). None of the baseline characteristics (age, ethnicity, or sex) were significant in the regression model.

The repeated measures mixed model without the time x treatment interaction revealed a statistically significant treatment effect for strength of desire to smoke

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Statistical differences cannot be inferred across time or between conditions from this figure. Strength of desire to smoke is measured on a 7-point scale from 1-7.
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\( F_{[2,96]} = 5.51, p = .0054 \) and a main effect for time \( F_{[5,563]} = 7.29, p < .0001 \). There were significant differences between light and vigorous conditions (\( p = .0075 \)), and moderate and vigorous conditions (\( p = .01 \)).

3.3.5 TOBACCO WITHDRAWAL SYMPTOMS

Figures 6, 7, 8, and 9 show the raw mean hunger, restlessness, tension, and composite withdrawal scores, respectively, for the three treatment conditions. Non-significant reductions were observed in raw mean scores for all of these variables between baseline and five minutes post exercise under all three conditions. The reductions were followed by gradual increases in withdrawal symptoms thereafter. There were no trends across time for the other withdrawal symptoms.

A series of repeated measures mixed models were conducted for each of the TWS measured by the MPSS, as well as an overall measure of composite MPSS score. There were no statistically significant time x treatment interaction effects for any of the individual withdrawal symptoms or composite withdrawal score. None of the baseline characteristics (age, ethnicity, or sex) were significant in any of the regression models for TWS.

The repeated measures mixed model analyses for TWS without the time x treatment interaction revealed statistically significant treatment effects for restlessness \( F_{[2,123]} = 3.27, p = .04 \), hunger \( F_{[2,103]} = 6.38, p = .0024 \), and composite MPSS score \( F_{[2,117]} = 3.62, p = .03 \). The treatment effect for depression also approached statistical significance \( F_{[2,103]} = 3.02, p = .05 \). Main effects for time were observed for restlessness \( F_{[5,543]} = 3.70, p = .003 \), hunger \( F_{[5,571]} = 6.39, p < .0001 \), and composite withdrawal score \( F_{[5,568]} = 3.92, p = .0017 \). There were no treatment or time effects for tension, but mean scores did show a large decrease in all three conditions immediately after exercise (see Figure 5).
Statistical differences cannot be inferred across time or between conditions from this figure. Hunger is measured on a 7-point scale from 1-7.
FIGURE 8: RAW MEAN TENSION SCORES BY CONDITION ACROSS TIME.\textsuperscript{5}

FIGURE 9: RAW MEAN COMPOSITE MPSS SCORES BY CONDITION ACROSS TIME.\textsuperscript{3}

\textsuperscript{5} Statistical differences cannot be inferred across time or between conditions from this figure. Restlessness is measured on a 7-point scale from 1-7.

\textsuperscript{3} Statistical differences cannot be inferred across time or between conditions from this figure. Tension is measured on a 7-point scale from 1-7.
3.3.6 AFFECT AND AROUSAL

Figure 10 shows the mean scores across time for the three treatment conditions, for affect. There were no obvious trends for affect or arousal.

Overall, there was no statistically significant interaction effect between time points and treatment conditions for affect ($p=0.77$) or arousal ($p=0.73$). None of the baseline characteristics (age, ethnicity, or sex) were significant in the regression models for affect and arousal. The repeated measures mixed models without the time x treatment interaction also revealed no statistically significant treatment effects for affect or arousal.

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7 Statistical differences cannot be inferred across time or between conditions from this figure.
8 Statistical differences cannot be inferred across time or between conditions from this figure. Affect is measured on an 11-point scale from -5 to +5.
Chapter 3: Crossover Trial

It was initially proposed that the mediating effects of affect and arousal on the exercise-cigarette cravings relationship would be explored. However, mediation analyses were not conducted on these variables because there were no statistically significant effects, nor trends towards effects, of exercise on affect and arousal.

3.3.7 FOOD CRAVINGS

Figure 11 shows the mean food cravings scores across time for the three treatment conditions.

![Figure 11: Raw mean food cravings scores by condition across time.](image)

Overall, there was no statistically significant interaction effect between time points and treatment conditions ($p=0.71$). None of the baseline characteristics (age, ethnicity, or sex) were significant in the regression model.

*Statistical differences cannot be inferred across time or between conditions from this figure. Possible values for the FCQ-S range from 15 – 75.*
The repeated measures mixed model without the time x treatment interaction revealed a statistically significant treatment effect for food cravings ($F_{[2,78]} = 3.13, p = .049$) and a main effect for time ($F_{[2,235]} = 9.31, p < .0001$). There were significant differences before Tukey-Kramer adjustment between light and vigorous conditions (unadjusted $p = .04$), and moderate and vigorous conditions (unadjusted $p = .03$), but these differences were not statistically significant after adjustment (see Table 3).

### 3.3.8 HEART RATE VARIABILITY

Table 7 presents the means and normalised standard errors at baseline for each of the HRV measures. Figure 12 shows the raw mean heart rate in beats per minute for the three conditions across time.

**TABLE 7: MEAN (STANDARD ERROR) FOR EACH HEART RATE VARIABILITY MEASURE AT BASELINE IN EACH CONDITION**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Light</th>
<th>Baseline Moderate</th>
<th>Baseline Vigorous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean HR</td>
<td>72.3(1.14)</td>
<td>72.64(0.93)</td>
<td>71.3(1.12)</td>
</tr>
<tr>
<td>RMSSD</td>
<td>32.56(2.3)</td>
<td>39.86(2.27)</td>
<td>55.04(4.68)</td>
</tr>
<tr>
<td>pNN50</td>
<td>24.9(1.7)</td>
<td>17.9(1.65)</td>
<td>25.57(2.61)</td>
</tr>
<tr>
<td>Ln HF power</td>
<td>6.21(0.12)</td>
<td>5.73(0.14)</td>
<td>6.2(0.22)</td>
</tr>
</tbody>
</table>
As expected, the repeated measures mixed model analysis for mean heart rate found a statistically significant interaction effect ($F_{(10, 557)} = 81.29$, $p < .0001$), with statistically significant differences in least square means between light and vigorous conditions, light and moderate conditions, and moderate and vigorous conditions up to 25-35 minutes post-exercise. The difference between light and vigorous conditions remained significant at 45-55 minutes post-exercise. Differences in least square means for heart rate and all HRV measures are presented in Table 8.

Figures 13 and 14 present the time domain measures of HRV, RMSSD and pNN50.

Statistical differences cannot be inferred across time or between conditions from this figure. The mean heart rate for each condition at each time-point represents the mean of the average heart rate over a five or ten minute segment for each individual participant.
**TABLE 8: DIFFERENCES IN LEAST SQUARE MEANS BETWEEN CONDITIONS FOR MEASURES OF HEART RATE AND HEART RATE VARIABILITY AT EACH TIME POINT DURING AND POST-EXERCISE**

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Treatment difference</th>
<th>Mean Heart Rate</th>
<th>RMSSD</th>
<th>pNN50</th>
<th>Ln (HF power)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Estimate</td>
<td>SE</td>
<td>Adj P</td>
<td>Estimate</td>
</tr>
<tr>
<td>0-5 mins</td>
<td>L-M</td>
<td>-19.72</td>
<td>1.93</td>
<td>&lt;.0001</td>
<td>12.09</td>
</tr>
<tr>
<td></td>
<td>L-V</td>
<td>-24.35</td>
<td>1.91</td>
<td>&lt;.0001</td>
<td>17.06</td>
</tr>
<tr>
<td></td>
<td>M-V</td>
<td>-4.63</td>
<td>1.93</td>
<td>0.6043</td>
<td>4.97</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-10 mins</td>
<td>L-M</td>
<td>-30.87</td>
<td>1.94</td>
<td>&lt;.0001</td>
<td>16.58</td>
</tr>
<tr>
<td></td>
<td>L-V</td>
<td>-47.18</td>
<td>1.91</td>
<td>&lt;.0001</td>
<td>18.04</td>
</tr>
<tr>
<td></td>
<td>M-V</td>
<td>-16.31</td>
<td>1.93</td>
<td>&lt;.0001</td>
<td>1.46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-15 mins</td>
<td>L-M</td>
<td>-35.18</td>
<td>1.94</td>
<td>&lt;.0001</td>
<td>16.11</td>
</tr>
<tr>
<td></td>
<td>L-V</td>
<td>-58.76</td>
<td>1.91</td>
<td>&lt;.0001</td>
<td>15.03</td>
</tr>
<tr>
<td></td>
<td>M-V</td>
<td>-23.58</td>
<td>1.94</td>
<td>&lt;.0001</td>
<td>-1.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-30 mins</td>
<td>L-M</td>
<td>-11.22</td>
<td>1.94</td>
<td>&lt;.0001</td>
<td>24.01</td>
</tr>
<tr>
<td></td>
<td>L-V</td>
<td>-20.93</td>
<td>1.91</td>
<td>&lt;.0001</td>
<td>34.53</td>
</tr>
<tr>
<td></td>
<td>M-V</td>
<td>-9.71</td>
<td>1.93</td>
<td>0.0001</td>
<td>10.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-50 mins</td>
<td>L-M</td>
<td>-6.90</td>
<td>1.94</td>
<td>0.041</td>
<td>20.45</td>
</tr>
<tr>
<td></td>
<td>L-V</td>
<td>-14.35</td>
<td>1.92</td>
<td>&lt;.0001</td>
<td>26.43</td>
</tr>
<tr>
<td></td>
<td>M-V</td>
<td>-7.45</td>
<td>1.93</td>
<td>0.0146</td>
<td>5.99</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-70 mins</td>
<td>L-M</td>
<td>-4.24</td>
<td>1.95</td>
<td>0.7678</td>
<td>16.81</td>
</tr>
<tr>
<td></td>
<td>L-V</td>
<td>-3.93</td>
<td>1.93</td>
<td>0.0002</td>
<td>20.42</td>
</tr>
<tr>
<td></td>
<td>M-V</td>
<td>-5.15</td>
<td>1.93</td>
<td>0.4085</td>
<td>3.61</td>
</tr>
</tbody>
</table>

*p < .05, **p<.01, ***p<.001, ****p<.0001, SE: Standard error, RMSSD: Square root of the mean squared differences between successive R-R intervals, pNN50: percentage of the number of successive R-R interval pairs that differ by more than 50 ms, Ln (HF power): natural log of the high frequency power.
FIGURE 13: MEAN RMSSD (ms) BY CONDITION ACROSS TIME\textsuperscript{11}

Statistical differences cannot be inferred across time or between conditions from this figure. The mean RMSSD for each condition at each time-point represents the mean of the average heart rate over a five or ten minute segment for each individual participant.

FIGURE 14: MEAN PNN50 (%) BY CONDITION ACROSS TIME\textsuperscript{12}
Chapter 3: Crossover Trial

The repeated measures mixed model analysis for mean RMSSD found a statistically significant interaction effect \( (F_{10, 557} = 2.42, p = .0079) \). After Tukey-Kramer adjustment, the differences between conditions were not significant during the exercise period, but there were statistically significant differences between light and vigorous conditions at all the recovery time points, with the largest difference occurring at 5-15 minutes post-exercise (LSM difference [standard error] = 34.5 [5.15], \( p < .0001 \)). Differences were also significant at 5-15 minutes and 25-35 minutes post-exercise between light and moderate conditions. There were no differences between moderate and vigorous exercise at any time point.

The repeated measures mixed model for mean pNN50 found a statistically significant interaction effect \( (F_{10, 556} = 6.18, p < .0001) \). As per the RMSSD analysis, there were no statistically significant differences between conditions for pNN50 during the exercise period, or between moderate and vigorous conditions during the recovery period. The difference in least square means between light and vigorous conditions was statistically significant at all three recovery time points. The difference between light and moderate conditions was statistically significant at 5-15 minutes and 25-35 minutes post-exercise.

Figure 15 presents the frequency domain measure, the mean natural log of the high frequency power, for the three conditions across time.

\[ \text{Statistical differences cannot be inferred across time or between conditions from this figure. The mean pNN50 for each condition at each time-point represents the mean of the average heart rate over a five or ten minute segment for each individual participant.} \]
FIGURE 15: THE MEAN NATURAL LOG OF THE HIGH FREQUENCY POWER (ms$^2$) BY CONDITION ACROSS TIME$^{13}$

The repeated measures mixed model for the natural log (ln) of the HF power also revealed a statistically significant interaction effect ($F_{[10, 511]} = 7.25$, $p < .0001$). Pairwise comparisons revealed statistically significant differences between light and vigorous exercise conditions during the exercise period and up to 25-35 minutes post-exercise, and between light and moderate exercise during the exercise period and up to 5-15 minutes post-exercise.

3.3.9 MEDIATION ANALYSES

Additional repeated measures mixed model analyses for desire to smoke and strength of desire to smoke were conducted to examine the mediating effects of mean heart rate, RMSSD, pNN50, and ln(HF power). Mediation analyses revealed no effect of any of the HRV measures on the relationship between condition and

---

$^{13}$ Statistical differences cannot be inferred across time or between conditions from this figure. The mean natural log of HF power for each condition at each time-point represents the mean of the average heart rate over a five or ten minute segment for each individual participant.
desire to smoke or strength of desire to smoke. Moreover, additional linear regression analyses were conducted to determine whether changes in the HRV measure in each condition from baseline to exercise and from exercise to recovery affected change in desire to smoke and strength of desire to smoke from baseline to post-exercise in that condition. There were no significant effects for any of these regression analyses.

3.3.10 PERIPHERAL MARKERS SUB-STUDY ANALYSES

3.3.10.1 Participants

The flow of participants in the sub-sample is presented in Figure 16. Of the 135 smokers that contacted the study expressing interest in participating, 26 males were asked whether they would participate in the peripheral markers sub-sample component of the study. Of these, 12 participants were either unable to be contacted, ineligible, or declined to participate, and 6 chose to participate in the study without taking part in the sub-study. A total of eight participants took part in the sub-study.
Registered participants (N=90)

Approached to participate in sub-study (N = 26)

Not eligible: n = 1
Declined: n = 1
Unable to be contacted: n = 6

Attended screening (N = 18)

Declined further participation n =3
Unable to be contacted: n = 1

Randomised participants (N = 8)

Chose to participate in the study, but not the sub-study: n =6

Completed all sessions (N = 8)

FIGURE 16: FLOW DIAGRAM FOR THE PERIPHERAL MARKERS OF NEUROBIOLOGICAL CHANGES SUB-STUDY
3.3.10.2  Baseline characteristics

Demographic characteristics for the sub-sample are presented in Table 9. All were male and were, on average, slightly younger and had lower levels of baseline carbon monoxide levels than the wider study sample. All other measures were similar to the total sample at baseline.

TABLE 9: BASELINE PARTICIPANT DEMOGRAPHIC DATA FOR SUB-SAMPLE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>33.4 ± 12.6</td>
</tr>
<tr>
<td>Ethnicity*</td>
<td></td>
</tr>
<tr>
<td>NZ European, n (%)</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>Māori, n (%)</td>
<td>4 (37.5%)</td>
</tr>
<tr>
<td>Pacific, n (%)</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>Other (Indian), n (%)</td>
<td>1 (27.5%)</td>
</tr>
<tr>
<td>BMI, mean ± SD</td>
<td>26.6 ± 6.3</td>
</tr>
<tr>
<td>Number of cigarettes/day, mean ± SD</td>
<td>16.8 ± 4.0</td>
</tr>
<tr>
<td>Age of smoking onset, mean ± SD</td>
<td>14.9 ± 3.0</td>
</tr>
<tr>
<td>Years smoked, mean ± SD</td>
<td>16.4 ± 14.3</td>
</tr>
<tr>
<td>Fagerstrom Test of Nicotine Dependence score, mean ± SD</td>
<td>5.8 ± 1.7</td>
</tr>
<tr>
<td>Baseline expired carbon monoxide level (ppm), mean ± SD</td>
<td>11.8 ± 12.6</td>
</tr>
</tbody>
</table>

* Participants were asked to indicate all ethnic groups they belonged to in line with statistics NZ ethnicity protocols, so totals exceed 100%

Table 10 presents the means and normalised standard errors for all variables measured in the sub-sample (plasma cortisol, saliva cortisol, adrenaline, noradrenaline, glucose, and insulin) at baseline (30 minutes before exercise) in each condition.
TABLE 10: MEAN (STANDARD ERROR) FOR ALL DEPENDENT VARIABLES AT BASELINE BY CONDITION

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Light</th>
<th>Moderate</th>
<th>Vigorous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma cortisol (pg/ml)</td>
<td>4415 (384.4)</td>
<td>5570 (497.2)</td>
<td>6896 (654.6)</td>
</tr>
<tr>
<td>Salivary cortisol (pg/ml)</td>
<td>2361 (297.9)</td>
<td>3023 (261.9)</td>
<td>3524 (449.3)</td>
</tr>
<tr>
<td>Adrenaline (ng/ml)</td>
<td>71 (11.4)</td>
<td>66 (7.7)</td>
<td>88 (20.5)</td>
</tr>
<tr>
<td>Noradrenaline (ng/ml)</td>
<td>1064 (112.9)</td>
<td>1166 (195.5)</td>
<td>989 (197.8)</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.00 (.11)</td>
<td>5.05 (.11)</td>
<td>4.88 (.09)</td>
</tr>
<tr>
<td>Insulin (µU/mL)</td>
<td>10.00 (1.03)</td>
<td>9.36 (1.41)</td>
<td>7.13 (.78)</td>
</tr>
</tbody>
</table>

3.3.10.3 Plasma cortisol

Figure 17 shows the mean plasma cortisol scores across time for the three treatment conditions. Overall, there was no statistically significant interaction effect between time points and treatment conditions. Baseline characteristics (age or ethnicity) were not significant in the regression model.
The repeated measures mixed model without the time x treatment interaction found a statistically significant main effect for time for plasma cortisol (F[4, 93] = 3.44, p = .01). The main effect for treatment approached statistical significance (F[2, 22] = 3.22, p = .059). There was a significant difference between light and vigorous conditions (p = .048). Table 11 presents differences in least square means between conditions in the treatment effect for all outcomes (with the exception of noradrenaline, see below). The asterisks denote significance between treatments after Tukey-Kramer adjustment to reduce type 1 error.

\[ \text{Statistical differences cannot be inferred across time or between conditions from this figure.} \]
TABLE 11: DIFFERENCES OF LEAST SQUARE MEANS BETWEEN CONDITIONS

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Estimate (Standard error)</th>
<th>L-M</th>
<th>L-V</th>
<th>M-V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma cortisol</td>
<td>1375.8 (1155.7)</td>
<td>2927.7 (1155.7)*</td>
<td>1551.9 (1127.9)</td>
<td></td>
</tr>
<tr>
<td>Salivary cortisol</td>
<td>.07 (.11)</td>
<td>.10 (.11)</td>
<td>.03 (.11)</td>
<td></td>
</tr>
<tr>
<td>Adrenaline</td>
<td>30.5 (41.7)</td>
<td>28.8 (41.7)</td>
<td>59.3 (40.8)</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>.39 (.54)</td>
<td>.42 (.54)</td>
<td>.81 (.52)</td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>.69 (2.01)</td>
<td>2.74 (2.01)</td>
<td>3.43 (1.96)</td>
<td></td>
</tr>
</tbody>
</table>

*p < .05

3.3.10.4 Salivary cortisol

Figure 18 shows the mean salivary cortisol scores across time for the three treatment conditions. Trends were similar across the three conditions.

FIGURE 18: MEAN SALIVARY CORTISOL CONCENTRATION (pg/ml) BY CONDITION ACROSS TIME.15

15 Statistical differences cannot be inferred across time or between conditions from this figure.
Overall, there was no statistically significant interaction effect between time points and treatment conditions. Baseline characteristics (age or ethnicity) were not significant in the regression model.

The repeated measures mixed model without the time x treatment interaction revealed a statistically significant time effect for salivary cortisol ($F_{[4,92]} = 4.29, \ p = .0032$). There was no effect for treatment ($p = .64$).

The Bland-Altman plot of agreement between the raw data for plasma cortisol and salivary cortisol is presented in Figure 19. The LoA were -11167 to 13616 pg/ml.
In accordance with Bland and Altman, when the scatter of the differences increases as the mean increases, as in Figure 20, a logarithmic transformation of both variables should be conducted and a second Bland-Altman plot created. Figure 13 presents the difference between the natural log of plasma cortisol and the natural log of salivary cortisol, against the natural log of the mean of the two measures. The LoA were -2.1 to 2.7.

**FIGURE 20: AGREEMENT BETWEEN PLASMA CORTISOL AND SALIVARY CORTISOL AFTER LOG TRANSFORM**
3.3.10.5  Adrenaline

Figure 21 shows the mean adrenaline scores across time for the three treatment conditions.

FIGURE 21: MEAN ADRENALINE CONCENTRATION (ng/ml) BY CONDITION ACROSS TIME.\(^{16}\)

Overall, there was no statistically significant interaction effect between time points and treatment conditions. Baseline characteristics (age or ethnicity) were not significant in the regression model.

The repeated measures mixed model without the time x treatment interaction found no statistically significant differences between treatments or over time.

\(^{16}\) Statistical differences cannot be inferred across time or between conditions from this figure.
Figure 22 shows the mean scores across time for the three treatment conditions for noradrenaline.

![Graph showing mean noradrenaline concentration (ng/ml) by condition across time.](image)

**FIGURE 22: MEAN NORADRENALINE CONCENTRATION (ng/ml) BY CONDITION ACROSS TIME.**

Overall, there was a statistically significant interaction effect between time points and treatment conditions for noradrenaline ($F_{[8, 72]} = 2.23, p = .03$). Baseline characteristics (age or ethnicity) were not significant in the regression model for noradrenaline. Statistically significant differences in least square means were observed between light and vigorous conditions (LSM difference [SE] = 2850 [592], $p < .0001$) and between moderate and vigorous conditions (1816 [587], $p = .003$) at 5 minutes post-exercise. The difference between light and vigorous exercise remained

---

*Statistical differences cannot be inferred across time or between conditions from this figure.*
significant after Tukey-Kramer adjustment (p = .0007). However, the difference between moderate and vigorous conditions was no longer significant after Tukey-Kramer adjustment.

3.3.10.7 Glucose

Figure 23 shows the mean glucose scores across time for the three treatment conditions.

**FIGURE 23: MEAN GLUCOSE CONCENTRATION (mmol/L) BY CONDITION ACROSS TIME.**

Overall, there was no statistically significant interaction effect between time points and treatment conditions. Baseline characteristics (age, sex, and ethnicity) were not significant in the regression model.

---

18 Statistical differences cannot be inferred across time or between conditions from this figure.
The repeated measures mixed model without the time x treatment interaction revealed a statistically significant main effect for time for glucose ($F_{[4,92]} = 3.37, p = .013$). There was no statistically significant treatment effect ($F_{[2,16]} = 1.20, p = .33$).

3.3.10.8 Insulin

Figure 24 shows the mean insulin scores across time for the three treatment conditions.

Overall, there was no statistically significant interaction effect between time points and treatment conditions ($p=0.71$). Baseline characteristics (age, sex, and ethnicity) were not significant in the regression model.

Statistical differences cannot be inferred across time or between conditions from this figure.
Chapter 3: Crossover Trial

The repeated measures mixed model without the time x treatment interaction revealed a statistically significant main effect for time for insulin ($F_{[4,87]} = 2.70, p = .036$). There was no statistically significant treatment effect ($F_{[2,19]} = 1.70, p = .2$).

3.3.10.9 Mediation analyses in the sub-sample

It was initially proposed that the mediating effects of the peripheral markers on the exercise-cigarette cravings relationship would be explored. However, given the small sample of participants ($n = 8$) there was insufficient statistical power to explore these relationships meaningfully.

3.4 DISCUSSION

This study sought to determine the effects of three different intensities of exercise on cigarette cravings and TWS during temporary smoking abstinence, and to explore the mechanisms underlying the relationship between exercise and cigarette cravings. Overall, compared with light- and moderate-intensity exercise, vigorous-intensity exercise had the greatest impact on the variables of interest, but the magnitude and duration of effects on TWS and cravings were small. This discussion will summarise the findings for each variable of interest in turn, relate these findings to previous literature, and provide recommendations for future research.

3.4.1 CIGARETTE CRAVINGS

The greatest reductions in cigarette cravings (desire to smoke and strength of desire to smoke) were observed following vigorous exercise compared with moderate and light intensity exercise. Statistically significant differences between conditions were only evident up to five minutes post exercise. Previous studies have observed differences in cravings up to 30 minutes after treatment when comparing exercise with a passive control. There were no statistically significant differences between light and moderate exercise.
The magnitude of the reduction in cravings in all three conditions was small. For desire to smoke, there were reductions of -1.5, -0.73, and -0.69 between baseline and 5 minutes post vigorous, moderate, and light exercise, respectively. Eight studies have reported a higher mean reduction in desire to smoke between baseline and immediately post-exercise ranging from -1.90 to -4.90.\textsuperscript{66, 78, 98, 99, 101, 102, 145} The exercise in all of these studies was of moderate intensity or higher.

For strength of desire to smoke, there were reductions of -1.68, -0.86, and -0.96 between baseline and 5 minutes post vigorous, moderate, and light exercise, respectively. Five studies reported greater reductions in strength of desire to smoke, ranging from -1.80 to -4.50.\textsuperscript{66, 77, 96, 102, 103} One of which was observed following isometric exercise (a relatively light intensity exercise modality in comparison with the vigorous exercise condition of the current study).\textsuperscript{103} Notwithstanding this, there are also studies that have observed lesser reductions in cravings from baseline to immediately post exercise.\textsuperscript{80, 93, 97, 100, 101, 116, 145}

There are a number of factors that could explain the variability in magnitude across studies, including sample characteristics, the study environment, and the length of abstinence prior to exercise. However, as Haasova et al. discussed in their recent review,\textsuperscript{69} the largest effect sizes have been observed in studies with the highest level of mean baseline cravings, which suggests that level of nicotine dependence may moderate the effect of acute exercise on cravings. More research is needed to examine the moderating effects of nicotine dependence.

The current study findings support the findings of a previous study, which also found greater reductions in cigarette cravings following exercise of higher intensity than a lower intensity condition.\textsuperscript{163} They showed that cycling at 40%-60% HRR for 5 minutes reduced desire to smoke compared with cycling at 10%-20% HRR. However, the current study is the first to show a difference in cravings between moderate and
vigorous intensity exercise. Previous studies have found no significant differences between moderate- and vigorous-intensity exercise.\textsuperscript{96, 102, 116} However, two of these studies did report a difference in cigarette cravings between both moderate and vigorous exercise conditions and a passive control,\textsuperscript{96, 102} and the most recent of these suggested that the lack of difference between moderate- and vigorous-intensity exercise may reflect the presence of a ceiling or threshold effect of exercise intensity, as opposed to a dose-response relationship.\textsuperscript{102} They proposed that a certain level of intensity must be obtained to impact cigarette cravings, but beyond this level, perhaps there is little additional benefit. The current findings suggest this may not be the case. This is discussed with respect to the findings from the peripheral markers of neurobiology variables below.

### 3.4.2 TOBACCO WITHDRAWAL SYMPTOMS

There were few differences between conditions for TWS. Treatment effects were observed for restlessness, hunger and the composite MPSS score, and an effect for depression approached statistical significance. Raw mean scores suggest that there were small reductions in these variables from baseline to immediately post-exercise, followed by gradual increases thereafter, across all conditions. Collectively, these findings suggest that light-intensity exercise is as effective as moderate- or vigorous-intensity exercise for reducing TWS.

The current study findings reflect the findings of twelve previous studies, which also found a positive effect of exercise on at least one withdrawal symptom in comparison with a control condition.\textsuperscript{66, 72-76, 78, 80, 81, 94, 96, 103} The magnitude of the reductions in withdrawal symptoms from baseline to 5 minutes post-exercise in the current study ranged from -0.1 to -0.82 (on a 7-point scale), which are comparable with reductions observed in some previous studies.\textsuperscript{74, 76, 80, 106} However, other studies have found reductions of much greater magnitude,\textsuperscript{66, 72, 74, 103} including a study of very-light-intensity exercise.\textsuperscript{103} Baseline withdrawal symptoms were lowest in the vigorous...
exercise condition across most of the withdrawal symptoms. This was an unexpected finding, and most likely due to chance. However, there is a possibility that the anticipation of vigorous exercise may have lowered baseline withdrawal symptoms. One third of participants were able to anticipate their vigorous exercise assessment, having had completed light- and moderate-intensity exercise during previous bouts. This may have affected the mean withdrawal scores. Indeed, previous research by Harper\textsuperscript{87} showed that participants in high exercise expectancy and high exercise credibility groups experienced a greater, albeit non-significant, reduction in withdrawal symptoms following exercise than those in the low expectancy and credibility groups, which supports these findings.

3.4.3 AFFECT AND AROUSAL

In contrast to most of the previous studies,\textsuperscript{73 79 93 95 96 104} there were no statistically significant interaction effects or main effects for time or treatment on affect. In the current study, affect was measured with the 1-item Feeling Scale,\textsuperscript{109} and arousal was measured with the 1-item Felt Arousal Scale.\textsuperscript{110} Two previous studies\textsuperscript{93 145} have also used these measures to explore affect. The Feeling scale assesses the dimension of affective valence (pleasure-displeasure) and the Felt Arousal Scale assesses the dimension of activation. Both studies examined self-paced brisk walking in comparison with a passive control condition, and reported time by condition interaction effects for affective valence,\textsuperscript{93 145} thus the null effect seen in this study may be related to the lack of a passive control condition. It is possible that light-intensity exercise may increase affect at levels comparable to moderate and vigorous exercise, thus attenuating any effect. Indeed, in the current study, the magnitude of change for affect from baseline up to 30 minutes post-exercise was higher in the light intensity condition than the vigorous condition. Although there were no significant differences between conditions in affect, there were at least trends across the three
conditions, whereby affect increased slightly between baseline and 5 minutes post-exercise and then maintained post-exercise levels thereafter.

The measure of arousal on the other hand showed no trends. This is consistent with the study by Arbour-Nicotopoulou et al.,\textsuperscript{93} which also showed no effect for activation, but inconsistent with Taylor et al.,\textsuperscript{78} who reported a time by condition interaction effect for activation. Taylor et al.\textsuperscript{78} surmised that the limited change in arousal may be explained by an elevated level of baseline arousal as a result of the unfamiliar environment (an exercise laboratory). This may also explain the lack of effect in the study by Arbour-Nicotopoulou et al.,\textsuperscript{93} but the baseline levels of arousal in the current study were low, so increases in arousal after exercise were expected. It is possible that exercise had no effect on arousal levels in this population; however, as some of the participants required assistance to understand this item, the lack of trends may actually reflect difficulties with comprehension of this item.

3.4.4 FOOD CRAVINGS

Overall, there was a significant treatment effect for food cravings, as well as a main effect for time. Differences between light and vigorous conditions, and moderate and vigorous conditions, were statistically significant before Tukey-Kramer adjustment for multiple comparisons suggesting a trend towards lower food cravings after vigorous exercise.

Similar to the TWS items, baseline food cravings were lower in the vigorous exercise condition compared to the moderate and light conditions. Again, this may be due to chance, but also may reflect some kind of anticipation effect of vigorous exercise. Evidence suggests that bouts of vigorous exercise may suppress appetite.\textsuperscript{136} It is possible that the anticipation of vigorous exercise may have suppressed appetite prior to exercise.
As this was the first study to explore the effect of food cravings, it was also the first in this context to instruct participants to fast overnight to stimulate food cravings prior to each assessment. It is unclear whether fasting had any effect on the magnitude of baseline cigarette cravings. After abstaining from both cigarettes and food there were some participants that anecdotally reported that they did not experience any cravings for food because, as is common for smokers, they were accustomed to starting their day without breakfast. Although efforts were made to stimulate food cravings by presenting a selection of foods (fresh bread, chocolate, potato chips) on a tray in the laboratory, these participants were unlikely to crave food until after they had their usual ‘breakfast’ of coffee and a cigarette. Other participants anecdotally reported the opposite however, whereby they craved food more than the cigarette on arrival. It is unclear whether, for these participants, baseline cigarette cravings were lower than they otherwise would have been if participants had been allowed to eat prior to the assessment and were not experiencing a potentially overpowering craving for food. More research is needed to examine the effect of overnight fasting on cigarette cravings during temporary smoking abstinence to determine whether the presence of food cravings lowers the desire to smoke.

3.4.5 HEART RATE VARIABILITY

It was hypothesised that there would be statistically significant differences in HRV between conditions, and that these differences would mediate the relationship between exercise intensity and cigarette cravings. Greater reductions in HRV were observed during moderate and vigorous exercise than during light exercise, although differences between conditions during exercise were largely statistically non-significant. In the recovery phase, significant differences were observed between light and moderate, and light and vigorous intensity conditions up to 35 minutes post-exercise for the time domain measures of HRV (RMSSD and pNN50). There are two features of these results that are worthy of discussion and future research. First,
although differences in mean heart rate during exercise were statistically significant between moderate and vigorous conditions, the HRV response during the exercise phase was remarkably similar (no significant differences between the two conditions). The low levels of HRV (RMSSD, pNN50, ln(HF power)) observed during both moderate and vigorous exercise suggests complete withdrawal of the parasympathetic system during both those conditions, and that a threshold of vagal withdrawal was reached during moderate exercise. The additional increase in heart rate in the vigorous exercise condition is therefore beyond the threshold of vagal withdrawal, and most likely reflects additional sympathetic activity, which may be explained by an increase in a sympathetic mediator, such as the increase in noradrenaline observed following vigorous activity in the sub-sample. More research is required to confirm this hypothesis.

Second, there were differing rates of recovery observed following each condition of exercise. The HRV time-domain variables increased to pre-exercise levels almost immediately following light-intensity exercise, but by comparison, the moderate and vigorous exercise conditions had a much slower rate of increase. Moreover, although not statistically significant, there were trends to suggest a slower rate of increase following vigorous exercise compared with moderate exercise. The mediation analysis of the HRV measures on the exercise-cravings relationship did not find an effect, but the slower increase in HRV following vigorous exercise may explain the greater reduction in cravings in this condition in a larger sample. One emerging area of research interest is the concept of neurovisceral integration, in which HRV regulates a set of neural structures involved in cognitive, affective, and autonomic regulation (the central autonomic network\textsuperscript{164}). Studies by Thayer and colleagues have demonstrated the link between cognitive performance, HRV and prefrontal neural function that suggests that when HRV is reduced and one is in a state of fight or flight response, the higher cognitive areas in the prefrontal cortex essentially shut
Given that the lowest levels of HRV were observed after vigorous exercise, and vigorous exercise showed the greatest reduction in cravings, HRV could explain the relationship between vigorous exercise and cravings. It is plausible that whilst HRV is low following vigorous exercise and the autonomic nervous system is in a state of fight or flight, the higher cognitive centres associated with cravings are switched off. This may explain why participants in the current study experienced reduced cravings following vigorous exercise.

This hypothesis also supports the work of Janse Van Rensberg and colleagues who found, using fMRI, selective impairment of the prefrontal cortex following exercise in abstaining smokers. Specifically, they showed a substantial reduction in activation in the dorso-lateral prefrontal cortex (in comparison with control scanning), and increased activation in Broadman’s Area 10. Janse Van Rensberg et al. surmised that their findings align with Dietrich’s ‘Transient Hypofrontality’ hypothesis. According to this hypothesis, parts of the brain (i.e. areas of the frontal lobe involved in higher cognitive processing and addiction processes) that are not essential to the performance of exercise and the maintenance of homeostasis are temporarily inhibited during, and for a short time after, exercise. Janse Van Rensberg et al. concluded that this reduction in activation in areas associated with addiction processes may explain post-exercise reductions in cigarette cravings. Further research into the relationships between HRV, exercise, and cigarette cravings is required to provide further support to the findings of Janse Van Rensberg et al.

Beyond the acute effects, the effects of chronic smoking on perseverative cognition (a common response to stress manifested in worry and rumination) may also be influenced by HRV. We surmise that the reduction in HRV that results from chronic smoking causes a decrease in the ability of the prefrontal cortex to process higher cognitive functioning and addiction processes appropriately. This poor executive function causes the smoker to be stuck in a perseverative loop, and the
inability to break this cycle may explain not only addiction to nicotine, but addiction processes in general. The findings from the current study suggest that vigorous exercise appears to interrupt this cycle, whereas moderate and light exercise intensities do not. Further research into the relationship between vigorous exercise, HRV, and cigarette cravings is required to examine this hypothesis. However, the question still remains, if vigorous exercise is the answer to breaking this perseverative loop, how do we get smokers who physiologically are less conditioned to vigorous exercise, to exercise at a sufficient intensity to have an effect on cigarette cravings and smoking cessation?

3.4.6 PERIPHERAL MARKERS OF NEUROBIOLOGY OUTCOMES

It is important to state upfront that the findings from the subsample are exploratory. Despite the presence of statistically significant interaction effects for some outcomes, the results must be viewed with caution considering the small sample size, high between-subject variability in hormonal responses, and the high number of outcomes examined. Nevertheless, the findings from the peripheral markers of neurobiological changes component of the study are noteworthy, and will hopefully inform future research hypotheses.

3.4.6.1 Cortisol

It was hypothesised that there would be a significant difference in both plasma and salivary cortisol between conditions, with the greatest increases observed following vigorous exercise. There were no statistically significant interaction effects for plasma and salivary cortisol, and no statistically significant differences before or after adjustment for multiple comparisons for salivary cortisol. A difference in plasma cortisol between light and vigorous conditions was statistically significant after adjustment for multiple comparisons, indicating higher levels of plasma cortisol after vigorous exercise.
Three previous studies have explored the role of cortisol and its relationship between exercise and cigarette cravings. However, two of these explored the effect of exercise on cortisol in non-abstaining smokers. The third study reported higher cortisol levels post exercise compared with a passive control, but the differences in cortisol concentration were not associated with changes in cigarette cravings. However, Scerbo et al. used an abstinence period of only three hours, which may not have been sufficient to increase cigarette cravings, and possibly attenuated the effect of cortisol. The current study was therefore the first study to examine the effect of exercise on cortisol after overnight smoking abstinence. Unlike studies of the effect of exercise on cortisol in non-smokers, which show substantial increases in cortisol post-exercise, the current study, like the study by Scerbo et al., reported decreases in cortisol levels from pre- to post-exercise in all conditions.

In the present study, the greatest attenuation of the effect of abstinence on cortisol levels was expected to occur between baseline and 5 minutes post-exercise. However, attenuation actually occurred between 5 and 20 minutes post-exercise in all three conditions for both salivary and plasma cortisol. This contrasts with the study by Ho, which observed an increase in both saliva and plasma cortisol from baseline to immediately post exercise. The difference between the two studies may be explained by a) the length of abstinence prior to the exercise bout between the two studies (i.e. no abstinence versus overnight abstinence), b) the different modality of exercise examined (cardiovascular versus resistance exercise), or c) the duration of the exercise bout. The exercise bout in the study by Ho (six resistance exercises), may have been of longer duration than the 15-minute bout in the current study, and therefore more time may have elapsed between the onset of exercise and the first measurement after exercise, allowing more time for cortisol to increase. Unfortunately the length of time taken to complete the six resistance exercises was not reported so this cannot be confirmed.
Chapter 3: Crossover Trial

One of the aims of the study was to compare the findings of the salivary cortisol assay with plasma cortisol in order to determine whether one could be used as a proxy measure of the other. The advantage of this for future studies is that salivary cortisol is non-invasive, is less time consuming, less burdensome on participants, and more cost-effective than the collection of plasma. Collecting saliva via salivettes also allows for the collection of samples at times when participants are not present in the laboratory. Data from this study suggest that these two methods agree well and salivary cortisol can be considered a useful proxy measure. However, an important caveat is that, given the large differences observed between plasma and salivary cortisol concentrations, it may be inappropriate to use saliva as a proxy measure of cortisol if an accurate measure of cortisol concentration is the outcome. However, salivary cortisol may be a useful approach if the researcher is interested in relative change from baseline, and less concerned about absolute values. Further research is needed to corroborate these findings.

Cortisol, a fundamental component of the stress response, plays an important role modulating central nervous system activity during times of stress.\(^\text{174}^{175}\) The withdrawal symptoms experienced during smoking abstinence (irritability, depression, restlessness, anxiety, tension) resemble those that occur in response to stress.\(^\text{176}\) Thus, reductions in cortisol on the first day of abstinence may explain the intensity of withdrawal symptoms experienced. Baseline cortisol levels prior to temporary smoking abstinence were not measured in the current study, so it was not possible to determine the change in cortisol associated with the withdrawal of nicotine. However, reductions in cortisol on the first day of abstinence have been noted previously,\(^\text{155}^{156}\) and are predictive of relapse and severity of withdrawal.\(^\text{155}\) Although there was insufficient power in this sub-sample to determine the relationship between cortisol and cravings with respect to exercise, the increase in cortisol following vigorous exercise suggests that vigorous exercise may be able to attenuate reductions in
cortisol on the first day of abstinence for quitting smokers and hence alleviate withdrawal symptoms. More research is needed to determine the effects of cortisol in a larger sample size comparing vigorous exercise with a passive control condition.

3.4.6.2 Catecholamines

As with cortisol, catecholamines were assessed to determine their mediating effects on cigarette cravings. It was hypothesised that both adrenaline and noradrenaline would increase from baseline to post-exercise, with the greatest increase occurring at the first measurement point after exercise (5 minutes). It was also expected that increases would be proportional to the intensity of exercise such that the greatest increases would occur after the vigorous exercise condition.

A time by condition interaction effect was observed for noradrenaline, and as expected, the greatest increase occurred at 5 minutes post-vigorous exercise. The difference between light-intensity exercise and vigorous-intensity exercise was significant at this time point, whilst the difference between vigorous and moderate conditions approached statistical significance. As expected, the noradrenaline response was short, and reduced substantially at 10 minutes post-exercise.

In contrast, no differences were observed for adrenaline between the three conditions. Adrenaline increased after all three conditions, but an effect proportional to exercise was not observed. This contrasts with the only previous study to measure catecholamines after exercise in smokers (albeit non-abstaining smokers), which found similar increases in both adrenaline and noradrenaline after high-intensity exercise compared with lesser increases in adrenaline and noradrenaline after low-intensity exercise.\textsuperscript{171}

The differential effects on these two variables is difficult to explain; however, as the co-efficient variation (CV) for adrenaline was higher than the acceptable CV reported
in the assay manual, perhaps the results of the adrenaline assay are not an accurate depiction of the adrenaline response.

The findings for noradrenaline corroborate with the HRV measures in the full sample. Considering its role as a sympathetic mediator to increase heart rate, the large increase in noradrenaline post vigorous exercise, relative to moderate and light conditions, may relate to the increase in sympathetic activity required during vigorous exercise to increase heart rate when the vagal withdrawal threshold is reached. Future studies of exercise and HRV in abstaining smokers should include measurement of noradrenaline.

3.4.6.3 Insulin and Glucose

There were no statistically significant differences in the concentrations of glucose between conditions. It was hypothesised that a dose-response relationship would be present whereby the greatest increase in glucose would be observed following vigorous exercise, then moderate exercise, then light exercise, but no statistically significant differences were observed. It was also hypothesised that increases in glucose might mediate the exercise-craving relationship. Unfortunately, it was not possible to explore this in the current study. There were also no statistically significant differences in insulin concentrations between conditions. Insulin levels increased from baseline to five minutes post exercise, and then gradually decreased to baseline levels by 60 minutes post-exercise, during all three conditions.

One participant had to be withdrawn from the analyses of glucose and insulin because of abnormally high glucose levels. This participant was telephoned after the assay, and he confirmed that he had recently been diagnosed with type 2 diabetes mellitus. It was considered appropriate to include this participant’s data for the other peripheral marker outcomes, but as his glucose and insulin readings significantly elevated the sample mean for these variables, and as a diagnosis of diabetes was
part of the initial exclusion criteria, this participant’s insulin and glucose data was excluded from the analyses.

This was the first study to explore insulin and glucose in this context. The sample was too small to detect any differences between conditions, and there were no trends of note. It may be worth exploring these variables in a larger sample comparing exercise against a passive control condition; however, these exploratory findings suggest that efforts should be focused elsewhere.

3.4.7 STRENGTHS

This study is the largest crossover trial conducted in this area to date, and adds to the growing body of literature on the effects of different intensities of exercise on cigarette cravings.

This was the first study to examine and compare three different exercise intensities, and the first to examine noradrenaline, adrenaline, insulin, and glucose, in this context. Findings for these variables are inconclusive, but do illustrate the need for future examination of these variables.

It was also the first study to examine HRV before, during, and after exercise in smokers undertaking a period of smoking abstinence, and findings suggest that the relationship between vigorous exercise and HRV should be explored further in abstaining smokers.

It was also the first study to explore the effects of exercise on plasma and salivary cortisol after overnight smoking abstinence. As expected, the attenuation effect observed in previous studies, caused by high levels of baseline cortisol resulting from short pre-assessment abstinence periods, was not observed in this study.

This was also the first study of its kind to include an ethnically diverse sample (albeit with small numbers of each ethnicity). Ethnicity has not always been reported in
previous studies, but those that have, have generally reported a predominantly Caucasian sample. The current study included 15 participants who self-identified as being of NZ Māori ethnicity. More research is needed with larger and more ethnically diverse samples to establish whether differences between ethnicities exist with regard to how cravings are expressed and the effect exercise has on them.

The use of light-intensity cardiovascular exercise as a pseudo-control condition is both a strength and a limitation of the study. Its inclusion provides assurance that observed effects between vigorous exercise and the control are due to the exercise intensity, as opposed to a form of cognitive mechanism such as distraction. Although the mechanism of distraction has largely been discounted, the recent work by Harper on exercise expectancy and credibility does suggest that cognitive mechanisms may still play a minor role. However, in hindsight, including a pseudo-control was also a limitation. Given the exploratory nature of the research on peripheral markers of neurobiology outcomes, it may have been more beneficial to compare moderate and vigorous exercise with a passive control condition for these outcomes. The findings for adrenaline, cortisol, glucose, and insulin may have been more pronounced if compared with a passive control condition. Although it was expected that changes in all these variables after exercise would be proportional to the exercise intensity, it is possible, given participants were considered insufficiently active upon entry into the study, that light-intensity exercise was sufficient to see changes in these variables.

Another strength of this study is the use of linear mixed models to analyse these data. Most previous studies have used repeated measures ANOVA, which allow for comparisons of differences between conditions at each time-point. Linear mixed model analyses were used in this case because comparing differences between three conditions across up to six time-points for multiple variables increases the chance of a Type 1 error. Moreover, unlike the linear mixed model approach, the
repeated measures ANOVA approach does not account for missing data. For consistency with previous studies, it would have been ideal to use repeated measures ANOVA and report differences between conditions at each time-point for each variable. However, I considered this statistically inappropriate to do so in this case.

3.4.8 LIMITATIONS

Although common to most previous studies in this area, the study took place in an exercise laboratory, and the findings are not necessarily generalisable to other environments. Ussher et al.\textsuperscript{103} showed that isometric exercise reduced cravings for up to 30 minutes in a laboratory setting, while the effect only lasted for 5 minutes in the participants’ usual environment. In the current study, efforts were made to elicit cravings with the presence of smoking-related cues in the laboratory, as has also been used in previous studies. However, smokers are still likely to have lower cigarette cravings in situations where they know they can’t smoke, such as a laboratory. In contrast, there are constant reminders of cues to smoke in the participants’ usual environment that can reduce the effect of attempts to alleviate cravings. More research is needed to examine these effects in a more ecologically valid setting.

Moreover, as suggested by Everson et al.,\textsuperscript{96} participants undergoing a period of temporary abstinence may experience cravings, withdrawal symptoms, and affective responses differently than they would if they were actually attempting to quit smoking. These findings are therefore not necessarily generalisable to participants undergoing a quit attempt.

This study contained a number of repeated measures, both within each session and between conditions. It is possible that participants may have answered questions
based on memory (i.e. how they answered previously) rather than an accurate depiction of how they were feeling at the time.

The MPSS was used for all measures of withdrawal symptoms. The MPSS has been used in many previous studies and, as an assessment of total withdrawal, shows a high degree of sensitivity to abstinence and good reliability. But it has been shown to be less sensitive to individual items (namely anxiety and hunger), which may have impacted on the ability to determine differences between conditions for these variables.

Finally, as previously mentioned, the sample size for the peripheral markers sub-study was small, and future research with a larger sample is required. Moreover, a larger sample would also aid interpretation of HRV findings.

3.5 CONCLUSIONS

- Vigorous exercise reduces cravings relative to light- and moderate-intensity exercise

- Light and moderate exercise intensities have no detectable influence on psychological and biological markers during smoking abstinence

- These findings support the use of vigorous exercise over moderate- or light-intensity exercise to reduce cravings up to 5 minutes after treatment

- There were statistically significant differences between light and vigorous conditions for all measures of HRV. A larger sample is required to determine the mediating effects of HRV
Noradrenaline and cortisol both increased following vigorous exercise. These increases may explain greater reductions in cravings in comparison with light and moderate exercise.

This study was exploratory. More research is required with a larger sample size to examine HRV and peripheral markers of neurobiological changes.

One of the underlying assumptions regarding the role of exercise as a smoking cessation aid is that exercise and nicotine invoke similar neurobiological processes in the brain. Whilst the results from this crossover trial are exploratory, they provide further support to a neurobiological basis for the relationship between acute exercise and cigarette cravings. Noradrenaline has previously been identified as one of a number of neurotransmitters that might explain the relationship between exercise and cigarette cravings because of the similar effects of exercise and nicotine on these pathways. The findings for noradrenaline, cortisol, and HRV are novel, and the potential relationships between these variables, exercise and cigarette cravings needs to be explored further.

Aside from these neurobiological processes, exercise has also been proposed as a smoking cessation aid because of its positive effects on weight gain when quitting and psychological variables, such as affect and self-esteem. Unlike previous studies, this study showed no effect of exercise on affect, but this may reflect the lack of comparison to a passive control condition. The potential effect of exercise on weight gain was explored acutely by examining food cravings. It was hypothesised that vigorous exercise would suppress acute cravings for food, and could therefore be promoted to assist quitting smokers to avoid snacking whilst undergoing their quit attempt. No effect of exercise intensity on food cravings was observed in this study, but further research including a passive control condition is warranted. The long-term effects of exercise on weight gain during a quit attempt are
explored below. The hypothesis that exercise acts a distraction from somatic thoughts was not explored in this study because previous research indicated that distraction does not play a major role.\textsuperscript{74}
CHAPTER 4  SYSTEMATIC REVIEW – EXERCISE INTERVENTIONS FOR SMOKING CESSATION

4.1 INTRODUCTION

This chapter presents a review and meta-analysis of studies examining the effect of exercise interventions on smoking cessation. A Cochrane review of exercise interventions for smoking cessation was first published in 2005, and included 11 studies that examined the effect of exercise on smoking cessation compared with a control group. The Cochrane review was updated in 2008, and most recently in 2012. The purpose of this review was not to replicate the Cochrane review but rather to present a meta-analysis of the effect of exercise on smoking abstinence, and to review secondary outcomes. Ussher et al., did not conduct a meta-analysis, citing the heterogeneity of included studies. The rationale for undertaking a meta-analysis in this review is that the criteria for studies included in the Cochrane review were stricter than the criteria set here. Specifically, this review included all RCTs examining the effect of exercise on smoking abstinence regardless of length of follow-up, whereas Ussher et al. restricted inclusion to studies with a follow-up of 6 months or greater. Furthermore, unpublished theses and dissertations were included in this review. The inclusion of these unpublished studies and studies of short duration has both merits and limitations. Although the shorter studies do not provide an assessment of long-term effectiveness, their inclusion does allow for discussion of some of the more novel intervention approaches that have been piloted. Moreover, whilst the pilot studies can only measure the efficacy, rather than the effectiveness, of exercise, the more recent studies have often used a pragmatic design which provides insight into the potential effectiveness in the real world and the feasibility of the intervention for a large trial.
In order to set the context for the meta-analysis, a summary of the findings of the Cochrane review is first presented, followed by the findings of the present review and meta-analysis.

4.1.1 SUMMARY OF FINDINGS FROM THE USSHER et al., 2012 COCHRANE REVIEW

The Cochrane review of exercise interventions for smoking cessation identified 15 RCTs (n=4298) with at least 6 months’ follow-up. Only 3 of the 15 trials showed significantly higher abstinence rates in an active (intervention) group compared with participants in the control group at the end of 8-12 weeks’ treatment, and only one study reported higher long-term abstinence rates (at 12 months) in the physically active group, 11.9% versus 5.4%, but this was not statistically significant (odds ratio OR 2.36, 95% CI 0.97, 5.70). With respect to secondary outcomes, Ussher et al. also discussed the effect of the study interventions on weight gain, fitness and psychological measures. The following review will also discuss these outcomes, and will refer to the Cochrane review where appropriate.

4.1.2 OBJECTIVES

The aim of the present review was to update and evaluate the effectiveness of exercise interventions on smoking cessation. Specific objectives were:

1) To conduct meta-analyses of the effect of exercise interventions in combination with a behavioural intervention and/or NRT on smoking abstinence rates compared with the same behavioural intervention and/or NRT alone.

2) To conduct a narrative review of the effect of exercise interventions on various secondary outcomes: physical activity, physical fitness, weight, and psychological variables.
Chapter 4: Systematic Review of Intervention Studies

4.2 METHOD

This review was conducted using methods broadly based on the Cochrane guidelines for systematic reviews of interventions (Version 5.1.0).\textsuperscript{92}

4.2.1 SELECTION CRITERIA

4.2.1.1 Study design

Eligible studies were parallel-arm, randomised or quasi-RCTs.

4.2.1.2 Study participants

Trials involving male and female smokers (18 years or older) of all ethnicities, either wishing to quit or recent quitters, were eligible for inclusion.

4.2.1.3 Interventions

Eligible trials were those where at least one group of participants received a programme of supervised or unsupervised exercise alone or as an adjunct to a smoking cessation intervention, compared with a smoking cessation intervention alone. Control groups were defined as groups receiving either: (1) usual care; (2) a health and/or wellness programme; (3) NRT; or (4) a combination of these.

4.2.1.4 Outcomes

Eligible outcomes were: (1) point prevalence smoking abstinence of five or more days and (2) continuous smoking abstinence (measured via self-report and/or carbon monoxide or salivary cotinine) measured at the longest follow-up. Secondary outcomes reviewed were (1) physical activity, (2) physical fitness, (3) anthropometry outcomes, and (4) psychological variables.

4.2.1.5 Duration

Interventions of all durations were included.

4.2.1.6 Exclusion Criteria

Interventions in which exercise was included as part of a multiple component smoking cessation programme were excluded, as the specific effects of exercise on
smoking outcomes could not be assessed. Multiple risk factor interventions, in which
smoking cessation was included as one of a number of health-related outcomes,
were also excluded if the specific effects of exercise on smoking outcomes could not
be assessed.

4.2.2 DATA SOURCES AND SEARCH STRATEGY
Trials were identified through searches of electronic databases, and hand searching
of reference lists of all relevant articles. The initial search included all studies
published up to November 2011. This was later updated to include all studies up to
June 30th 2012.

4.2.2.1 Databases searched
A systematic search of the literature was conducted using online searches of the
following electronic data bases: Sports Discus, MEDLINE, PubMed, EMBASE (1980-
present), PsycINFO, CINAHL Plus, Cochrane Tobacco Addiction Group specialized
register, the ETD Digital Library- Networked Digital Library of Theses and
Dissertations, and Proquest Digital Dissertations.

4.2.2.2 Search terms
The search terms included were smoking, smoking cessation, nicotine, tobacco,
exercise, physical activity, and fitness. Searches were limited to randomised or
quasi-RCTs published in English, with human adult (aged 18 years old or over)
participants.

4.2.3 STUDIES IDENTIFIED VIA SEARCH STRATEGY
4.2.3.1 Study selection
A total of 1869 potentially eligible studies published between 1970 and June 2012
were identified, and entered into an Endnote library. Titles and abstracts of all studies
were reviewed for inclusion. Of the 1869 studies identified, 1849 were studies that
did not examine the effect of an intervention on smoking cessation or did not meet
the exclusion criteria outlined above. Trials of adolescent and adult participants were
excluded if the mean age of the sample was less than 18 years of age. After reviewing all abstracts, full-text copies of all potentially relevant studies were obtained and reviewed. The reference lists of all potentially relevant trials were inspected, and full text copies of all formerly unidentified studies were attained. A second reviewer was available to resolve any doubts regarding the eligibility of specific studies.

4.2.3.2 Description of included studies
Twenty studies met the inclusion criteria for review as at June 30, 2012. Full details for each study are presented in Table 12. Six studies had more than one associated publication. One study was unpublished research from a doctoral dissertation.

4.2.3.3 Data extraction and synthesis
The following data were extracted from each study included in the review: setting, study design, study objectives, method of recruitment, method of randomisation, participant characteristics (age, sex, ethnicity, smoking behaviour, FTND score, exercise level at baseline), inclusion and exclusion criteria, sample size, intervention and control programme descriptions (including number of sessions, and duration), rates of treatment adherence, duration of follow-up, definition and measure of smoking cessation, method of validation, quality information, loss to follow-up, results, and limitations. Where data from a publication were not adequately described, additional information was sought from the authors.

Results of studies that were sufficiently alike in terms of comparison groups and outcomes were combined in the meta-analyses. The final decision regarding which studies to include in the meta-analysis was made in consultation with two senior researchers and a biostatistician. Meta-analyses were conducted where there were a sufficient number of studies (n=4) for a particular outcome of smoking abstinence, and the published data were in a suitable format. Secondary outcomes that were assessed in at least two studies were also reviewed. Data synthesis and statistical
analyses were conducted using the Cochrane Collaboration Review Manager (RevMan, version 5.1; The Cochrane Collaboration, Copenhagen, Denmark), with ORs and 95% confidence intervals reported. Statistical heterogeneity was tested with the Chi-squared ($I^2$) statistic, which determines the percentage of variation due to heterogeneity, and not due to chance. If statistical heterogeneity was present, a random effects model (rather than a fixed effects model) was used. Sensitivity analyses excluding studies that were assessed as having a high risk of bias were conducted to determine if estimates of effect changed substantially.

4.2.4 ASSESSMENT OF RISK OF BIAS

Assessment of study quality was conducted in accordance with the Cochrane guidelines for assessing risk of bias. A detailed description of the assessment process is outlined in Chapter 2 on pages 7-8 of this thesis. The following determinants of study quality were considered: 1) sequence generation, 2) allocation concealment, 3) blinding of participants, personnel and outcome assessors, 4) incomplete outcome data, 5) selective outcome reporting, and 6) other sources of bias. Other sources of bias considered were: whether the intervention and control/comparison groups were comparable in key characteristics at baseline (as indicators of selection bias), whether there was differential percentage loss to follow-up/drop outs (as indicator of attrition bias), and how selection and/or attrition bias was avoided and managed (i.e. was ITT analysis employed?). Whether a target sample size was calculated a priori was also considered (as an indicator of precision).
### TABLE 12: SUMMARY OF INCLUDED STUDIES

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects characteristics</th>
<th>Exercise and control characteristics</th>
<th>Measures of abstinence and exercise</th>
<th>Design, length of treatment, length of follow-up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Al-Chalabi et al.</strong></td>
<td>19 m &amp; 21 f.</td>
<td>a) weekly emails with instructions for body scan and isometric exercises + behavioural support + NRT</td>
<td>Abstinence measure – Prolonged abstinence (CO verified)</td>
<td>2-arm pilot RCT 4-week treatment Follow-up at EOT</td>
<td>Smoking abstinence rates at 4 weeks: (a) 45% (b) 55%. 81% of (a) intended to carry on with isometric exercise and 25% intended to continue to use body scan. Intervention well received</td>
</tr>
<tr>
<td></td>
<td>Mean age = (a) 33 yrs (b) 37 yrs.</td>
<td>b) behavioural support + NRT alone. Isometric exercise (series of six static muscular contractions for 1 min each (jaw clenching, fist clenching, pushing hands down onto thighs, pushing palms together, squeezing thighs together, and pressing soles of the feet down into the floor)</td>
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<tr>
<td></td>
<td>Mean cigs = (a) 18 per day, (b) 20 per day.</td>
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<tr>
<td></td>
<td>Mean FTND = (a) 4.9, (b) 5.4</td>
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<tr>
<td></td>
<td>Mean baseline CO = (a) 23, (b) 29</td>
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<tr>
<td></td>
<td>Exercise: no criteria</td>
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<tr>
<td><strong>Bize et al.</strong></td>
<td>272 m &amp; 209 f.</td>
<td>a) 9 weekly 60 min sessions of moderate intensity group based PA plus encouragement to exercise for 30 mins 4 times per week + usual care (9-week smoking cessation programme). b) usual care + a 9-week healthy lifestyle programme</td>
<td>Abstinence measure – Prolonged abstinence at 12 months verified by CO &lt;10ppm Exercise measure - PA frequency questionnaire,</td>
<td>2-arm parallel RCT 9-week treatment 1-year follow-up</td>
<td>Abstinence rates at EOT = (a) 46%, (b) 47%. 1-year: (a) 29% (b) 27%. Exercise at EOT: (a) 1606 MET min/week (b) – 1275 (p = 0.04). At 6-months (a) 1419 (b) 987 (p=.03). No sig differences for withdrawal, depression, stress, weight, but trends in favour of intervention</td>
</tr>
<tr>
<td></td>
<td>Mean age = 42 yrs</td>
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<tr>
<td></td>
<td>Mean cigs = 27 per day.</td>
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</tr>
<tr>
<td></td>
<td>Mean FTND = (a) 5.3, (b) 5.5</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Baseline exercise inclusion criteria: &lt;150 minutes moderate or &lt;60mins vigorous per week</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exercise: inclusion criteria:</td>
<td></td>
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<tr>
<td></td>
<td>excluded &gt;3 days moderate or &gt;2 days vigorous per week</td>
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</tr>
<tr>
<td><strong>Bock et al.</strong></td>
<td>55 f.</td>
<td>a) 60 min group-based Vinyasa style yoga 2 x/week + CBT smoking cessation group based counselling 1x/week</td>
<td>Abstinence measure – 7-day PPA at 8 weeks (EOT) and 3 and 6 months follow-up verified by saliva cotinine &lt; 15ng/ml</td>
<td>2-arm pilot RCT 8-week treatment 6-month follow-up</td>
<td>Abstinence rates at EOT= (a)13/32 (b) 3/23 (p = .03). At 6 months (a) 7/32 (b) 2/23 (a) = 3 x greater reduction in negative affect cf (b).</td>
</tr>
</tbody>
</table>
Ciccol et al. 184

<table>
<thead>
<tr>
<th>Study</th>
<th>Gender</th>
<th>Participants</th>
<th>Age</th>
<th>Cigarettes</th>
<th>FTND</th>
<th>Baseline Exclusion Criteria</th>
<th>Intervention</th>
<th>Abstinence Measure</th>
<th>Follow-Up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12 m &amp; 13 f.</td>
<td>All participants – 15-20min smoking cessation counselling session +8-weeks nicotine patches</td>
<td>Mean age = 37 yrs</td>
<td>Mean cigs = 18 per day.</td>
<td>Mean FTND = 4.0</td>
<td>Baseline exercise exclusion criteria: &gt;60min regular exercise/wk</td>
<td>2-arm pilot RCT</td>
<td>7-day PPA at 12 weeks (EOT) and 6 months verified by CO &lt;10ppm</td>
<td>6-month follow-up</td>
<td>At 3 months - 7 day PPA: (a) 46%, (b)17%. Prolonged abstinence: (a)15%, (b) 8%. At 6 months, 7 day PPA: (a)38% (b) 17%. Prolonged abstinence (a) 15% (b) 8% (a) = mean reduction in body weight, and fat at 3 months, of mean increase in (b). PA increased for (a) at 3 months and decreased for (b), but increased for both groups at 6 months.</td>
</tr>
</tbody>
</table>

Hill 1985 185

<table>
<thead>
<tr>
<th>Study</th>
<th>Gender</th>
<th>Participants</th>
<th>Age</th>
<th>Cigarettes</th>
<th>Baseline CO</th>
<th>Baseline Exclusion Criteria</th>
<th>Intervention</th>
<th>Abstinence Measure</th>
<th>Follow-Up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 m &amp; 26 f.</td>
<td>a) group facility based exercise, 30 mins, 2 x per week for 5 weeks + home activity + cessation programme 2 x weekly for 5 weeks</td>
<td>Mean age = 40 yrs</td>
<td>Mean cigs = 32 per day.</td>
<td>35ppm</td>
<td>Baseline exercise exclusion criteria: not currently walking for exercise</td>
<td>2-arm RCT</td>
<td>7-day PPA at 1, 3 and 6 months follow-up verified by CO &lt;10ppm</td>
<td>6-month follow-up</td>
<td>No statistically sig differences were observed between groups for smoking abstinence</td>
</tr>
</tbody>
</table>

Hill 1993 186

<table>
<thead>
<tr>
<th>Study</th>
<th>Gender</th>
<th>Participants</th>
<th>Age</th>
<th>Cigarettes</th>
<th>FTND</th>
<th>Baseline CO</th>
<th>Baseline Exclusion Criteria</th>
<th>Intervention</th>
<th>Abstinence Measure</th>
<th>Follow-Up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>39 m &amp; 43 f.</td>
<td>a) Behavioural treatment (BT)only, b)BT + nicotine gum, c) BT + ex, d) ex only.</td>
<td>Mean age = 59.</td>
<td>Mean cigs = 28 per day.</td>
<td>Mean FTND = 6.5</td>
<td>Mean baseline CO = 35ppm</td>
<td>Baseline exercise exclusion criteria: not currently walking for exercise</td>
<td>4-arm RCT</td>
<td>5-day PPA at EOT, 1, 4 and 9 months follow-up verified by CO &lt;10ppm</td>
<td>9-month follow-up</td>
<td>5day PPA- 3 months – (a) 46% (c) 33%, 4 months – (a) 32% (c) 34%, 7 months – (a) 27% (c) 22%, 12 months – (a) 32% (c) 28%</td>
</tr>
</tbody>
</table>

Kinnunen et al. 187

<table>
<thead>
<tr>
<th>Study</th>
<th>Gender</th>
<th>Participants</th>
<th>Age</th>
<th>Cigarettes</th>
<th>FTND</th>
<th>Baseline CO</th>
<th>Baseline Exclusion Criteria</th>
<th>Intervention</th>
<th>Abstinence Measure</th>
<th>Follow-Up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>182 f.</td>
<td>a) Supervised 40 minute exercise sessions for 5 weeks (from 3 weeks pre quit to 2 weeks post) then 1 session per week for remaining 14 weeks +BT and nicotine gum. b) equal contact control condition consisting of health and wellness lectures and discussions +BT and nicotine gum. c) BT and nicotine gum</td>
<td>Mean age = 39</td>
<td>Mean cigs = 19 per day.</td>
<td>Mean FTND = 4.9</td>
<td>Baseline exercise exclusion criteria: &lt;3 x /wk</td>
<td>3-arm RCT</td>
<td>Prolonged abstinence at 1 week, 1, 4 and 12 months follow-up verified by CO &lt;10ppm and salivary cotinine Exercise measure – PA self-report (Helasoya), VO2max</td>
<td>12-month follow-up</td>
<td>Abstinence rates - one week – (a): 60%, (b) - 54%, 1 month – (a) 41%, (b) - 39%, 4 months – (a) 24%, (b) - 23%, 12 months – (a)10%, (b) 13%. No sig diffs, Increase in PA and VO2max from baseline to EOT for (a) and (b), with greater increases for (a). Not measured at follow-up</td>
<td></td>
</tr>
</tbody>
</table>

184 Ciccol et al., 185 Hill 1985, 186 Hill 1993, 187 Kinnunen et al.
### Chapter 4: Systematic Review of Intervention Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Mean Age</th>
<th>Mean Cigs</th>
<th>Baseline Exercise Exclusion Criteria</th>
<th>Intervention A</th>
<th>Intervention B</th>
<th>Abstinence Measure</th>
<th>Study Design</th>
<th>Follow-up Period</th>
<th>Abstinence Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linke 1996</td>
<td>15 males &amp; 23 females</td>
<td>43.6</td>
<td>16 per day</td>
<td>No criteria</td>
<td>a) internet-based CP + received weekly emails with instructions to exercise intermittently throughout the day in response to their cigarette cravings. Encouraged to engage in a variety of different types of exercise and to incorporate a balance of aerobic, strengthening and stretching exercises.</td>
<td>b) internet-based CP</td>
<td>7-day PPA at 3 months</td>
<td>2-arm pilot RCT</td>
<td>3-month treatment</td>
<td>Baseline exercise exclusion criteria: no criteria</td>
</tr>
<tr>
<td>Marcus 1991</td>
<td>20 females</td>
<td>39</td>
<td>28 per day</td>
<td>Exercised ≤ 1 time per week for the last 6 months</td>
<td>a) CP plus exercise. CP = eight 1-hour behaviour modification sessions over 4 weeks.</td>
<td>b) CP alone with equal contact control (3 health education lectures/week for 15 weeks). Ex = 3 supervised sessions per week for 15 weeks, including 30-45 mins of cycle ergometry at vigorous intensity. Training started 3 weeks before quit date.</td>
<td>7-day PPA at 1, 3, 12 months, verified by saliva cotinine &lt; 10ng/ml</td>
<td>2-arm RCT</td>
<td>15 weeks treatment (3 weeks pre quit, 12 weeks post)</td>
<td>12 month follow-up</td>
</tr>
</tbody>
</table>
| Marcus 1995 | 20 females | 38 | 23 per day | Exercised ≤ 1 time per week for the last 6 months | a) CP plus exercise. CP = once a week for 12 weeks. | b) CP alone with equal contact control (3 health education lectures/week for 15 weeks). Ex = 3 supervised sessions per week for 15 weeks, including 30-45 mins of cycle ergometry at vigorous intensity. Training started 3 weeks before quit date. | Prolonged abstinence at 1, 3, 12 months, verified by saliva cotinine < 10ng/ml | 2-arm RCT | 15 weeks treatment (3 weeks pre quit, 12 weeks post) | 12 month follow-up | Abstinence rates at 24 hours: (a) 80%, (b) 70%; 7 days: (a) 50%, (b) 0%; 1 month: (a) 40%, (b) 0%; 3 months: (a) 30%, (b) 0%; 12 months: (a) 20%, (b) 0% | Abstinence rates at 3 months: (a) 27%; (b) 25%. No sig diffs. Higher adherence predicted sig greater reduction in smoking rates among Int group.
## Marcus 1999\textsuperscript{174}

*281 f.*
*Mean age = 40*
*Mean cigs = 22 per day.

Baseline exercise inclusion criteria: exercised ≤ 2 times per week for the last 6 months

- **a)** CP + exercise. CP = once a week for 12 weeks
- **b)** CP + equal contact control (3 health education lectures/ per week for 12 weeks).
Ex = 3 supervised sessions per week for 12 weeks, including 30-40 mins of cycle ergometry at vigorous intensity. Training started 3 weeks before quit date.

**Abstinence measure** – prolonged abstinence at 3, 12 months, verified by saliva cotinine < 10 ng/ml, and CO < 8 ppm

**2-arm RCT**
- 15 weeks treatment (3 weeks pre quit, 12 weeks post)
- 12 month follow-up

Abstinence rates: EOT – (a) 31%, (b) 22%, 3 months – (a) 25%, (b) 14%, 12 months – (a) 19%, (b) 14%. Sig diffs at EOT and 3 months. Approached sig at 12 months.

VO2 peak increased significantly in (a) from baseline (25) to EOT (28), but was unchanged in (b): baseline (25), EOT (25)

## Marcus 2005\textsuperscript{171}

*217 f.*
*Mean age = 43*
*Mean cigs = 21 per day.*

Baseline exercise inclusion criteria: exercised < 90 minutes per week of moderate exercise

- **a)** CBT + EX
- **b)** CBT + equal contact control
  - CBT = 8 week group based CP, once/week.
  - Ex = 1 x 60min session/ wk. moderate intensity CV exercise. + 4 days of home-based exercise of at least 30 mins.
  - Contact control - 8 week wellness programme 1 hr/ week.

**Abstinence measure** – 7-day PPA at 7 days, 6 and 12 months verified by CO < 10 ppm

**Exercise measures:**
- Peak VO2.
- Other measures: weight gain

**2-arm RCT**
- 8 weeks treatment
- 12 month follow-up

Abstinence rates: 7-day PPA EOT-
- Con - 19%, Ex-20%. Continuous abstinence Con - 11%; Ex - 15%. 3 months - 7day PPA - Con 5%, Ex 12%, continuous – Con 4%, Ex 8%, 12 month - 7 day – Con 8%, Ex 7%, continuous con 1% vs ex 1%

VO2 peak sig increased from baseline to EOT (+5.51%) but was relatively unchanged in the CBT group (-.6%).

Not measured at follow-up

No sig diffs between groups for weight gain at 12 months

## Martin et al\textsuperscript{173}

*113m & 92 f.*
*Mean age = 42*
*Mean cigs = 27 per day.*

Baseline exercise inclusion criteria: < once per week

- **a)** - behavioural counselling plus exercise
- **b)** - behaviour counselling plus Nicotine gum
- **c)** - Standard treatment (CP for 8 weeks then Nicotine anonymous meetings for 4 weeks.
  - Behavioural counselling - 8 weekly 60-75 min sessions.
  - EX - mod aerobic ex prescriptions progressing from 15-45 min on site and at home.

**Abstinence measure** – 7-day PPA at 7-days, 6 and 12 months verified by CO < 10 ppm

**3-arm RCT**
- 12 weeks treatment
- 12-month follow-up

Abstinence rates: EOT: (a) = 60%, (b) 52%, (c) 31%. No differences at 6 or 12 months
### McKay et al. 1999

- **Participants:**
  - n = 684 males & 1634 females
  - 78% ≥ 30 years of age
  - 83% ≥ 10 cigs per day
  - Baseline exercise inclusion criteria: no criteria

- **Intervention:**
  - a) Internet-based programme to encourage PA incl. access to a peer-support forum.
  - b) Internet-based programme to encourage smoking cessation incl. peer support forum.

- **Abstinence measure:**
  - 7-day PPA at 3 and 6 months, unverified
  - Exercise measures:
    - Self-reported PA (BRFSS)

- **Outcomes:**
  - 2-arm RCT
  - 6 months treatment
  - 6 months follow-up

- **Results:**
  - Abstinence rates:
    - 3 months: (a) 99/504, (b) 103/524
    - 6 months: (a) 120/461, (b) 112/448
  - Engagement in vigorous PA:
    - 6 months: (a) 163/429, (b) 173/430
  - Engagement in moderate PA:
    - 6 months: (a) 344/433, (b) 332/433

- **Notes:**
  - No sig differences between groups

---

### Prapavessis et al. 2002

- **Participants:**
  - 142 females
  - Mean age = 38
  - Mean baseline CO = a+b - 16ppm, c+d - 17ppm
  - Baseline exercise inclusion criteria: no criteria

- **Intervention:**
  - a) EX + nicotine patch
  - b) EX + no nicotine patch
  - c) CBT + nicotine patch
  - d) CBT + no nicotine patch

- **Exercise:**
  - CV activity, 45 min 60-75% HRR
  - 3 times/week for 12 weeks

- **Abstinence measure:**
  - Prolonged abstinence at 6 weeks, 3, 12 months, verified by saliva cotinine < 10ng/ml, and CO <10ppm
  - Other measures:
    - Weight gain, CSEQ

- **Outcomes:**
  - 4-arm RCT
  - 12 weeks treatment
  - 12 months follow-up

- **Results:**
  - Abstinence rates:
    - 7-day PPA:
      - EOT (a) 28/33, (b) 18/35, (c) 21/26, (d) 19/27
      - 12 months:
        - (a) 12/33, (b) 6/35, (c) 11/26, (d) 12/27
    - No sig differences for continuous abstinence rates.
    - Consistently higher rates were seen when NRT was added to both treatments.
    - Combined Ex groups (a+b) sig increased fitness at 12 weeks, cf combined CBT groups (c+d). No differences at 12 month follow up.

---

### Russell et al. 2003

- **Participants:**
  - 42 females
  - Mean age = 28
  - Mean cigs = 23 per day
  - Baseline exercise inclusion criteria: no criteria

- **Intervention:**
  - a) PA - 9 one hour classes walk/jog activity program. Exercise at 70-80% of their age predicted max HR 3 times per week for 20-30 mints. 2 sessions done outside of class.
  - b) Group 2 - Support group 9 one hour educational meetings on diet exercise and coping with stress.
  - c) Contact control met briefly with therapists to collect measures

- **Abstinence measure:**
  - quit (not defined)

- **Outcomes:**
  - 3-arm RCT
  - 9 weeks treatment
  - 16 months follow-up

- **Results:**
  - No sig differences between groups for abstinence.
  - Sig increase in tension-anxiety scores in (a) cf (b) & (c)
### Chapter 4: Systematic Review of Intervention Studies

<table>
<thead>
<tr>
<th>Study Authors</th>
<th>Gender</th>
<th>Mean Age</th>
<th>Exercise Inclusion Criteria</th>
<th>Intervention Details</th>
<th>Abstinence Measure</th>
<th>Study Design</th>
<th>Follow-up</th>
<th>Outcome Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taylor et al., 2006</td>
<td>68 m.</td>
<td>Mean age = 52 (for the 203 enrolled participants)</td>
<td>Baseline exercise inclusion criteria: no criteria Men post AMI</td>
<td>a) Intervention 1 - CV activity - 30-40 min 70-85% HR max +CP. b) Intervention 2 Home exercise 20 min 5/wk. c) Control. d) Intervention 3 - Fitness test at baseline and end of treatment, CP. a &amp; b pooled together as ‘training’ group c &amp; d pooled together as ‘no-training’ group</td>
<td>Abstinence measure – Self-report non-smoking verified by plasma thiocyanate Exercise measures - Functional capacity – peak treadmill workload in METs</td>
<td>4-arm RCT</td>
<td>23 weeks follow-up</td>
<td>At 23 weeks: Prevalence of smoking lower in training group (13/42) than no-training groups (10/26). Peak treadmill workload was sig greater in training than no-training groups.</td>
</tr>
<tr>
<td>Ussher et al., 2007, 2003</td>
<td>111 m &amp; 188 f.</td>
<td>Mean age = 43</td>
<td>Mean cigs = 22 per day. Baseline exercise exclusion criteria: &gt;30 mins moderate exercise on 5 days/week, or &gt;20 mins vigorous exercise on 3 days/week</td>
<td>a) Exercise counselling (once a week for 7 weeks) + CP (once a week for 7 weeks). Exercise began one week prior to quit date b) CP + brief health education once/week for 7 weeks.</td>
<td>Abstinence measure – prolonged abstinence at 6 weeks, 12 months, verified by CO &lt;10ppm Other measures - Weight gain, body fat gain</td>
<td>2-arm RCT</td>
<td>7 weeks treatment 12 months follow-up</td>
<td>Smoking abstinence rates at 6 weeks were: (a) 40% (b) 39%. At 12 months: (a) 9% (b) 12%. No diffs between groups in weight gain or body fat gain Ratings of tension anxiety and stress lower in (a) cf. (b)</td>
</tr>
<tr>
<td>Vickers et al., 2005</td>
<td>60 f.</td>
<td>Mean age = 41</td>
<td>Mean cigs = 22 per day. Mean FTND = 4.9 Baseline exercise inclusion criteria: exercise &lt; 20mins/day on &lt;3 days/week Women with depression</td>
<td>a) - weekly individually-tailored exercise counselling sessions designed to motivated increased regular PA and short bouts of ex in response to negative affect and urges to smoke. b) health education counselling received into on a variety of health topics incl. sleep hygiene, nutrition, and health screening tests for women. All participants received smoking cessation counselling and nicotine patches</td>
<td>Abstinence measure – 7-day PPA at 10 weeks, 24 weeks, verified by CO &lt;8ppm Exercise measures - Exercise stage of change PA recall Other measures - PANAS206 HRSD207</td>
<td>2-arm RCT</td>
<td>10 weeks treatment 24 weeks follow-up</td>
<td>Smoking abstinence rates at week 10 were 17% for (a) and 23% for (b). Ex stage of change - no diff between groups at baseline. At week 10. 74% of ex group in action phase, compared with 40% of con group. EX counselling participants sig increased PA at weeks 10 and 24. PANAS – (a) sig improved PANAS scores at week 24 HRSD – (b) sig &gt; reduction in depression scores at week 10 cf. (a)</td>
</tr>
</tbody>
</table>
## Williams et al.

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Intervention Details</th>
<th>Outcome Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 f. female, Mean age = (a) 41, (b) 43</td>
<td>a) 3 sessions/week of brisk walking for 50min/session, performed on treadmills at the research centre. 50-70% age predicted max HR. b) wellness contact control - watched films on a variety of health and lifestyle issues 3 times per week (30 mins each)</td>
<td>Abstinence measure – 7-day PPA and prolonged abstinence at 8 and 12 weeks, verified by CO &lt;10ppm. Exercise measures – 7-day PAR&lt;sup&gt;20&lt;/sup&gt;. Other measures – Weight, MPSS,&lt;sup&gt;84&lt;/sup&gt; weight concerns, weight efficacy after quitting, Smoking self-efficacy, QIDS&lt;sup&gt;10&lt;/sup&gt;.</td>
</tr>
<tr>
<td>Baseline exercise inclusion criteria: &lt;60min/week of routine exercise</td>
<td>2-arm pilot RCT 8 weeks treatment 12 weeks follow-up</td>
<td>At EOT -7 day PPA: (a)48% (b) 23%. Prolonged abstinence: (a) 35% (b) 20%. No sig diffs. At follow up - 7 day PPA: (a) 21% (b) 13%. Prolonged abstinence: (a) 17% (b) 13%. No effects of treatment on weight, nicotine withdrawal symptoms, weight gain concerns, self-efficacy for maintaining weight after quitting smoking, smoking cessation self-efficacy or negative affect</td>
</tr>
</tbody>
</table>

<sup>M</sup> male, <sup>F</sup> female, cigs cigarettes; FTND Fagerström Test for Nicotine Dependence, <sup>CO</sup> Carbon Monoxide, <sup>Ex</sup> Exercise, <sup>NRT</sup> Nicotine Replacement Therapy, <sup>EOT</sup> End of treatment, <sup>RCT</sup> Randomised controlled trial, ppm Parts per million, <sup>MET</sup> Metabolic equivalent, <sup>PPA</sup> Point-prevalence abstinence, <sup>CBT</sup> Cognitive behaviour therapy, <sup>cf.</sup> compare, <sup>BT</sup> Behavioural therapy, <sup>PA</sup> physical activity, <sup>CP</sup> cessation programme, <sup>sig diffs</sup> Significant differences, <sup>BRFSS</sup> Behavioural Risk Factor Surveillance System, <sup>CV</sup> Cardiovascular, <sup>CSEQ</sup> Cessation Self-Efficacy Questionnaire, <sup>POMS</sup> Profile of Mood State Questionnaire, <sup>PANAS</sup> Positive And Negative Affect Schedule, <sup>HRSD</sup> Hamilton Rating Scale for Depression, <sup>QIDS</sup> Quick Inventory of Depression Symptomatology
4.3 RESULTS

4.3.1 CHARACTERISTICS OF INCLUDED STUDIES

A total of 20 trials including 4661 participants were included in the review. Most of the trials were small (median sample size was 60, range: 20-2318) and were published between 1985 and 2011. Only one trial was from NZ. Fifteen were conducted in the US, two in the UK, and one each in Canada and Switzerland. Six studies had more than one associated publication (see Table 11).

4.3.2 CHARACTERISTICS OF INCLUDED PARTICIPANTS, INTERVENTIONS AND OUTCOMES

There was diversity in the types of participants, interventions, outcomes, trial design, and quality. The study populations were similar in age (median mean age = 41 years, range = 28–59 years), but there were some differences in health status. Although 17 studies recruited healthy, albeit predominantly sedentary individuals, three studies did target specific sub-groups of the smoking population: depressed women, recovering alcoholics, and those recovering from post-acute myocardial infarction. With regard to ethnicity, most participants were Caucasian; seven of the eight studies that reported ethnicity reported percentages of study participants of Caucasian ethnicity over 80%. Only Ciccolo et al. recruited an ethnically diverse sample representative of the population (53% Caucasian, 31% Hispanic, 12% Black). The other trials did not report ethnicity. Ten of the trials were conducted among women only, one among men only, and nine among men and women.

4.3.2.1 Exercise level

In order to ensure that predominantly sedentary/insufficiently active participants were included, 12 studies set a maximum level of exercise at baseline as part of their inclusion criteria. Levels of exercise ranged from less...
than once per week to less than 150 minutes of moderate-intensity exercise per week. The other eight studies did not exclude participants based on exercise level.

### 4.3.2.2 Other eligibility criteria

Physical and mental health criteria were consistent across almost all trials, with most trials specifying that participants needed to be in good health, with no known medical and/or psychological impairments, or not on any medications that would preclude involvement in exercise or make compliance to exercise difficult or unsafe. Abusers of alcohol and/or drugs were excluded in seven studies, and pregnant women were excluded in three studies.

### 4.3.2.3 Smoking topography at baseline

The median mean number of daily cigarettes smoked at baseline was 23 in the fourteen studies that reported this variable (range = 16-32). Four studies reported the mean number of years participants had been smoking prior to baseline (range = 17-24 years), and six studies measured and reported a mean baseline carbon monoxide (CO) level (range = 15-36 ppm). The FTND was used to measure baseline levels of nicotine dependence in nine studies. Participants demonstrated a moderate level of nicotine dependence across all studies, with mean baseline participant FTND scores ranging from 4 (2.6) to 6.5 (1.6).

### 4.3.2.4 Exercise interventions

The exercise interventions employed varied greatly in mode of delivery, intervention duration, frequency of contact with study researchers/exercise counsellors, and the intensity, frequency, and duration of prescribed exercise. Mode of delivery of the exercise programme varied from structured, supervised exercise bouts performed solely at a research centre, to supervised exercise bouts with an
additional prescribed unsupervised home- or facility-based exercise component,\textsuperscript{181,185} to face-to-face exercise counselling,\textsuperscript{203,205} to home-based exercise prescribed remotely (via email or a website) with little or no face-to-face contact with the research team.\textsuperscript{179,180,196}

4.3.2.5 \textit{Intervention duration}

Intervention duration varied from 4 weeks\textsuperscript{180,193} to 24 weeks,\textsuperscript{202} with most interventions lasting between 8 and 16 weeks (median = 11 weeks, interquartile range = 7.5 – 13.5 weeks). Exercise programmes were initiated at six,\textsuperscript{198} four,\textsuperscript{205} three,\textsuperscript{178,187-189} or one week\textsuperscript{179,181,183,185,203} prior to the quit date, on the quit date,\textsuperscript{180,184} or one week post-quit date.\textsuperscript{191,200} One study failed to state the timing of the exercise programme relative to quit date.\textsuperscript{196} The frequency of contact throughout the interventions also varied. Eight studies provided one contact per week for the duration of the exercise intervention involving either a supervised exercise session,\textsuperscript{181,187,191,193} face-to-face exercise counselling,\textsuperscript{203,205} or a weekly email.\textsuperscript{179,180} Additionally, two of these studies\textsuperscript{181,191} encouraged participants to engage in four sessions of unsupervised exercise per week. Three studies\textsuperscript{183-185} provided two supervised exercise sessions per week, and seven studies\textsuperscript{178,186,188,189,198,200,208} provided three supervised sessions. One study began the intervention with three supervised exercise sessions, and gradually decreased the number of supervised sessions whilst simultaneously increasing the prescribed number of unsupervised sessions, over the 3-month intervention.\textsuperscript{186} One study did not specify the frequency of contact,\textsuperscript{202} and one study had no specified contact sessions, but provided an online forum where participants could obtain advice from smoking cessation counsellors.\textsuperscript{196}

4.3.2.6 \textit{Exercise intensity}

Early trials focused on the effect of vigorous-intensity cardiovascular exercise on smoking cessation.\textsuperscript{178,185,188,189,200,202} However, there has been a shift more recently
to trials of moderate-intensity cardiovascular exercise,\textsuperscript{181, 186, 187, 191, 193, 198, 203, 205, 208} as well as other modes of exercise such as isometric exercise (a series of six static muscular contractions (e.g. fist clenching) performed over a 6-minute period in response to craving),\textsuperscript{180} resistance exercise (10 weight lifting exercises),\textsuperscript{184} yoga,\textsuperscript{183} or a combination of aerobic, resistance, and stretching exercises.\textsuperscript{179}

4.3.2.7 Duration of exercise
With the exception of one study,\textsuperscript{196} which did not report the type of exercise prescribed, and two other studies,\textsuperscript{179, 180} in which participants were prescribed short (5- to 15-minute) bouts of exercise in response to craving, the prescribed exercise duration was between 20 and 60 minutes.

4.3.2.8 Control conditions
There was marked variation in the control conditions employed across studies. Early trials used behavioural counselling with or without NRT as the control, but suffered from unequal contact time between treatment and control groups.\textsuperscript{185, 188, 193, 202} More recent trials have attempted to reduce bias associated with uneven contact time between groups, by including a control treatment of equal contact time.\textsuperscript{178, 183, 184, 186, 187}\textsuperscript{189, 191, 193, 200, 203, 205, 208} However, as some studies\textsuperscript{184, 208} asked control group participants to attend sessions to watch a video, the “equal contact time” did not necessarily equate to an equal amount of social support. Many trials used either standard care,\textsuperscript{180, 181} no contact,\textsuperscript{202} or health and wellness education,\textsuperscript{184, 187, 205, 208, 188} for the control condition; however, others designed the control treatment to incorporate and/or adapt existing smoking cessation programmes already offered in the local community\textsuperscript{185, 186, 193} or developed their own smoking cessation programme incorporating behavioural support and/or NRT.\textsuperscript{178, 183, 188, 189, 191, 196, 198, 200, 203} Three trials altered existing smoking cessation programmes to match the duration and frequency of the exercise intervention.\textsuperscript{185, 193, 203}
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Four trials examined the effect of exercise alone against a form of behavioural support (counselling or education).

Eleven trials examined exercise + behavioural support against the same behavioural support alone or standard care.

Six of the more recent trials examined exercise + behavioural support + NRT versus behavioural support + NRT, or exercise + NRT versus behavioural support + NRT.

Six studies compared the effect of more than two treatment groups, examining various combinations of the three treatments: exercise, behavioural support, and NRT (see Table 11).

### 4.3.2.9 Primary outcomes

The primary outcome in 17 of the trials was smoking abstinence. The other three studies were pilot studies which focused primarily on feasibility outcomes such as rates of treatment adherence, changes in exercise behaviour, and attrition, but measured smoking abstinence as a secondary outcome. There were discrepancies in the measurement and verification of smoking abstinence. Six trials reported continuous or prolonged smoking abstinence, eight trials reported either 5-day or 7-day point prevalence smoking abstinence, and three trials reported both of these outcomes. Two trials did not define their self-report measure of smoking abstinence, but reported biochemical verification of smoking abstinence. Fifteen studies used a measure of carbon monoxide in expired air to verify smoking abstinence. Four of these also measured salivary cotinine. Two studies used salivary cotinine as the only method of verification, and one measured plasma thiocyanate concentration, and two studies did not biochemically verify smoking abstinence.
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4.3.2.10  Secondary outcomes

There was an array of secondary outcomes assessed. This review will focus on four broad secondary outcome categories: physical activity, physical fitness, anthropometry, and psychological variables.

With respect to physical activity, many different measures were used. Four studies\textsuperscript{191, 203, 205, 208} used the Blair 7-day recall questionnaire;\textsuperscript{209} one study\textsuperscript{181} used the Bernstein physical activity frequency questionnaire,\textsuperscript{212} one study\textsuperscript{187} the Finbalt Health Response survey,\textsuperscript{213} and one\textsuperscript{196} the Behavioural Risk Factor Surveillance System.\textsuperscript{197} One study\textsuperscript{184} used a 3-month physical activity recall questionnaire,\textsuperscript{214} one used\textsuperscript{179} the Godin and Shephard Leisure Time Exercise Questionnaire,\textsuperscript{148} and three studies\textsuperscript{191, 203, 205} measured exercise stage of change based on the Transtheoretical Model.\textsuperscript{215}

The predominant physical fitness measure was a submaximal predicted VO\(_{2\text{max}}\) test.\textsuperscript{185, 187-189, 191, 198, 200, 205} Functional capacity,\textsuperscript{202} flexibility,\textsuperscript{179} and muscular strength,\textsuperscript{179} were also assessed.

Nine studies measured anthropometric measures. These included changes in weight status,\textsuperscript{178, 179, 181, 184, 188, 189, 191, 198, 203} body fat,\textsuperscript{203} BMI,\textsuperscript{203} and body composition measured by dual x-ray absorptiometry.\textsuperscript{184}

Psychological outcomes included depression or depressive symptoms,\textsuperscript{179, 181, 183, 187, 191, 196, 205, 208} positive and/or negative affect,\textsuperscript{179, 183, 187, 191, 205, 208} weight concerns associated with quitting,\textsuperscript{183, 187, 191, 205, 208} self-efficacy,\textsuperscript{179, 191, 208} perceived stress,\textsuperscript{181, 187, 191} and social support.\textsuperscript{196, 198} There were a number of other psychological outcomes, each measured in only one study. These will not be reviewed here.

4.3.2.11  Length of follow-up

Length of follow-up ranged from end of treatment (three pilot studies\textsuperscript{179, 180, 208}) to 18 months.\textsuperscript{200} The majority of studies included a follow-up assessment at 6 and/or 12 months.\textsuperscript{178, 181, 183-189, 191, 193, 198, 200, 202, 203, 205}
4.3.3 RISK OF BIAS IN INCLUDED STUDIES

The assessment of risk of bias was based on the guidelines in the Cochrane handbook for Systematic reviews of interventions. As a whole, the earlier studies were generally more likely to have a higher risk of bias. The following is a summary of the evaluation for risk of bias.

4.3.3.1 Sequence generation and allocation concealment;

All 20 trials included in the review were described as RCTs. However, only seven\textsuperscript{178} reported how their random allocation sequence was generated, all of which were computer generated. A further four trials stated that block randomisation was used,\textsuperscript{186} \textsuperscript{187} \textsuperscript{193} \textsuperscript{208} but did not describe how the random allocation sequence was generated. Seven trials reported concealment of the random allocation sequence, three used opaque sealed envelopes,\textsuperscript{181} \textsuperscript{205} \textsuperscript{208} and the other four did not describe the method of concealment.\textsuperscript{180} \textsuperscript{191} \textsuperscript{198} \textsuperscript{203}

4.3.3.2 Blinding

As each study involved at least one exercise condition versus a non-exercise control group, blinding of participants was not possible. However, it is unlikely that lack of participant blinding would bias results associated with smoking abstinence. No studies reported blinding researchers to the treatment condition. Non-blinding of researchers was deemed to not be a risk of bias with regard to the primary outcome in 18 of the 20 studies, as smoking abstinence, the primary outcome in all studies, was objectively verified. Although, even when a subjective measure of smoking abstinence was employed,\textsuperscript{179} \textsuperscript{196} it was unlikely that this biased the results to favour the intervention group, as there is little evidence in smoking cessation research for statistically significant differences between intervention and control groups in false-reporting of smoking abstinence.\textsuperscript{216}
4.3.3.3  Loss to follow-up

Overall loss to follow-up was reported in 17 studies. However, three of these trials did not report loss by treatment group. Only one of the remaining 14 studies that reported loss by intervention group reported differential loss to follow-up, observing higher loss to follow-up in the exercise groups (40%) than the CBT groups (23%) at 12 months follow-up, but no differential loss at the earlier time-points. Loss to follow-up was not reported in three studies.

4.3.3.4  Incomplete outcome data

Eleven studies employed an ITT approach. Of these, three studies did not state their process for managing incomplete data but the approach could be determined by the reported denominators at each time-point. Three studies presented both ITT and per-protocol (as treated) analyses results. All ITT analyses across all studies assumed participants lost to follow-up to be smoking. Five studies used a per protocol analysis method whereby only those participants who completed the follow-up assessment were included in the analyses. Hill et al. stated that they conducted a sensitivity analysis including the data of those lost to follow-up, and the results were the same. One study did not report how they handled missing data.

4.3.3.5  Other potential sources of bias

Sixteen studies were considered free of other sources of bias. Two studies did not have sufficient statistical power based on their small sample size. In one study, randomisation to the standard care control was terminated early as preliminary findings indicated that this condition fared considerably worse than the exercise and equal contact control conditions, and one study had very high rates of attrition.

4.3.3.6  Comparable groups at baseline

All studies, except one reported baseline characteristics. Thirteen studies reported no significant differences between groups on any variables at baseline. The
remaining six studies reported significant differences between groups on certain secondary outcomes, $VO_{2\text{max}}$ and positive affectivity, Nicotine Dependence Syndrome Scale score, current employment status, weight, BMI, years abstinent from alcohol, age, level of exercise stage of change, restlessness and sleep disturbance. Of these, only Ussher et al. reported accounting for baseline differences as a potential confounder in their statistical analyses. However, there were no significant differences between groups in the primary outcome measure at baseline in any of the studies.

4.3.3.7 A priori sample size calculation

Six studies reported calculating a sample size a priori. It was unclear how the sample size was chosen in four of the earlier studies. Five trials asserted that they were pilot studies and that larger trials were required.

4.3.3.8 Summary of study quality

None of the 20 studies were considered to have a high risk of bias. Fifteen studies were classified as having an “Unclear” risk of bias. The remaining five studies were considered to have a low risk of bias across all domains.

4.3.4 EFFECTS OF EXERCISE INTERVENTIONS

The following section describes the effects of exercise on smoking abstinence (continuous and point prevalence abstinence). Meta-analyses of continuous and point prevalence smoking abstinence at end of treatment, 6 months’ follow-up, and 12 months’ follow-up are presented first. This is followed by a review of other important secondary outcomes. The review and meta-analyses results are then discussed with respect to potential mediators that may explain the relationship between physical activity and smoking cessation.
4.3.5 META-ANALYSES

All studies published to date were reviewed for inclusion in a meta-analysis of the effect of exercise on smoking abstinence. In smoking cessation studies, there are two predominant measures of smoking abstinence, continuous abstinence and point prevalence abstinence. Continuous abstinence is defined either as complete abstinence between quit day and follow-up,\(^{218}\) or no more than five cigarettes since the start of the abstinence period (referred to as the Russell Standard\(^{219}\)). The former definition of complete continuous abstinence is often considered too stringent, and excludes participants who smoke a few cigarettes in the first few days during the abstinence period but progress to lifetime abstinence. Therefore, the Russell Standard\(^{219}\) is the approach used most commonly in more recent studies. The term continuous abstinence hereafter refers to both of these definitions. Point prevalence abstinence is defined as the prevalence of abstinence during a specified time period (commonly seven days) immediately preceding follow-up.\(^{218}\) All of the reviewed studies chose to use one or both of these as their measure of abstinence. Studies were heterogeneous in regard to the length of follow-up. Most studies presented outcome data at end of treatment, but follow-up durations varied. A sufficient number of trials assessed smoking abstinence at 6 months’, and 12 months’ follow-up to conduct meta-analyses for these two time points. Therefore six meta-analyses are presented, one for continuous abstinence and one for point-prevalence abstinence, at each follow up time-point (end of treatment, 6 months, and 12 months) (Figures 25-30). Studies were excluded from the meta-analyses if they did not compare exercise in combination with a smoking cessation programme (behavioural treatment and/or NRT) with the same smoking cessation programme alone.\(^ {193\ 196\ 198\ 200\ 202}\) Of these, two studies employed a different smoking cessation programme for the control group than the programme used for the intervention, which made it difficult to assess the impact on exercise alone.\(^ {193\ 196}\) one study compared exercise with cognitive behavioural therapy (CBT) with and without NRT, but did not compare exercise and
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CBT against CBT alone,\textsuperscript{198} and two studies\textsuperscript{200, 202} compared exercise with a control condition and no behavioural therapy was offered to either group. Of the remaining studies, two did not follow an ITT approach in their analyses,\textsuperscript{181, 187} but both reported dropouts by treatment group so it was possible to calculate the treatment effect from all randomised participants. It was unclear in one study whether an ITT approach was followed,\textsuperscript{186} and another study\textsuperscript{179} did not objectively verify smoking abstinence. The study by Hill\textsuperscript{186} was included in the meta-analyses of point prevalence abstinence at the end of treatment and 12 months, as was the study by Linke\textsuperscript{179} (end of treatment analysis only); however, subsequent sensitivity analyses were also conducted excluding these studies. Despite the apparent heterogeneity across studies in terms of exercise programme design, it was considered appropriate to conduct meta-analyses combining these studies. These meta-analyses provide an overall indication of the general effect of some form of exercise programme on smoking abstinence. Given the heterogeneity across studies, it is not possible to distinguish what type, intensity, or duration of exercise is needed to increase abstinence rates, and these meta-analyses results must be interpreted with this in mind. Sensitivity analyses controlling for dose of intervention received were considered, but with such heterogeneity across studies it was difficult to establish how and where to divide the studies. Therefore, such analyses were not conducted.

A total of nine trials measured and reported continuous smoking abstinence rates at the end of treatment (Figure 25). One of the nine trials found a statistically significant effect on continuous abstinence in favour of exercise (19.4% vs 10.2%, \( p = .03 \)).\textsuperscript{178} The OR for objectively verified continuous abstinence was 1.19. This was in favour of exercise but not statistically significant (95% CI 0.95, 1.49; \( p = 0.13 \)). A fixed effects model was used as significant heterogeneity was not evident (\( I^2 = 0\% \), \( p = 0.59 \)).

A total of nine trials measured and reported point prevalence smoking abstinence rates at the end of treatment (Figure 26). One study found a statistically significant
effect on point prevalence abstinence in favour of exercise (41% vs 13%, p = 0.03). The OR for point prevalence abstinence at end of treatment was 1.57 in favour of exercise (95% CI 1.13, 2.19; p = 0.007). A fixed effects model was used as significant heterogeneity was not evident ($I^2=23\%$, p = 0.24). A sensitivity analysis was conducted excluding one study where it was unclear whether an ITT approach was followed, and one study that did not verify smoking abstinence. The pooled weighted intervention effect changed only slightly with the two studies excluded (1.72; 95% CI 1.21, 2.45; p = 0.002).

Four trials measured and reported continuous smoking abstinence rates at six months (Figure 27). One study found a statistically significant effect on continuous abstinence in favour of exercise (19% vs 10%, p = .03). The OR for objectively verified continuous abstinence rate was 1.19 (95% CI 0.87, 1.64; p = 0.28). A fixed effects model was used as significant heterogeneity was not evident ($I^2=41\%$, p = 0.17).

A total of five trials measured and reported point prevalence smoking abstinence rates at six months (Figure 28). One trial found a statistically significant effect on point prevalence abstinence at six months in favour of exercise (25% vs 14%, p = .02). The OR for point prevalence abstinence at six months was 2.23 in favour of exercise (95% CI 1.38, 3.60; p = 0.001). A fixed effects model was used as significant heterogeneity was not evident ($I^2=0\%$, p = 0.56).

Six trials measured and reported continuous smoking abstinence rates at 12 months (Figure 29). None of the six trials found a statistically significant effect in favour of exercise; however, one study by Marcus et al. approached significance (11.9% vs 5.4%, p = .05). The OR for objectively verified continuous abstinence rate was 1.01 (95% CI 0.74, 1.37; p=0.96). A fixed effects model was used as significant heterogeneity was not evident ($I^2=17\%$, p = 0.30).
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**FIGURE 25: META-ANALYSIS OF CONTINUOUS ABSTINENCE AT END OF TREATMENT**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Exercise Events</th>
<th>Control Events</th>
<th>Odds Ratio M-H Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Chalabi 2008</td>
<td>9</td>
<td>20</td>
<td>4.44% 0.67 [0.15, 3.33]</td>
</tr>
<tr>
<td>Elze 2010</td>
<td>167</td>
<td>229</td>
<td>42.0% 1.04 [0.73, 1.50]</td>
</tr>
<tr>
<td>Ciccolo 2011</td>
<td>2</td>
<td>13</td>
<td>0.6% 2.00 [0.16, 25.43]</td>
</tr>
<tr>
<td>Kimmunea 2008</td>
<td>22</td>
<td>56</td>
<td>0.9% 1.94 [0.47, 7.90]</td>
</tr>
<tr>
<td>Marcus 1995</td>
<td>3</td>
<td>10</td>
<td>6.6% 0.56 [0.33, 0.95]</td>
</tr>
<tr>
<td>Marcus 1999</td>
<td>20</td>
<td>134</td>
<td>9.6% 2.12 [1.07, 4.10]</td>
</tr>
<tr>
<td>Marcus 2005</td>
<td>19</td>
<td>149</td>
<td>7.4% 0.36 [0.06, 1.97]</td>
</tr>
<tr>
<td>Ussher 2007</td>
<td>61</td>
<td>145</td>
<td>25.1% 1.04 [0.65, 1.86]</td>
</tr>
<tr>
<td>Williams 2010</td>
<td>10</td>
<td>29</td>
<td>2.8% 2.11 [0.65, 3.23]</td>
</tr>
<tr>
<td><strong>Total (5%)</strong></td>
<td>700</td>
<td>780</td>
<td>1.10 [0.95, 1.40]</td>
</tr>
</tbody>
</table>

Total events: 256 230
Heterogeneity: Chi² = 8.54, df = 8 (P = 0.59), I² = 0%
Test for overall effect: Z = 1.52 (P = 0.13)

**FIGURE 26: META-ANALYSIS OF POINT PREVALENCE ABSTINENCE AT END OF TREATMENT**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Exercise Events</th>
<th>Control Events</th>
<th>Odds Ratio M-H Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bock 2012</td>
<td>13</td>
<td>32</td>
<td>3.7% 4.58 [1.13, 18.57]</td>
</tr>
<tr>
<td>Ciccolo 2011</td>
<td>5</td>
<td>13</td>
<td>2.0% 4.29 [0.86, 27.78]</td>
</tr>
<tr>
<td>Hill 1993</td>
<td>5</td>
<td>18</td>
<td>10.8% 0.60 [0.17, 2.18]</td>
</tr>
<tr>
<td>Linke 2011</td>
<td>3</td>
<td>19</td>
<td>4.5% 1.00 [0.27, 3.72]</td>
</tr>
<tr>
<td>Marcus 1991</td>
<td>3</td>
<td>10</td>
<td>0.8% 9.80 [0.44, 219.25]</td>
</tr>
<tr>
<td>Marcus 1999</td>
<td>31</td>
<td>134</td>
<td>33.5% 1.05 [0.63, 2.50]</td>
</tr>
<tr>
<td>Marcus 2005</td>
<td>22</td>
<td>109</td>
<td>28.4% 1.11 [0.57, 2.18]</td>
</tr>
<tr>
<td>Vickers 2003</td>
<td>8</td>
<td>30</td>
<td>6.4% 0.72 [0.15, 3.54]</td>
</tr>
<tr>
<td>Williams 2010</td>
<td>14</td>
<td>29</td>
<td>6.3% 3.07 [1.00, 9.28]</td>
</tr>
<tr>
<td><strong>Total (5%)</strong></td>
<td>394</td>
<td>401</td>
<td>1.57 [1.13, 2.18]</td>
</tr>
</tbody>
</table>

Total events: 111 91
Heterogeneity: Chi² = 10.32, df = 8 (P = 0.24), I² = 23%
Test for overall effect: Z = 2.38 (P = 0.007)
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### FIGURE 27: META-ANALYSIS OF CONTINUOUS ABSTINENCE AT 6 MONTHS

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Exercise</th>
<th>Control</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Bize 2010</td>
<td>78</td>
<td>229</td>
<td>0.95</td>
</tr>
<tr>
<td>Ciccolo 2011</td>
<td>2</td>
<td>12</td>
<td>2.20</td>
</tr>
<tr>
<td>Marcus 1999</td>
<td>24</td>
<td>154</td>
<td>2.21</td>
</tr>
<tr>
<td>Marcus 2005</td>
<td>8</td>
<td>109</td>
<td>2.06</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>484</strong></td>
<td><strong>519</strong></td>
<td><strong>1.19</strong></td>
</tr>
</tbody>
</table>

Total events: 110, 106
Heterogeneity: Ch2 = 5.66, df = 3 (P = 0.17), I² = 41%
Test for overall effect: Z = 1.08 (P = 0.28)

### FIGURE 28: META-ANALYSIS OF POINT PREVALENCE ABSTINENCE AT 6 MONTHS

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Exercise</th>
<th>Control</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Bock 2012</td>
<td>8</td>
<td>32</td>
<td>1.54</td>
</tr>
<tr>
<td>Ciccolo 2011</td>
<td>5</td>
<td>13</td>
<td>6.03</td>
</tr>
<tr>
<td>Marcus 1999</td>
<td>33</td>
<td>134</td>
<td>2.07</td>
</tr>
<tr>
<td>Marcus 2005</td>
<td>13</td>
<td>109</td>
<td>2.78</td>
</tr>
<tr>
<td>Vickers 2009</td>
<td>1</td>
<td>30</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>318</strong></td>
<td><strong>320</strong></td>
<td><strong>2.23</strong></td>
</tr>
</tbody>
</table>

Total events: 53, 30
Heterogeneity: Ch2 = 4.65, df = 4 (P = 0.20), I² = 0%
Test for overall effect: Z = 3.29 (P = 0.001)
Chapter 4: Systematic Review of Intervention Studies

FIGURE 29: META-ANALYSIS OF CONTINUOUS ABSTINENCE AT 12 MONTHS

FIGURE 30: META-ANALYSIS OF POINT PREVALENCE ABSTINENCE AT 12 MONTHS
Four trials measured and reported point-prevalence smoking abstinence rates at 12 months (Figure 30). The OR for point prevalence abstinence at 12 months was 1.29 (95% CI 0.79, 2.11; p = 0.31) and favoured exercise, but was not statistically significant. A fixed effects model was used as significant heterogeneity was not found ($I^2=0\%$, p = 0.31). A sensitivity analysis was conducted excluding one study where it was unclear if an ITT approach was followed. The pooled weighted intervention effect changed only slightly with this study excluded (1.37; 95% CI 0.82, 2.32; p = 0.23).

### SECONDARY OUTCOMES

#### Anthropometric outcomes

Ten studies examined the effect of interventions on changes in weight. Of these, two showed a significant difference in weight gain between treatment groups in favour of exercise. However, in one of these, baseline differences in weight between groups were observed, which was not controlled for in the analyses. Prapavessis et al. found that participants in the exercise only treatment group had significantly less weight gain than those in the group receiving only cognitive behavioural therapy (CBT) at the end of treatment; however, this group also had the lowest rate of quitting of the four groups studied. No other studies showed any effect of exercise on change in weight when compared to a control group. As Ussher et al. suggest, some of these studies were too small to detect any differences in weight, and the larger trials provided NRT to both treatment arms, which may have attenuated post-cessation weight gain. Indeed, whereas Prapavessis et al. observed a difference in weight gain between exercise only and CBT only groups, they found no difference in weight gain between the exercise + NRT group and the CBT + NRT group. Two studies found trends towards a significant difference in weight gained in favour of exercise among participants who were abstinent at 12 months post-quit date (p=0.06).
With respect to other anthropometric outcomes, Ussher et al.\textsuperscript{204} found no differences between groups in percentage body fat or BMI at six weeks post-quit date. Ciccolo et al.\textsuperscript{184} found trends for body composition and body fat in favour of the resistance exercise condition compared to the control group at three and six months post-quit date, but the sample size was too small to detect a statistically significant difference.

### 4.3.6.2 Physical activity

As Ussher et al. stated in their Cochrane review,\textsuperscript{68} most studies did not measure and/or report physical activity levels among the control group, which makes it difficult to summarise the effect of exercise interventions for smoking cessation on physical activity levels. Of the studies that did report physical activity levels for both intervention and control groups, there were mixed results. Three studies\textsuperscript{181, 184, 205} found a statistically significant difference in favour of the exercise group at the end of treatment for physical activity level (measured in METS\textsuperscript{181, 184} or total minutes of physical activity\textsuperscript{205}), whereas others found no difference between groups for physical activity at end of treatment.\textsuperscript{187, 196, 204} Hill et al.\textsuperscript{185} reported that the exercise group increased their activity levels throughout the course of treatment compared with no change in the control group, but did not report whether this difference was statistically significant. Of the three studies that reported an effect at the end of treatment, only the effect in the study by Bize et al.\textsuperscript{181} was maintained to one year follow-up. However, three studies showed increased levels of exercise in the control group from end of treatment to follow-up, which may have attenuated any apparent effect of the intervention.\textsuperscript{184, 203, 205}

### 4.3.6.3 Physical Fitness

Seven studies reported an increase in physical fitness at the end of treatment.\textsuperscript{178, 184, 186, 189, 191, 198, 202} Of these, only Prapavessis et al. measured fitness at follow-up and found that the increase in physical work capacity in the exercise group from baseline to end of treatment returned to baseline levels after one year.\textsuperscript{198} Vickers et al.\textsuperscript{205}
found no change in VO$_{2\text{max}}$ scores from baseline to end of treatment in either group, and whilst Kinnunen et al.\textsuperscript{187} showed a greater increase in VO$_{2\text{max}}$ in the exercise group than the equal contact and standard treatment control groups, the difference between groups was not statistically significant.

### 4.3.6.4 Psychological variables

Of the eight studies that reported changes in TWS,\textsuperscript{178 180 181 183 187 191 200 203} only two showed a difference between groups. Ussher et al.\textsuperscript{203} found significant interaction effects for tension, anxiety, and stress, up to one week smoking abstinence, for irritability up to two weeks abstinence, and for restlessness up to three weeks abstinence, such that ratings of these symptoms were lower in the exercise group compared to the control group. Bock et al.\textsuperscript{183} found significant reductions in anxiety in participants undertaking a yoga exercise programme compared with no change in the control group at the end of an 8-week programme. Conversely, Russell et al.\textsuperscript{200} found that tension-anxiety scores were increased in the exercise group compared with controls at four months follow-up, suggesting that increased exercise had a detrimental effect on anxiety. However, as Ussher et al.\textsuperscript{68} stated in their Cochrane review, this may have reflected extraneous variables that could not be controlled for with such a small sample.

Negative affect was reduced in the exercise group compared to the control group in two studies,\textsuperscript{183 205} whereas one study\textsuperscript{193} found no significant differences between groups for mood or depression.
4.4 DISCUSSION

This chapter has systematically reviewed the evidence regarding the effect of exercise on smoking cessation, and has raised a number of pertinent issues. First, although the majority of studies have failed to find a significant effect of exercise on smoking cessation, findings from these meta-analyses suggest that exercise does have an effect on point prevalence smoking abstinence, at least up to six months. The weighted OR for point prevalence abstinence at six months was 2.23 in favour of exercise (95% CI 1.38, 3.60; p = 0.001). However, meta-analyses for continuous abstinence as the outcome measure found no effect. Although continuous abstinence is generally considered to be the gold standard measure of abstinence, it does not account for delayed intervention effects, nor those participants who relapse to smoking during the treatment period but quit again before the end of treatment (or follow-up assessment). Such participants would be better reflected using point prevalence measures of abstinence at follow-up.

Second, the positive effect of exercise on point prevalence abstinence found at 6 months was not observed at 12 months. All of the exercise programmes from the studies in the two meta-analyses examining point prevalence abstinence at 6 and 12 months were between 8 and 15 weeks in duration. The results of these meta-analyses suggest that the effect of exercise on smoking abstinence following a 2- to 4-month programme may last up to 6 months, but these effects dissipate by 12 months. Unfortunately, there are too few studies in each meta-analysis, and only two studies in both meta-analyses, to reliably draw conclusions regarding the temporal effects of exercise on smoking abstinence, or the intensity and duration of these programmes.

Third, the strong effect observed in the meta-analysis of point prevalence abstinence at six months’ follow-up was largely due to the contribution of one study. The study by Marcus et al. was the first of the larger trials conducted (those with a sample
size greater than 65). Their exercise programme comprised of a structured supervised programme of facility-based vigorous-intensity exercise 3 times per week for 12 weeks. They therefore recommended that subsequent research establish the effectiveness of lighter exercise intensities, and exercise in unsupervised settings. Indeed, moderate-intensity exercise has been shown to have a higher feasibility of adoption, lower risk of injury, and requires less need for supervision. It may also promote better adherence. However, subsequent trials of moderate-intensity exercise incorporating an unsupervised component did not produce a statistically significant effect between treatments for smoking abstinence.

The dearth of statistically significant results in favour of exercise across studies may be explained by findings observed for some secondary outcomes. None of the reviewed studies found an effect on physical fitness, weight gain, or psychological outcomes beyond the end of treatment, and only one study showed an effect for physical activity in favour of the intervention at one year follow-up. If exercise interventions for smoking cessation do not increase long term exercise levels then, in such cases, any intervention effect on smoking abstinence could not be attributed to the exercise itself per se. However, as few studies have examined secondary outcomes beyond the end of treatment, it is difficult to determine the relationship between these secondary outcomes and smoking cessation rates.

Although there were no differences in weight gained beyond the end of treatment in any study, there were trends towards a significant difference in weight gain among those abstinent at 12 months in two studies. Neither study was powered to detect differences in weight for abstinent smokers, but findings suggest that for those participants who do manage to quit smoking, exercise may be beneficial in reducing weight gain. It would be useful to determine whether exercise interventions for smoking cessation can positively effect weight gain long term among abstinent former smokers. However, given existing rates of smoking cessation, the power
required to detect a difference in weight gained among abstinent smokers may result in a required sample size beyond that which is practically achievable given research funding constraints. Future studies need to measure weight at follow-up in abstaining smokers, in order to combine results in a meta-analysis.

4.4.1 POSSIBLE MODERATORS

4.4.1.1 Cessation self-efficacy or confidence

Three studies examined smoking cessation self-efficacy and/or confidence to quit as a potential moderator. Ussher et al.\textsuperscript{203} found that abstinence at 12 months was associated with greater self-confidence in quitting ability at baseline. Hill et al.\textsuperscript{186} showed that among all participants, regardless of treatment condition, those who had quit smoking at one year follow-up had higher self-efficacy for smoking cessation at baseline than control participants. Williams et al.\textsuperscript{208} found a significant baseline self-efficacy by treatment interaction effect on abstinence at post-treatment and follow-up, such that those with higher self-efficacy for smoking cessation at baseline were more likely to quit if they were in the exercise group relative to the control group, than those with low baseline self-efficacy. This was the case for both 7-day point prevalence abstinence and continuous abstinence.

4.4.1.2 Age

Age has been shown to be another potential moderator. Bize et al.\textsuperscript{181} found that when participants were split into two sub-groups based on the median age, younger participants in the exercise group were more likely to quit than younger participants in the control group, whereas the reverse was observed for the older participants. The authors proposed that future research should aim to test for explanatory mechanisms of this relationship, suggesting that older smokers may have less ability to cope with two behaviour change processes at once, or are simply less compliant with exercise interventions. However, contrary to this finding, Ussher et al.\textsuperscript{203} showed that smoking
abstinence at 12 months was significantly associated with older age, suggesting that any effects of age may be sample specific.

4.4.1.3 Exercise adherence

Lack of adherence to exercise treatment was a limitation of many of the reviewed studies. As Hill et al. stated, given the high number of non-adherent exercise group participants, it is difficult to determine whether exercise is responsible for smoking cessation or is simply an indicator of another secondary variable, such as participant motivation. There was also a general reduction in exercise adherence following the end of treatment in all studies. Marcus et al. proposed that exercise adherence beyond treatment may be increased if the intensity or frequency of exercise is lowered.

A summary of the rates of treatment adherence for each study was presented in the Cochrane review by Ussher et al.; however, they did not summarise the effect of adherence on smoking cessation. In the present review, five studies reported positive effects of exercise adherence on exercise group cessation rates. Marcus et al. showed that the odds of achieving smoking cessation at the end of treatment increased by 40% with a 1-week increase in the number of weeks exceeding 110 minutes of physical activity. Kinnunen et al. found a significant association between post-quit exercise adherence and lower risk of relapse at all assessment points, including one year follow-up. However, there was no relationship between pre-quit exercise adherence and smoking relapse. Marcus et al. conducted multiple logistic regression analyses to determine the efficacy of treatment condition while adjusting for programme attendance, and found that exercise participants were 36% less likely to have relapsed at one year follow-up. Taylor et al. reported that those who had quit smoking had higher exercise adherence rates than those who continued to smoke, and Linke found that those exercise participants who reported
more exercise days on the study website throughout the intervention experienced greater reduction in smoking rates.

4.4.2 SUMMARY

The above review highlights the growing body of research to examine exercise interventions for smoking cessation. Although most individual trials have been unable to detect a difference in smoking abstinence rates between intervention and control groups, results from meta-analyses suggest that exercise has a significant positive effect on point prevalence abstinence up to six months. There are a number of methodological issues pertaining to the reviewed studies that limit the internal and external validity of these trials. The following summarises these issues with regard to exercise setting and delivery, and intervention duration.

*Exercise setting and delivery:* Most of the reviewed studies provided structured exercise in a supervised setting or a combination of both facility and home-based programmes lasting between 5 and 15 weeks in duration. Surprisingly, no studies have trialled community-based exercise programmes. However, such programmes may offer greater efficacy and potential for large scale implementation, greater participant adherence, and have greater appeal to sedentary smokers. There is good evidence from the physical activity literature that community-based exercise is related to greater adherence compared with facility-based programmes. A systematic review of randomised clinical trials reported a greater effect size for unsupervised versus supervised facility-based exercise programmes for self-reported exercise. Community-based interventions often incorporate a home-based component. There is a need to determine whether inexpensive community-based exercise interventions (including a home component) of greater frequency and grounded in behaviour change theory can augment smoking cessation outcomes, and maintain exercise, weight and fitness changes, as well as reduce smoking relapse. This review highlights the lack of clinical trials which
have evaluated the effectiveness of home and community-based lifestyle exercise maintenance interventions in assisting quitters to maintain exercise, fitness and weight following the termination of exercise aided smoking cessation programs, and hence prevent (or reduce) smoking relapse. Although cost-effectiveness data are lacking, community-based interventions have more scope for sustainability.

Three recent studies have explored ways to increase home- and community-based exercise using the internet. Exercise prescription was delivered either via a website or email in all three studies, and none found an effect on smoking abstinence. Two of these studies were not statistically powered to determine an effect on cessation outcomes. However, the findings of the two pilot studies do suggest that delivering exercise prescription remotely has potential to increase home- and community-based exercise participation, and possibly impact smoking abstinence.

As well as delivering exercise prescription remotely, another approach to aid and encourage home and community based exercise is the use of remote exercise counselling (i.e. counselling that is not conducted in a face-to-face setting). Although none of the reviewed trials offered counselling remotely, the efficacy of exercise counselling has been examined. Vickers et al. delivered Social Cognitive Theory-based exercise counselling sessions to their study population of depressed female smokers, providing 10 weekly face-to-face counselling sessions (the duration of each session was not reported). Although the study was not adequately powered to detect a difference in smoking abstinence rates, there was a significant difference in physical activity levels between groups at both 10 weeks’ (end of treatment) and 24 weeks’ follow-up.

The trial by Ussher et al. (n=299) involved brief periods of exercise counselling (five minutes of counselling in the first session, and two minutes thereafter for each
subsequent session) that were not sufficiently intense to achieve the desired level of exercise. The authors concluded that the frequency and nature of their counselling was not intensive enough to result in an effect. They suggested that future studies focus on an intervention that combines exercise counselling with some form of supervision. Moreover, receiving professional support was suggested to have an important role in increasing exercise adherence.\textsuperscript{204}

Another study,\textsuperscript{229} not included in this review as results have not been published yet, utilised trained counsellors to provide two dedicated ‘in-house’ physical activity sessions to promote moderate-to-vigorous activity (including pedometer administration, step count monitoring and goal setting). During the smoking relapse prevention programme (20 weeks) counsellors encouraged on-going step monitoring with biweekly 10\% increases in steps towards meeting the goal of 10,000 steps per day. Smoking cessation outcomes have not yet been published but increased moderate-to-vigorous physical activity was associated with greater abstinence. The overall effect of exercise was also greater for interventions that prompted activity more frequently (5+ occasions) compared to low level prompting (0-4 occasions). The authors concluded that interventions, which provide people with professional guidance about starting an exercise regimen and then provide ongoing support, may be more effective in encouraging uptake of the behaviour.

\textit{Intervention duration:} The duration of the intervention is also important. More trials of interventions of longer than 2-3 months’ duration are needed. The meta-analyses show that exercise programmes are effective at increasing smoking cessation rates up to the end of the treatment, but few studies have found statistically significant effects on smoking abstinence at follow-up. Interventions therefore need to be long enough to allow participants time to reach the maintenance stage of exercise behaviour change. Moreover, participants need to be provided with the skills, and
counselling to build self-efficacy during the intervention, to enable maintenance of the exercise behaviour to be sustained once the intervention ends.

4.5 CONCLUSION

Exercise shows promise as a useful adjunct to smoking cessation programmes. Most trials to date have provided structured exercise as a supervised programme but have been too small and therefore underpowered (11 of the 20 reviewed trials sampled less than 65 participants), and/or too low in intensity or duration to conclude that there is an effect of intervention. Exercise interventions varied in intensity and duration from study to study and in particular may not have been sufficiently intense or reliably sustained to achieve the desired effect. Meta-analyses results suggest that exercise is effective for smoking cessation, but the most effective modality, intensity, frequency, and duration of exercise, method of intervention delivery, and exercise setting, remain unclear. Moreover, only six trials reported physical activity outcomes, and of these only three found statistically significant differences in physical activity between intervention and control groups at the end of treatment. Due to the lack of reporting of physical activity outcomes across studies it is unclear whether exercise interventions for smoking cessation have been unsuccessful because they did not increase exercise behaviour, or because exercise is not a good smoking cessation aid. The majority of studies have also suffered from poor exercise adherence, which also exacerbates the problem of assessing the effectiveness of exercise as a smoking cessation aid. The Cochrane review concluded that further trials are needed with larger sample sizes, sufficiently intense exercise interventions, and measures of exercise adherence. This conclusion is echoed in the findings presented in this chapter. The lack of effect of exercise on smoking cessation rates observed in most studies is in contrast to the statistically
significant effects of acute exercise on cigarette cravings observed across most studies reviewed in Chapter 2. This apparent discordance highlights the complexity of the role of exercise as a smoking cessation aid. It is possible exercise only acts acutely to reduce cigarette cravings, and does not aid smoking cessation. However, exercise does aid quitting for some individuals so it may be that personal characteristics, such as attitude and motivation towards exercise, determine whether exercise is a useful adjunct to smoking cessation. The confounding role of individual differences will be discussed further in the remaining chapters.

Despite the assumption that exercise should minimize weight gain during a quit attempt, few studies have found this to be the case. However, this likely reflects the inability of interventions to date to increase exercise behaviour, rather than the inability of exercise to reduce weight gain among quitting smokers. Improvements in exercise adherence are required before exercise-based reductions in weight gain during smoking cessation will be observed. With the observed rates of exercise adherence to date, NRT does appear to attenuate any effect of exercise on post-cessation weight gain. It is unclear whether greater exercise adherence would reduce weight gain over and above the effects of NRT.

The assumption that exercise aids smoking cessation via its effects on self-esteem, confidence, or self-efficacy has not been tested in trials of exercise interventions for smoking cessation.
CHAPTER 5  EXERCISE TO ENHANCE SMOKING CESSATION OUTCOMES: THE FIT2QUIT TRIAL

5.1  INTRODUCTION
The systematic review in Chapter 4 highlights that, while exercise shows promise as a useful adjunct to smoking cessation programmes, there are insufficient data to conclusively support its effect, and thus, additional research is required. Previous trials have provided structured exercise as a supervised programme, have included small sample sizes, and have been of low intensity or duration, which may have contributed to the lack of effect observed to date. This chapter will present the results of a large RCT designed to address these methodological issues. The study incorporated a telephone counselling intervention to provide exercise prescription and support for people to exercise in their home and/or community environment. Ten contacts (face-to-face and telephone) over 6 months with referral to community-based activities and programmes was provided.

5.1.1  OBJECTIVES
The primary objective was to determine the effect of an exercise intervention on smoking cessation rates at six months when added to usual care (smoking cessation support + NRT) in comparison with usual care alone.

Secondary objectives were:

- To examine the effect of exercise and control conditions on change in physical signs and symptoms associated with withdrawal and urges to smoke
- To examine the effect of exercise and control conditions on smoking behaviour (the number of cigarettes currently smoked per day [for those still smoking], information on NRT use)
- To examine the effect of exercise and control conditions on change in self-
reported physical activity

- To determine the cost effectiveness of the intervention to improve smoking cessation
- To determine the effect of exercise and control conditions on change in weight and BMI, physical fitness, leisure exercise, self-efficacy, and motivation in a sub-sample

5.1.2 HYPOTHESES

The addition of exercise to usual care will produce greater 6-month abstinence rates than usual care alone.

Secondary hypotheses are that:

1) In comparison to usual care, the exercise intervention group will increase self-reported physical activity levels at eight weeks and six months

2) Among sub-sample participants, relative to usual care participants, the intervention group will:
   a. gain less weight at six months
   b. increase self-efficacy
   c. increase fitness

3) the programme will be cost-effective compared to usual care

5.2 METHOD

5.2.1 DESIGN

A prospective, parallel, two-arm randomized controlled trial was conducted between January 2010 and January 2012. A pragmatic study design was chosen to evaluate the benefits of an exercise intervention in addition to existing smoking cessation support, in a real or everyday approach. Pragmatic trials answer questions about the overall effectiveness of an intervention package, rather than investigate the
contributions of its different components. Eligible participants were randomised in a 1:1 ratio to either an exercise intervention plus usual stop smoking support or to usual stop smoking support alone (i.e., usual care), following a baseline assessment. Randomisation was via a computerised central randomisation service, stratified by study centre (Auckland and Waikato), sex (male and female) and ethnicity (Māori and non-Māori).

5.2.2 PARTICIPANT RECRUITMENT
Study procedures and terms were approved by the NZ Multi-region Ethics Committee (MEC/09/08/090). Participants were recruited through Quitline (the national smoking cessation helpline in NZ, http://www.quit.org.nz/). Contact details of Quitline callers who agreed to be contacted about research and who went on to receive the usual Quitline programme of eight weeks of NRT (patch, gum and/or lozenge) and behavioural support, were forwarded to the study coordinating centre. The research team attempted to contact all referrals to inform them of the trial. Interested participants were registered for the study once they had provided oral informed consent. A research assistant recorded each potential participant's details (participant initials, date of birth, and sex) and assigned them a registration number, prior to screening for eligibility. Participants were eligible for the study if they were at least 18 years of age, a resident in the greater Auckland and Waikato areas, interested in quitting, wanted to be physically active, smoked at least 10 cigarettes per day (including roll your own), smoked their first cigarette within 30 minutes of waking, contactable by telephone, and able to provide written informed consent. Participants were excluded if they had a stroke or heart-related condition in the last two weeks, were enrolled in competing smoking cessation programs, had a medical condition which limited their ability to exercise safely, currently participated in an exercise program, or participated in greater than 150 minutes of physical activity per
week. Once eligibility was determined a baseline assessment session was scheduled.

5.2.3 SAMPLE SIZE

The estimated effect size of the intervention on quit rates at 6 months needed to be realistic, yet clinically significant. The percentage of successful quit attempts at 6 months achieved through Quitline in 2008 (when the trial was designed) was 15%. The effect size was estimated at 7.5% which was half that of the control group (Quitline) quit rate. This effect size was chosen because a 7.5% difference between groups represented a 50% improvement in quit rates, which would be clinically relevant. A sample size of 1,400 participants (700 per arm) was calculated to provide 90% power at 5% level of significance to detect an increase in quit rates over baseline from 15% to 22.5% at six months, assuming a dropout rate of 20%.

Given the high prevalence of smoking among Māori, this study aimed to recruit at least 25% of participants (n=350 with 175 per arm) who self-identify as Māori, to determine consistency of effects for this population. Based on the targeted sample size for Māori, and maintaining equal explanatory power for Māori (90% power at 5% level of significance), it was calculated that we would be able to detect a 15% difference between groups, which would represent a doubling of quit rates over baseline at six months.

Early on in the trial it was clear that we would not recruit 1400 participants. Based on the current recruitment rate at the time, it was estimated that 970 participants (485 per group) would be recruited. Using this revised target and working backwards to determine the size of the effect that we would be able to detect, a revised power calculation estimated a minimum difference of 10% in smoking cessation rates (adjusting for 20% loss to follow-up) could be detected with 90% power at the 5% level of significance.
5.2.4 PROCEDURE AND SETTING

Two approaches to collecting participant data were used in the present study. The primary approach was to administer questionnaires via a telephone assessment. A sub-group of participants completed a face-to-face assessment, during which they provided additional information to those in the telephone assessments (full details are provided below).

5.2.4.1 Telephone administered assessment procedures

During the registration phone call, eligible participants were given the option to attend a telephone assessment or face-to-face assessment. For those who chose a telephone-based assessment a research assistant recited the Participant Information Sheet (Appendix 13) and Informed Consent Form (Appendix 14) to the participant before proceeding further. Participants were given the opportunity to ask questions and clarify any information. The research assistant then signed an informed consent form on behalf of the participant. At the conclusion of the telephone call, participants were mailed a Participant Information Sheet, as well as a copy of their Informed Consent Form for their own records. Participants were then given the option to complete the baseline assessment in the same phone call, or at a scheduled time within the next three days. During the baseline assessment, participants completed questionnaires on smoking history, current smoking status, physical activity, and costs. Study researchers entered questionnaire responses directly into electronic case record forms on the study website. Participants were then randomised via a central randomisation web-based service to either intervention or control groups using three stratification factors: study centre (Auckland or Waikato), sex, and ethnicity (Māori or non-Māori).

Participants allocated to the control group were informed of their group allocation and encouraged to continue with the Quitline programme and NRT. They were informed they would be contacted in eight weeks for a follow-up telephone assessment.
Participants allocated to the intervention group were informed of their group allocation, and informed they would be contacted within the next week to set up an initial face-to-face interview with an exercise support person to commence the intervention.

5.2.4.2 **Face-to-face assessment procedures**

Following the registration phone call, participants were sent the face-to-face assessment Participant Information Sheet (Appendix 15) and Informed Consent Form (Appendix 16), and were scheduled for a baseline face-to-face assessment. Assessments were offered at a variety of locations within the Auckland region (the University of Auckland Tamaki campus in Glen Innes, Sport Auckland in Greenlane, and a community centre in Manukau), and the Sport Waikato office in Hamilton. Upon arrival at the baseline assessment, participants were offered the opportunity to ask any questions and returned signed consent forms. As per the telephone administered assessment, participants completed questionnaires on smoking history, current smoking status, physical activity, and costs. Additionally, participants completed psychological measures related to physical activity participation and a step test to measure aerobic capacity. Height and weight were also measured. Participants were then randomised to either intervention or control groups as per the procedure described above.

Repeat assessments were conducted at 8 and 24 weeks. For all participants the 8-week assessment was conducted by telephone, during which participants completed measures of smoking status, health care utilisation, and physical activity. Those participants who attended a face-to-face assessment at baseline also completed the psychological measures related to physical activity participation. Not every participant was available at 8 weeks, thus, anytime between week 7 and week 10 was considered acceptable. At least three attempts were made to contact each participant. If the participant could not be contacted within this time frame, the 8-week
assessment data were not collected. Identical procedures to the baseline assessments were conducted at six months, except that attempts were also made to verify quit status via salivary cotinine. Not every participant was available at 24 weeks, thus, anytime between week 24 and week 28 was considered acceptable. At least three attempts were made to contact each participant. If the participant could not be contacted in this time frame, the 24-week assessment data were not collected. See Figure 31 for a flow chart of study procedures.

5.2.5 MEASURES

5.2.5.1 Demographics and smoking history
Age, sex, ethnicity, employment status, primary occupation, level of education, marital status, household income level, and smoking history were collected at baseline. For smoking history, participants were asked to report the amount of cigarettes they usually smoke, whether they smoke ‘roll your own’ or tailor-made cigarettes, if they usually smoke cigars or tobacco from a pipe, the number of years they had been smoking continuously, history of previous quit attempts, services/products used in previous quit attempts, and the FTND. Participants were also asked whether they were using NRT and any non-study medications at baseline and at week eight. The paper case record forms for all measures used in the Fit2Quit trial are located in Appendices 17-21.

5.2.5.2 Smoking status
Self-reported 7-day point prevalence of smoking abstinence was assessed with a single item: “Have you had a single puff of a cigarette in the last seven days.” Self-reported continuous abstinence was measured with a single item: “Have you smoked more than 5 cigarettes since your nominated quit date,” as per the Russell Standard. Participants could respond to each of these questions with “Yes” or “No.”
5.2.5.3 Tobacco withdrawal symptoms

TWS were assessed using the Mood and Physical Symptoms Scale, a validated self-report instrument that assesses whether the participant was depressed, irritable, anxious, had disturbed sleep, or had poor concentration in the previous week, using a 5-point Likert-type scale ranging from 1 (not at all) to 5 (extremely) for each symptom. Participants were also asked to report the amount of time they felt urges to smoke in the previous week on a 6-point Likert-type scale ranging from 1 (not at all) to 6 (all of the time).
Chapter 5: The Fit2Quit Trial

**FIGURE 31: FLOW DIAGRAM OF STUDY PROCEDURES**
Physical activity levels were assessed using the International Physical Activity Questionnaire (IPAQ), one of the most reliable and valid self-report instruments, using a 7-day recall period, to provide a comprehensive evaluation of daily physical activities, and the time spent walking, and doing light-, moderate-, and vigorous-intensity activities across various domains. For analysis, both total physical activity score and total scores for each of the domains (work, active transport, domestic & garden, leisure-time) were calculated and reported in MET (metabolic equivalent) minutes per week.

Cost effectiveness information

Determining the cost-effectiveness of a smoking cessation programme requires comparing the costs and outcomes of those receiving the intervention with the costs and outcomes of the usual-care group. The analysis takes the perspective of the health-care funder by including direct medical expenses incurred by the funder and the individual. For the period of the trial, the costs incurred included the cost of delivering the programme (e.g., resources and staff time needed to travel to site and administer the programme, including a 50% overhead rate for all staff time). The long term costs of smoking cessation include the medical costs associated with avoiding lung cancer and cardiovascular disease. This was calculated by applying NZ costs and prices to NZ resources use, and international estimates when there was no NZ information available.

The primary outcome of the cost-effectiveness analysis was quality-adjusted life years (QALYs). Although utility scores (EQ-5D) were measured at the beginning and end of the study period, previous studies have demonstrated that the cost-effectiveness of smoking cessation programmes is dependent on the quit rates at 6 or 12 months and subsequent relapse rates. As the long-term benefits from smoking cessation (e.g., avoided cases of lung cancer) may not be evident for many
years, the analysis used a Markov state transition model to track costs and QALYs for a hypothetical cohort model of participants moving between specified health states at the end of each cycle. Utility values for each health state (e.g., early stage lung cancer [I&II], advanced stage lung cancer [III&IV], stable lung cancer, progressive lung cancer or no lung cancer) were assigned from a structured literature review of preference-based quality-of-life scores or utility weights for lung cancer. Long-term cost of cancer (e.g., early lung cancer 1st year, advanced lung cancer, ongoing costs of stable disease, progressive disease and terminal care) were taken from previous studies and adapted for NZ. The model tracked the hypothetical cohort of smokers from age 30 years over their lifetime. The Markov model used the trial results, NZ life tables, National Minimum Data Set and international evidence (for probabilities, relative risks, and costs) to estimate life-time events (cardiovascular disease and lung cancer), costs, and effects (QALYs) from the age of 30. Cost-effectiveness results were produced separately for two cohorts: all males, and all females. Both EQ-5D ITT analysis and unverified point prevalence and continuous abstinence rates were used in the cost-effectiveness model. In the Markov model, relapse rates for quitters were 10% for both arms (Fit2Quit and control) for the first six years, and then 0% per annum after that. The incremental cost-effectiveness ratios (ICERs) report the incremental cost per QALY gained. Costs and QALYs were discounted at 3.5% and reported in 2010 NZ dollars. In order to understand the robustness of the results to changes in relapse rates, sensitivity analysis examined alternative specifications (e.g., males only, females only) of successful quit attempts and continued abstinence. Using the Markov model and probabilistic sensitivity analysis (using information on the means and standard deviations from the trial when available and from the international literature otherwise) we examined the robustness of the results to uncertainty in parameter estimates. The analyses used a willingness-to-pay ICER threshold.
(implied NZ threshold) of $20,000 per QALY gained to guide the interpretation of the findings, a level in keeping with higher-end cost-effectiveness ratios found in previous evaluations of smoking-cessation programmes.\textsuperscript{239}

5.2.6 SUB-SAMPLE MEASURES
The following measures were examined in participants in the face-to-face sub-group only.

5.2.6.1 Body mass index
Anthropometric data were measured using standard practices.\textsuperscript{240} Weight was recorded to the nearest 0.1 kilogram using calibrated measurement scales (Tanita HD332, Tokyo). Height was measured using a stadiometer (Leicester Height Measure, UK) to the nearest 0.1 cm.

5.2.6.2 Psychological measures
Psychological variables were assessed to determine their potential mediating effect. Specifically, physical activity task efficacy was assessed using nine items adapted from the Self Efficacy Scale.\textsuperscript{241} Participants rated their level of confidence to perform physical activity at increasing intensity levels and increasing amounts of time most days of the week. Durations used were 10 minutes, 30 minutes and 60 minutes and intensities were labeled as light, moderate, and hard. Participants were provided with descriptions of the intensity levels and examples of types of physical activities at each level. Participants rate their confidence levels on a scale ranging from 0\% (I am not confident at all) to 100\% (I am completely confident). Scores from these items were summed, and divided by nine to give a mean score for task efficacy. Greater scores indicated greater efficacy to perform physical activity at harder intensities for longer periods of time.

Six items adapted from the Barriers Efficacy Scale\textsuperscript{241} were used to assess participants’ perceived confidence to perform regular physical activity in the face of
particular barriers (e.g. “If it is bad weather”). Participants rated their confidence levels on a scale ranging from 0% (I am not confident at all) to 100% (I am completely confident). Scores from these items were summed, and divided by six to give a mean score for barrier efficacy (BE). Greater scores indicated greater efficacy to perform physical activity in the face of a variety of barriers.

Self-determination to exercise was operationalised using the Locus of Causality for Exercise Scale (LCE); a reliable and valid 3-item self-report measure of the extent to which participants feel they choose to exercise with no sense of coercion. Participants rate how much they agree or disagree with each statement on a seven-item Likert scale from 1 (Strongly disagree) to 7 (Strongly agree) indicating their motivation to perform exercise. Scores from these items were summed and divided by three to provide a mean score for exercise motivation. High scores indicated greater self-determination or a more internal perceived locus of causality.

5.2.6.3 Exercise Behaviour
Exercise was assessed using the Leisure Score Index (LSI), which includes three items to assess the frequency of mild, moderate, and vigorous exercise performed during free time for at least 15 minutes during a typical week. The LSI is used to provide specific information on exercise behaviour rather than habitual physical activity, which was assessed with the IPAQ. Weekly exercise minutes for mild, moderate, and vigorous exercise, plus combined scores for moderate and vigorous exercise minutes were calculated. The LSI possesses acceptable test-retest reliability and concurrent validity.

5.2.6.4 Physical fitness
There were a number of considerations when choosing the appropriate measure of physical fitness for the study. Measuring aerobic fitness at the population level requires the use of a submaximal test, as direct tests of maximal oxygen consumption require the recording of breath-by-breath gas exchange. A submaximal
test allows the researcher to take the test out of the laboratory environment and into the field. Given the face-to-face assessments were to be conducted in office meeting rooms and community centres, it was important to choose a physical fitness test that a) could be conducted within a small space, and b) did not require the transport of heavy equipment between sites. This eliminated cycle ergometry and treadmill tests, as well as walking and running tests usually conducted on a running track or basketball court. Hence, a sub-maximal step test was chosen. A number of sub-maximal step tests have been developed to measure aerobic fitness. The Astrand-Ryhming step test was initially chosen, which requires participants to step up and down on a 40cm step (men) or 33cm step (women) at a rate of 22.5 body lifts per minute for 5 minutes. However, pilot tests revealed that this test, which was developed on active subjects, was too challenging for many of the sample of insufficiently active smokers to complete. Thus, a second test, which had been developed for use with the general population, was chosen.

In this trial, physical fitness was assessed using the Step Test, a simple field test of aerobic fitness, which has been found to correlate well with maximal oxygen consumption ($VO_{2\text{max}}$). The test was initially used to determine the reliability and validity of the Actiheart (Cambridge Neurotechnology Ltd, Papworth, UK), a single device designed to measure both movement and heart rate. However, it has since been employed as the measure of physical fitness in adults in the Health Survey for England (HSE), 2008. The Step Test was chosen for the health survey for practical reasons, as survey participants were assessed in their own homes and, as such, research nurses needed a fitness test that could be conducted in a small space with equipment that was easily transportable. As the requirements for the Fit2Quit study fitness test were similar, the Step Test used in the HSE was chosen for the Fit2Quit study.
During the Step Test participants were fitted with a heart rate monitor (a transmitter around the chest and wrist unit), and seated for five minutes prior to the test. Two different heart rate monitors were used, the Garmin Forerunner 305 GPS–enabled device with heart rate (Garmin [Europe] Ltd, UK), and the Polar F6™ Black Coal fitness heart rate monitor (Polar Electro Oy, Finland). The lowest recorded heart rate during the 5-minute seated period was recorded as the participant’s resting heart rate (rest phase). Participants were instructed to step on and off a fixed platform (height = 20cm for those aged 18-54, or 15cm for those aged 55 and over) in time with a digital audio file played on a laptop computer, for a maximum of 8 minutes. The starting step rate was 15 body lifts (up and down off the platform) per minute, which increased gradually throughout the test, reaching a maximum rate of 33 body lifts per minute by the end of the 8th minute (exercise phase). The participant’s heart rate was recorded at 30-second intervals throughout the test. On completion of the test, participants were seated and heart rate data were recorded for a further 2 minutes at 15-second intervals (recovery phase). For safety reasons, the test was terminated if their heart rate exceeded 85% of their estimated age-specific max heart rate (calculated as 208 - age x 0.7), or if they lost balance, could no longer keep in time with the beat, or wanted to stop.

*Step test data processing:* All heart rate measurements were recorded manually on a paper form during the assessment, and entered into a Microsoft excel spreadsheet for data processing. Data processing procedures were conducted by Dr Soren Brage and Dr Kate Westgate at the Medical Research Council Epidemiology Unit, Cambridge, England using data from a previous validation study, which calibrated the step test against maximal oxygen consumption.

Participants’ heart rate data were separated into three phases: rest, exercise, and recovery. Resting heart rate was recorded as the minimum heart rate observed during the rest phase. All heart rate observations in the exercise and recovery
phases were then expressed as heart rate above rest (HRaR). Based on the validation study in the UK, an estimation equation was derived for the physiological activity intensity (PAI) required throughout the step test to undertake the mechanical work to lift the body up and down the step (a product of step frequency, step height, and the gravitational constant). A linear regression was fitted between the estimated PAI and the HRaR values during the exercise phase to determine the slope and intercept of the straight line. The recovery heart rate values were then fitted in a quadratic regression equation against recovery time to determine the 1-minute recovery HRaR. An example of the graph produced following these calculations is provided in Appendix 22). Using the validation dataset, an estimate of sub-maximal PAI was derived from the slope and intercept of the straight line from the linear regression of the exercise phase, 1-minute recovery HRaR, step test duration, and resting heart rate. This relationship was then extrapolated up to age-predicted maximal heart rate to provide an estimate of the participant’s maximal oxygen uptake ($VO_{2\text{max}}$).

**Data cleaning:** First, to eliminate noisy observations (irrelevant or meaningless data) from the analysis, three equal observations in a row and/or outliers deviating by over 40bpm from the previous value were classified as noisy, and excluded in the linear regression. Second, alternative equations were derived for tests in which it was impossible to use the test phase or the recovery phase due to the number of noisy observations. For tests where it was not possible to obtain an accurate estimate of 1-minute recovery HRaR, due to noisy data during this phase, an alternative equation was used to determine $VO_{2\text{max}}$ based on the rest phase and exercise phase data. Similarly, if there were too many noisy observations in the test phase, an alternative equation was used to determine $VO_{2\text{max}}$ using the rest phase and recovery phase data. Finally, estimates of $VO_{2\text{max}}$ could not be derived for participants with step test durations of less than four minutes, and were therefore excluded from analyses.
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Following these processes, a manual check of the graphs of the revised data for each participant conducted to ensure all noisy data had been removed. For analysis, Mean VO$_{2\text{max}}$ is expressed relative to weight (ml/O$_2$/min$^{-1}$/kg$^{-1}$).

5.2.6.5 Exit interviews

A sub-sample of intervention group participants participated in a telephone-administered exit interview to evaluate participants’ perceptions of the Fit2Quit exercise intervention. Details of the methodology of the exit interviews are outlined in Chapter 6.

5.2.7 INTERVENTION

Participants randomised to the intervention group commenced a comprehensive 6-month home and community-based exercise programme in addition to usual Quitline smoking cessation support. The intervention started within one week of the baseline assessment and continued for the duration of the study (24 weeks). Participant’s quit date was recorded so the length of time between the quit date and the start of the exercise programme could be determined. Previous research has recommended exercise start before the quit date$^{252}$ to reduce the demand of coping with two major changes in health behaviour simultaneously.$^{253}$ $^{254}$ Unfortunately, this approach was not possible in the Fit2Quit study for two reasons. First, participants were recruited through Quitline and therefore had already initiated their quit attempt before they were contacted about the study. Second, participants had already received their ‘Quit Pack’ (containing information and NRT) before the exercise programme started.

The aim was to identify an intervention that was sufficiently intense to lead to a putative effect on withdrawal syndrome while being acceptable and tolerable to participants such that they would be likely to maintain physical activity levels over the duration required. The intervention also had to be feasible and easily replicable, which would allow it to be implemented on a widespread basis if successful. The intervention identified as a basis for the study intervention was Green Prescription
(GRx) services in NZ. A GRx is a referral from primary care to agencies that support physical activity, typically involving monthly telephone support for three months to become more physically active for health benefit. GRx providers assist with goal setting, information, and psychological support, and usually include healthy eating information and advice. An evaluation of the GRx programme found it to be an effective and cost-effective programme for increasing physical activity.

However, to maximize the impact of exercise among those trying to quit smoking, participants in the study were provided with a more intensive and comprehensive exercise programme than the usual GRx regimen. A total of 10 contacts (face-to-face and telephone support sessions) delivered over 6 months was offered, with the goal of individuals participating in a minimum of 30 minutes of moderate-to-vigorous aerobic-based exercise on most days of the week, in line with current recommendations.

Research has documented telephone-assisted exercise counselling as beneficial and cost-effective. Hence, in this study participants received 1-2 face-to-face support sessions and 8-9 telephone calls, in which the focus was on altering the key mediators of physical activity. Participants were also offered the opportunity to participate in existing community-based group physical activity programs.

Following randomisation, an introductory face-to-face meeting with a trained GRx participant support person (PSP) was scheduled with participants in the intervention group. During this session, the PSP ascertained the participant's exercise history, preferences for activity, and barriers to participation. Participants were given a pedometer to encourage physical activity, which was also used as a tool to monitor progress. Participants were asked to wear the pedometer for the first week to provide an indication of baseline physical activity.
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Following the face-to-face visit, the PSP conducted telephone calls to deliver the intervention on a weekly basis for four weeks, fortnightly for four weeks, then monthly as maintenance for the remaining three months. Contact was more intensive during the initiation period (eight weeks). Components included individual consultation, exercise prescription, and behavioural support to facilitate exercise initiation and maintenance.

In an attempt to enhance participants’ understanding of the link between exercise and smoking abstinence, during each telephone consultation, the PSP discussed the benefits of physical activity for smoking cessation, and ensured awareness of the reason for exercising. The PSP prescribed exercise duration, frequency, and intensity, with the aim of increasing activity (measured by pedometer step counts) by 10% per week until maintenance (goal) levels were achieved. Walking was the primary (default) mode of activity but other activities such as swimming, cycling and culturally specific activities (e.g. Kapa Haka [dance], Waka Ama [outrigger canoe paddling]) were encouraged based on individual preferences, past history, and access to facilities such as swimming pools and gyms. A role of the PSP was to assist individuals to find activities that ‘best fit’ their personal needs and then facilitate involvement. The exercise prescribed was aerobic in nature (e.g., walking) and performed at an intensity equivalent to between 50%-85% of VO\textsubscript{2max}. An equivalent perceived exertion level of 4-6 out of 10\textsuperscript{153} was used to assist participants to exercise at the appropriate intensity. By slowly increasing the frequency, intensity, and duration of exercise, participants gradually develop a sense of mastery and achievement, and hence, their own exercise identity.\textsuperscript{258}

In an attempt to overcome inequalities in affordability of access to physical activity participation the intervention group were also provided with exercise shoes and apparel if required. The need for this was addressed at the initial face-to-face interview with the GRx exercise facilitator. A relationship was established with ASICS
NZ (Brittain Wynyard & Co Ltd, Auckland, NZ), who agreed to provide sports shoes and apparel at cost-price for this study.

The Fit2Quit study exercise intervention was grounded in self-efficacy theory. Self-efficacy refers to “peoples’ beliefs about their capabilities to exercise control over events that effect their lives” (p. 1175). Self-efficacy is concerned with beliefs of personal capability; they are judgments of one’s capabilities to perform given actions and are often described as situation specific. Beliefs about behaviour outcomes are formed before the behaviour is performed. Initiation and maintenance of a particular behaviour is governed by one’s judgment and expectations of their ability to perform the behaviour. Most smokers making a quit attempt do not use physical activity to assist them but findings from surveillance research in the UK suggest that enhancing participant self-efficacy beliefs regarding physical activity as a smoking cessation aid may help increase the use of physical activity as a behavioural strategy.

There are various forms of self-efficacy. In terms of physical activity, task self-efficacy refers to one’s efficacious beliefs (or confidence) to complete a specific task (e.g. walking 30 minutes a day, 7 days a week). Barrier efficacy is one’s efficacious beliefs (or confidence) to overcome common obstacles to be physically active. Scheduling self-efficacy refers to one’s efficacious beliefs (or confidence) to make plans and schedule physical activity on a regular basis.

Generally self-efficacy has been proposed to come from four main sources: (1) past experiences (the most important source of self-efficacy – one’s previous achievements with the task at hand), (2) vicarious experiences (modeling- the process of comparing oneself with someone else), (3) social persuasions (positive encouragement from others), and (4) physiological factors (one’s perceptions of the physiological responses associated with unfamiliar situations, e.g. increased heart
rate during exercise). The intervention was designed to draw on all four of these sources at various stages of the programme.

A schematic presentation of the theoretical basis for the intervention is provided in Figure 32. As illustrated, the intervention was proposed to influence physical activity levels, which in turn would result in increased quit rates. The effect of the intervention on physical activity was proposed to be mediated through change in self-efficacy, and it is also possible that the effect of physical activity on quit rates could also be mediated by increased self-efficacy.

![Figure 32: A Schematic Diagram of the Theoretical Basis for the Study Intervention](image)

There have been a number of reviews that have discussed the role of self-efficacy in physical activity behaviour change. In one review of theory-based interventions to increase physical activity participation (18 interventions), Belanger-Gravel et al. found that Social Learning/Cognitive Theory was the most common theory applied, and that self-efficacy was the predominant variable targeted. Strategies to enhance self-efficacy have been shown to facilitate exercise initiation and maintenance in adults. Moreover, self-efficacy based interventions have been shown to be effective at increasing physical activity behaviour and adherence. Ashford et al. conducted a meta-analysis of the effectiveness of physical activity interventions to
increase self-efficacy, which revealed a small but statistically significant effect of physical activity interventions on physical activity self-efficacy (ES = 0.16; 95% CI 0.08, 0.25, p<.001).

Although numerous studies with adult participants have shown self-efficacy to predict physical activity behaviour (e.g.271-273), few have examined self-efficacy as a mediator of the intervention and physical activity behaviour relationship. To the best of my knowledge only four studies have tested self-efficacy as a mediator of intervention outcomes according to the guidelines for mediation outlined by Baron & Kenny162 (or similar guidelines274-276). Of these, two found significant mediating effects for self-efficacy,277 278 one found partial support,279 and one showed no mediation effect.280 More research is needed to properly test the mediating effects of self-efficacy. Moreover, as Bauman et al.281 suggested in their paper on the influences of physical activity, it is also possible that self-efficacy may moderate this relationship, such that an effect of a physical activity intervention on physical activity behaviour might only be evident in those with high physical activity self-efficacy, or even confound the relationship, as those with high self-efficacy are more likely to participate in a programme, and therefore will have greater increases in physical activity behaviour.

With respect to the moderation hypothesis, three studies have shown that participants with high exercise self-efficacy are more likely to act on plans to exercise than participants who doubted their ability.282 283 Based on the evidence outlined above, an intervention based on self-efficacy was considered the best approach to increase exercise behaviour in the Fit2Quit sample of previously insufficiently active smokers.

To ensure that the intervention focused on increasing self-efficacy, the PSPs were trained to use a number of important behaviour change techniques including: a) enhancing self-monitoring so participants could see what they had achieved (mastery experiences), b) providing support and encouragement (social persuasion) as well as
facilitating opportunities to exercise with others in a supportive environment (modeling), c) educating participants about the normal physiological responses to exercise and how to positively interpret their responses, and d) encouraging the participant to exercise with other successful exercisers (modeling or vicarious experiences). The PSP discussed strategies with participants focused on developing confidence to perform exercise, overcoming barriers to be active, increasing motivation to exercise, scheduling exercise into one’s daily routine, goal setting, and enhancing social support and networks to be physically active, as well as ensuring participant awareness of the benefit of exercise as a smoking cessation aid.

Additionally, PSPs were trained as Quitcard providers allowing them to provide participants with a Quitcard (a voucher) that participants could redeem at a community pharmacy for an 8-week supply of nicotine patches, gum, or lozenge. PSPs were trained to match the participant’s addiction level with the appropriate NRT dosage. Participants made a co-payment of NZ$3 for a 4-week supply of each NRT product. The first three PSPs attended the same training session to ensure intervention delivery was consistent across PSPs. There were two changes to PSP staff throughout the study. To ensure consistency of intervention delivery during staff changes, the initial PSPs were involved in the training of the new PSPs.

Table 13 provides a summary of the content of each of the intervention contacts. The content covered in each session varied depending on the progress of the participant. For example, if a participant indicated they had stopped exercising in week six, content for phone call four was altered accordingly. All telephone calls, including those with successful or unsuccessful contact were logged to help evaluate adherence with the intervention. Intervention phone calls were monitored throughout the study to ensure the fidelity of delivery. To achieve this, each PSP conducted a face-to-face interview and a ‘phone call 6’ while two study researchers were present. The study researchers provided feedback to the PSP on each participant contact,
focusing on any aspects of the intervention that were missed. This process was repeated six months later to ensure the PSPs continued their high standard of intervention delivery throughout the study. During the study new PSP staff were employed and the same monitoring process was applied.
### TABLE 13: SUMMARY OF THE CONTENT OF EACH INTERVENTION CONTACT

<table>
<thead>
<tr>
<th>Contact</th>
<th>Time</th>
<th>Session content</th>
<th>Self-efficacy variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Face-to-face</td>
<td>Week 1</td>
<td>Welcome participant to the program</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Explain the positive effects of regular physical activity on physical and mental health</td>
<td>Outcome expectancy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obtain exercise history - What activities have you enjoyed participating in in the past? What time of day do you prefer to exercise? What activities do you currently enjoy? In the past what factors helped you to participate in regular physical activity, and what factors hindered you?</td>
<td>Mastery experiences</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discuss normal physiological responses to exercise - highlighting what they are likely to experience</td>
<td>Physiological responses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Explain the benefit of monitoring progress with a pedometer and exercise log. Explain perceived exertion scale to monitor intensity of exercise</td>
<td>Mastery experiences and task efficacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exercise prescription - Prescribe exercise based on exercise history</td>
<td>Task efficacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Social persuasion - suggest the possibility of exercising with friends/family</td>
<td>Social persuasion/peer modeling</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discuss relapse - and the fact that if 'slips' occur (i.e. the participant has a cigarette, or misses an exercise session) they should not give up</td>
<td></td>
</tr>
<tr>
<td>2 - Phone call 1</td>
<td>Week 2</td>
<td>Discuss the barriers to exercise faced in the last week</td>
<td>Barrier efficacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discuss the physiological responses to exercise experienced in the previous week. Based on responses, reinforce that these are normal responses to exercise and any discomfort often improves with time</td>
<td>Physiological responses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discuss goal setting using the SMART principle - Set Specific, Measurable, Action-oriented, Realistic, Time-based Goals</td>
<td></td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Week</th>
<th>Phone call 1</th>
<th>Discuss common barriers to exercise - use the IDEA approach - Identify barriers, Develop a strategy, Evaluate, Assess. Prioritise the most common barriers to exercise and develop a strategy to overcome them</th>
<th>Barrier efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Phone call 2</td>
<td>Discuss the approach of changing the participant's perspective to exercise, from one of fitting exercise into their life to fitting their life around exercise</td>
<td>Scheduling efficacy</td>
</tr>
<tr>
<td>4</td>
<td>Phone call 3</td>
<td>Work through another barrier using the IDEA approach</td>
<td>Barrier efficacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Identify high risk situations that will challenge the participant's exercise compliance coping skills. Encourage the participant to seek out situations that make exercise convenient and enjoyable, and to avoid people, places or situations that may affect their ability to adhere to their exercise program</td>
<td>Coping efficacy</td>
</tr>
<tr>
<td>5</td>
<td>Phone call 4</td>
<td>Draw the participants attention to where they started and how far they have come</td>
<td>Mastery experiences</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discuss how physiological responses to exercise have improved over time</td>
<td>Physiological responses</td>
</tr>
<tr>
<td>6</td>
<td>Phone call 5</td>
<td>Plan long term maintenance of exercise behaviour by discussing opportunities for physical activity at local community facilities and organisations</td>
<td>Coping efficacy</td>
</tr>
<tr>
<td>7</td>
<td>Phone call 6</td>
<td>Discuss how to maintain focus on exercise in different environments, such as when on holiday - attempt to maintain a similar routine, use exercise as a way to explore surroundings etc.</td>
<td>Coping efficacy</td>
</tr>
<tr>
<td>8</td>
<td>Phone call 7</td>
<td>Discuss community options for exercise. Suggest exercise options in the community based on the participant's exercise interests. Set some goals regarding community exercise (if appropriate)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Phone call 8</td>
<td>Discuss community options for exercise. Ask the participant what activities they will continue to do in the community environment. Discuss location, cost, transport, with the participant. Help facilitate the participant joining an activity programme if needed.</td>
<td>Barrier and scheduling efficacy</td>
</tr>
<tr>
<td>10</td>
<td>Phone call 9</td>
<td>Review previous six months, reinforcing progress made to date, fitness improvements, barriers overcome, etc.</td>
<td>Mastery experiences</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Call 9</th>
<th><strong>Ensure participant is aware they need to continue to exercise regularly, maintaining or exceeding their prescribed level of exercise, scheduling exercise into their day, and exercising with others and/or participating in exercise options in the community (if appropriate)</strong></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>All calls</th>
<th><strong>Review progress since last contact. Provide positive feedback and encouragement regarding progress</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Discuss pedometer counts and exercise log</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Provide positive affirmations, support and encouragement regarding the participants progress</strong></td>
</tr>
</tbody>
</table>

**Mastery experiences**

**Social persuasion**

Discuss relapse if required. If relapse has occurred, discuss 'coping self-talk' with the participant, such as 'I'll continue to exercise as I did before… I know that once I get started, I really enjoy exercising’ etc.

Set goals for the time period until the next contact
5.2.8 USUAL CARE SMOKING CESsATION

All enrolled participants received usual smoking cessation services delivered by Quitline. People who phone Quitline are offered information and support by smoking cessation advisors to quit smoking. Participants were offered one-to-one telephone support for three months, as well as an exchange card (Quitcard) for up to eight weeks of subsidised NRT (patches, gum, or lozenge), which they redeemed at a local community pharmacy, and were encouraged to set a quit date.

5.2.9 OUTCOMES

The primary outcome for the Fit2Quit study was self-reported point prevalence (i.e., not a single puff of a cigarette in the past 7 days) at 6 months, confirmed by a salivary cotinine reading of less than 15ng/ml. The secondary outcomes were prolonged abstinence (i.e. no more than 5 cigarettes as per Russell Standard) verified by salivary cotinine (<15ng/ml) at 6 months after the quit date, self-reported 7-day point prevalence at 8 weeks after quit date, change from baseline in TWS at 8 weeks and 6 months, self-rated chances of quitting at 8 weeks, physical activity measured with the IPAQ at 8 weeks and 6 months, and cost effectiveness of the intervention to improve smoking cessation. Tertiary outcomes were examined in the face-to-face sub-group only, and included difference in change from baseline in weight, BMI, and physical fitness at six months; as well as psychological (self-efficacy, motivation) variables and the Leisure Score Index at eight weeks and six months. Qualitative exit interviews were conducted with a sub-sample of intervention group participants to explore themes regarding the acceptability and effectiveness of the intervention.

5.2.10 STATISTICAL ANALYSIS

Statistical analyses were performed using SAS version 9.2 (SAS Institute Inc. Cary NC) and R version 2.11.1 (R Foundations for Statistical Computing). All statistical tests were two-tailed and a 5% significance level was maintained throughout the
analyses. All treatment evaluations were performed on the principle of ITT using the observed data collected from all randomised participants. Participants with missing smoking status were assumed to be smoking, as has been recommended for smoking cessation studies.\textsuperscript{284}

Simple chi-squared analyses were used to evaluate the main treatment effect on the primary outcome, with estimation of relative risks (RR), 95\% confidence intervals and two-sided p-values. As a secondary analysis, the effect of the intervention was also evaluated using a logistic regression model adjusted for stratification factors (study center, ethnicity and sex), age, and other potential confounding factors at baseline if they were statistically significant at the 5\% level. ORs, 95\% confidence intervals and two-sided p-values are presented for comparison.

Statistical tests and regression models appropriate for continuous and categorical data were used for secondary and tertiary outcomes. Since no specific sample size was placed on the number of participants in the face-to-face sub-group, these tertiary outcomes were used to examine potential mechanisms mediating the effectiveness of the intervention. Sensitivity analyses were conducted to determine the effect of missing data due to loss to follow-up. Sub-group analyses by ethnicity (Māori and non-Māori [all other ethnicities]) were also conducted, and the consistency of effects tested.

If a statistically significant difference between groups was found for point prevalence and/or continuous abstinence in the face-to-face sub-group, and a tertiary outcome, logistic regression models were used to explore the mediating effects of the tertiary outcome at 24 weeks on the treatment effect for smoking abstinence in the sub-group.
5.3 RESULTS

5.3.1 PARTICIPANTS

Figure 33 shows screening of participants, recruitment and follow-up. Fifty-four per cent of screened eligible participants were randomised (906/1686). Follow up at 6 months was 92% (837/906) for the primary outcome. A total of 906 trial participants were randomised, with 455 and 451 in the intervention and control groups, respectively. For each group, loss to follow-up was 7% and 1% at 8 weeks, and 11% and 4% at 24 weeks for intervention and control groups, respectively.

**FIGURE 33: FLOW DIAGRAM OF PARTICIPANTS IN THE FIT2QUIT TRIAL**
5.3.2 BASELINE CHARACTERISTICS

Table 14 shows the baseline characteristics for participants in the intervention and control groups. There were no statistically significant differences between groups for any variables at baseline. Participants (n=906, mean age = 37.5 ± 12.2 years) were predominantly female (54%), of NZ European ethnicity (48%), and smoked an average of 19.6 cigarettes per day at baseline. The mean overall score for the FTND was 5.6, indicating a moderate level of dependence for the total sample population. Forty-four per cent of participants smoked 11-20 cigarettes per day at baseline and 56% had their first cigarette within 6-30 minutes of waking, suggesting a high level of dependence among these participants. The self-rated chance of quitting was reasonably high at baseline, with more than 40% of participants in both control and intervention groups rating a score of 5 ('very high').

5.3.3 SMOKING OUTCOMES

Cessation: Smoking abstinence rates at 24 weeks, as measured by 7-day point prevalence, were 23% in the intervention group (105/455) and 22% in the control group (98/451) (see Table 15). The RR for smoking was 0.98 (95% CI 0.92, 1.05; p=0.63). In other words, the difference between groups using this measure was not statistically significant. Continuous abstinence rates were lower in intervention and control groups (17% [78/455] and 18% [80/451], respectively; RR for smoking 1.01; 95% CI 0.95, 1.07; p=0.81), but again, there was no significant treatment difference between the groups. The ORs estimated in adjusted logistic regression analyses were similar to the RR. For those baseline factors adjusted for in the regression model, the probability of persistent smoking at 24 weeks was significantly higher in Māori participants (OR 1.63; 95% CI 1.12, 2.38, p=0.01) compared to non-Māori, and significantly higher in those with a higher baseline strength of urge to smoke (OR 1.28; 95% CI 1.11, 1.47, p=0.0006), using 7-day point prevalence as the outcome.
measure. Using continuous abstinence as the outcome measure, we found marginally higher ORs for both Māori ethnicity and higher strength of urge.

Of the 98 and 105 participants in control and intervention groups, respectively, who self-reported quitting smoking, only 62 (63%) and 54 (51%), respectively, completed a salivary cotinine test. In total, the proportion of participants who had salivary cotinine validation of their self-reported quit smoking status was 57%. The remaining 87 (43%) were unable to be contacted after arranging to meet for a salivary cotinine test, and/or failed to return a cotinine test via mail. Of those that completed the test, 41 (42%) and 39 (37%) participants in control and intervention groups, respectively, provided a salivary cotinine reading of less than 15ng/ml indicating that they had not smoked in the last 7 days. Similar results were found for continuous abstinence.

There were no differences in objectively verified smoking abstinence rates between control and intervention groups (RR = 1.01; 95% CI 0.97, 1.06, p=0.48).

**Sensitivity analysis:** No significant differences were found between groups for 7-day point prevalence or continuous abstinence using observed data only (i.e. no imputation). For 7-day point prevalence, the total number of complete cases was 683 (75% of those randomised, N = 906), with 328 and 355 in the intervention and control groups, respectively. Of these, 203 participants self-reported quitting at 24 weeks with 105 and 98 in the intervention and control groups, respectively (adjusted OR for smoking 0.86; 95% CI 0.62, 1.21, p=0.39). For continuous abstinence, the total number of complete cases was 680 (75%) with 326 and 354 in the intervention and control groups, respectively. Of these, 158 participants self-reported quitting at 24 weeks with 78 and 80 participants in the intervention and control groups, respectively (adjusted OR for smoking 1.01; 95% CI 0.70, 1.45, p=0.97).
TABLE 14: BASELINE DEMOGRAPHICS OF ALL RANDOMISED PARTICIPANTS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control (n=451)</th>
<th>Intervention (n=455)</th>
<th>Total (n=906)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>37.3 ± 12.2</td>
<td>37.6 ± 12.2</td>
<td>37.5 ± 12.2</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>207 (45.9)</td>
<td>208 (45.7)</td>
<td>415 (45.8)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>244 (54.1)</td>
<td>247 (54.3)</td>
<td>491 (54.2)</td>
</tr>
<tr>
<td>Prioritised ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Māori, n (%)</td>
<td>138 (30.6)</td>
<td>142 (31.2)</td>
<td>280 (30.9)</td>
</tr>
<tr>
<td>Pacific, n (%)</td>
<td>55 (12.2)</td>
<td>47 (10.3)</td>
<td>102 (11.3)</td>
</tr>
<tr>
<td>NZ European, n (%)</td>
<td>214 (47.5)</td>
<td>218 (47.9)</td>
<td>432 (47.7)</td>
</tr>
<tr>
<td>Asian, n (%)</td>
<td>11 (2.4)</td>
<td>13 (2.9)</td>
<td>24 (2.7)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>33 (7.3)</td>
<td>35 (7.7)</td>
<td>68 (7.5)</td>
</tr>
<tr>
<td>Number of cigarettes/day, mean ± SD</td>
<td>19.83 ± 9.2</td>
<td>19.41 ± 9.5</td>
<td>19.62 ± 9.3</td>
</tr>
<tr>
<td>Age of smoking onset, mean ± SD</td>
<td>15.47 ± 4.2</td>
<td>15.54 ± 4.2</td>
<td>15.5 ± 4.2</td>
</tr>
<tr>
<td>Years smoking continuously, mean ± SD</td>
<td>20.48 ± 11.9</td>
<td>20.15 ± 12.1</td>
<td>20.22 ± 12.0</td>
</tr>
<tr>
<td>FTND score, mean ± SD</td>
<td>5.63 ± 1.95</td>
<td>5.52 ± 1.90</td>
<td>5.57 ± 1.93</td>
</tr>
<tr>
<td>Previous quit attempts</td>
<td></td>
<td></td>
<td>19.4 ± 9.8</td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>348 (77.2)</td>
<td>368 (80.9)</td>
<td>716 (79)</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>10. (22.8)</td>
<td>87 (19.1)</td>
<td>190 (21)</td>
</tr>
<tr>
<td>Number of quit attempts in previous 12 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One, n (%)</td>
<td>83 (23.9)</td>
<td>93 (25.3)</td>
<td>176 (24.6)</td>
</tr>
<tr>
<td>Two, n (%)</td>
<td>28 (8.1)</td>
<td>37 (10.1)</td>
<td>65 (9.1)</td>
</tr>
<tr>
<td>Three, n (%)</td>
<td>14 (4.0)</td>
<td>15 (4.1)</td>
<td>29 (4.1)</td>
</tr>
<tr>
<td>Four or more, n (%)</td>
<td>18 (5.2)</td>
<td>20 (5.4)</td>
<td>38 (5.3)</td>
</tr>
<tr>
<td>None, n (%)</td>
<td>204 (58.6)</td>
<td>202 (54.9)</td>
<td>406 (56.7)</td>
</tr>
<tr>
<td>Don’t know, n (%)</td>
<td>1 (0.3)</td>
<td>1 (0.3)</td>
<td>2 (0.3)</td>
</tr>
</tbody>
</table>

* Participants were asked to indicate all ethnic groups they belonged to, so totals exceed 100%

TABLE 15: SMOKING ABSTINENCE RATES AT 8 AND 24 WEEKS AFTER THE NOMINATED QUIT DATE

<table>
<thead>
<tr>
<th>Abstinence measure</th>
<th>Control %</th>
<th>Intervention %</th>
<th>Relative Risk</th>
<th>95% lower CI</th>
<th>95% upper CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7-day point-prevalence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 weeks</td>
<td>130</td>
<td>136</td>
<td>29.9</td>
<td>0.99</td>
<td>0.91</td>
<td>1.07</td>
</tr>
<tr>
<td>24 weeks</td>
<td>98</td>
<td>105</td>
<td>23.1</td>
<td>0.98</td>
<td>0.92</td>
<td>1.05</td>
</tr>
<tr>
<td>Continuous</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 weeks</td>
<td>122</td>
<td>129</td>
<td>28.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 weeks</td>
<td>80</td>
<td>78</td>
<td>17.1</td>
<td>1.01</td>
<td>0.95</td>
<td>1.07</td>
</tr>
</tbody>
</table>
Chapter 5: The Fit2Quit Trial

**Smoking withdrawal and behaviour.** There were no statistically significant intervention effects on TWS (Table 16). For total mood and physical symptoms scores (range 1-25), the model-adjusted means were 9.90 (SE 0.21) and 9.92 (SE 0.20) in the intervention and control groups, respectively (p=0.96). However, there was a small but statistically significant difference in the number of cigarettes smoked in the previous 7 days (mean difference -0.92 cigarettes per day, 95% CI 0.06, 0.39; p=0.006) as well as in the number of cigarettes smoked since participants’ nominated quit date (mean difference -1.01 cigarettes per day, 95% CI -1.74, -0.09, p=0.02) in favour of the intervention group. Self-rated chance of quitting was also significantly lower in the intervention group compared to those in the control at 8 weeks (mean difference 0.23, 95% CI -1.90, -0.12; p=0.02).

**NRT use:** At baseline, 200 (44%) and 205 (45%) participants were using NRT in the control and intervention groups, respectively, whilst another 202 and 195, respectively, indicated that they had ‘not got around to it’ or the NRT products had not arrived yet. There was no effect of baseline NRT use on 7-day point prevalence abstinence at 24 weeks (OR 1.10; 95% CI 0.67, 1.83, p=0.70) in the regression model. The proportions of NRT use dropped to 27% and 28% at 8 weeks, and 9% and 11% at 24 weeks, in the two groups respectively. The most frequently used NRT product was Patch 21mg, with 32.6% and 33.4% at baseline in the control and intervention groups respectively. The numbers dropped to 15% at 8 weeks and 3%-6% at 24 weeks.

**5.3.4 PHYSICAL ACTIVITY OUTCOMES**

Total physical activity scores (MET-minutes per week) significantly increased from baseline for both the intervention and control groups, with the greatest change at 8 weeks followed by a reduction at 24 weeks. There were no statistically significant differences between groups (difference 154, 95% CI -684, +992, p=0.72). Similar patterns were observed for walking and vigorous intensity physical activity. However,
a significant positive intervention effect was found for leisure time physical activity. Overall, an increase of 527 minutes per week (SE 69.18) was observed in the intervention group and 308 minutes per week (SE 66.11) in the control group at 24 weeks (difference 219.11; 95% CI 52.7, 385.6, p=0.01). This was partially offset by an increase in physical activity in the domestic and garden domain in the control group compared with a decrease in the intervention group, but this difference was not statistically significant. Table 17 shows the least-squared means and standard errors for each of the different IPAQ derived measures of physical activity for intervention and control groups.
TABLE 16: TOBACCO WITHDRAWAL SYMPTOMS AND SMOKING BEHAVIOUR OUTCOMES

<table>
<thead>
<tr>
<th>Study Outcomes</th>
<th>Intervention</th>
<th>Control</th>
<th>Estimated Effect Size (Intervention - Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate (SE)</td>
<td>Estimate (SE)</td>
<td>Difference in Means</td>
</tr>
<tr>
<td>Total MPSS Score (1-25)*</td>
<td>9.90 (0.21)</td>
<td>9.92 (0.20)</td>
<td>-0.01</td>
</tr>
<tr>
<td>Total MPSS Score (self-reported abstainers only)*</td>
<td>8.57 (0.31)</td>
<td>8.23 (0.32)</td>
<td>0.35</td>
</tr>
<tr>
<td>Number of cigarettes smoked per day in the past 7 days*</td>
<td>4.75 (0.34)</td>
<td>5.67 (0.34)</td>
<td>-0.92</td>
</tr>
<tr>
<td>Number of cigarettes smoked per day since nominated quit date*</td>
<td>5.07 (0.37)</td>
<td>6.08 (0.36)</td>
<td>-1.01</td>
</tr>
<tr>
<td>Self-rated chance of quitting at 8 weeks**</td>
<td>3.96 (0.07)</td>
<td>3.73 (0.07)</td>
<td>0.23</td>
</tr>
</tbody>
</table>

* Repeated Measures Mixed Model adjusted for: baseline outcome (as appropriate), age, sex, Māori, centre, baseline Strength of Urge to Smoke (SUTS), and time.

** ANCOVA model adjusted for: baseline outcome, age, sex, Māori ethnicity, study centre, and baseline Strength of Urge to Smoke (SUTS).
### TABLE 17: CHANGE FROM BASELINE IN PHYSICAL ACTIVITY OUTCOMES ESTIMATED* AT 24 WEEKS

<table>
<thead>
<tr>
<th>IPAQ domain (MET minutes/week)</th>
<th>Intervention Estimate (SE)</th>
<th>Control Estimate (SE)</th>
<th>Estimated Effect Size (Intervention minus Control)</th>
<th>95% lower CI</th>
<th>95% higher CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total physical activity score</td>
<td>1134.04 (350.2)</td>
<td>1179.9 (336.7)</td>
<td>154.2 (426.8)</td>
<td>-683.8</td>
<td>992.2</td>
<td>0.61</td>
</tr>
<tr>
<td>Total walking score</td>
<td>364.5 (130.9)</td>
<td>207.9 (126.5)</td>
<td>156.6 (160.8)</td>
<td>-159.2</td>
<td>472.3</td>
<td>0.33</td>
</tr>
<tr>
<td>Total moderate physical activity score</td>
<td>330.8 (173.0)</td>
<td>410.1 (165.1)</td>
<td>-79.3 (211.6)</td>
<td>-494.8</td>
<td>336.2</td>
<td>0.70</td>
</tr>
<tr>
<td>Total vigorous physical activity score</td>
<td>871.4 (225.2)</td>
<td>725.0 (215.6)</td>
<td>146.4 (277.2)</td>
<td>-397.8</td>
<td>690.6</td>
<td>0.60</td>
</tr>
<tr>
<td>Change from baseline leisure domain</td>
<td>527.0 (69.2)</td>
<td>307.9 (66.1)</td>
<td>219.1 (84.8)</td>
<td>52.7</td>
<td>385.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Change from baseline work domain</td>
<td>580.9 (313.8)</td>
<td>538.1 (301.2)</td>
<td>42.8 (384.9)</td>
<td>-712.8</td>
<td>798.4</td>
<td>0.91</td>
</tr>
<tr>
<td>Change from baseline active transport domain</td>
<td>164.6 (52.9)</td>
<td>101.9 (50.7)</td>
<td>62.7 (65.0)</td>
<td>-64.9</td>
<td>190.3</td>
<td>0.34</td>
</tr>
<tr>
<td>Change from baseline domestic and garden domain</td>
<td>119.6 (124.8)</td>
<td>259.2 (119.7)</td>
<td>-139.6 (153.6)</td>
<td>-441.1</td>
<td>162.0</td>
<td>0.36</td>
</tr>
</tbody>
</table>

* Repeated Measures Mixed Model adjusted for: baseline outcome, stratification factors, age, and Strength of Urge to Smoke (SUTS).
5.3.5 MEDICATION AND ADVERSE EVENTS

At baseline, 129 (28%) participants in the control group and 149 (33%) participants in the intervention reported non-study medications. Serious adverse events were recorded in 17 control participants (3.8%) and 17 intervention participants (3.7%) at 8 weeks, and 15 (3.3%) and 14 (3.1%) participants reported serious adverse events in the control and intervention groups, respectively, at 24 weeks.

5.3.6 INTERVENTION ADHERENCE

The effect of adherence with the intervention on smoking abstinence rates was examined. This was achieved by recording the number of calls that were received by each participant. Table 18 provides the frequency of participants who adhered to the intervention based on number of calls received.

**TABLE 18: FREQUENCY AND CUMULATIVE FREQUENCY OF PARTICIPANTS ADHERENCE TO THE INTERVENTION BASED ON NUMBER OF CALLS RECEIVED**

<table>
<thead>
<tr>
<th>Number of calls delivered</th>
<th>Frequency</th>
<th>Percentage</th>
<th>Cumulative Frequency</th>
<th>Cumulative percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>34</td>
<td>8.02</td>
<td>34</td>
<td>8.02</td>
</tr>
<tr>
<td>1</td>
<td>27</td>
<td>6.37</td>
<td>61</td>
<td>14.39</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
<td>5.66</td>
<td>85</td>
<td>20.05</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>3.77</td>
<td>101</td>
<td>23.82</td>
</tr>
<tr>
<td>4</td>
<td>24</td>
<td>5.66</td>
<td>125</td>
<td>29.48</td>
</tr>
<tr>
<td>5</td>
<td>30</td>
<td>7.08</td>
<td>155</td>
<td>36.56</td>
</tr>
<tr>
<td>6</td>
<td>33</td>
<td>7.78</td>
<td>188</td>
<td>44.34</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>11.79</td>
<td>238</td>
<td>56.13</td>
</tr>
<tr>
<td>8</td>
<td>36</td>
<td>8.49</td>
<td>274</td>
<td>64.62</td>
</tr>
<tr>
<td>9</td>
<td>71</td>
<td>16.75</td>
<td>345</td>
<td>81.37</td>
</tr>
<tr>
<td>10</td>
<td>79</td>
<td>18.63</td>
<td>424</td>
<td>100</td>
</tr>
</tbody>
</table>

*Frequency missing = 31*

Adherence to the intervention and cessation outcomes: Of the 455 participants randomised to the intervention group, 52% completed at least 7 intervention calls (median = 7, IQR = 4-9). Overall, 125 participants received less than half of the scheduled intervention calls (≤ 4 calls). The number of intervention calls delivered significantly reduced the probability of smoking (OR 0.88, 95% CI 0.81, 0.97, p= 0.01) for those in the intervention group. When all
participants were included, a significant treatment effect on smoking cessation was found for those who received seven intervention calls or more (OR 0.67, 95% CI 0.46, 0.98, p=0.03).

5.3.7 EFFECT OF INTERVENTION ON MĀORI PARTICIPANTS

In total, 280 Māori (31% of the total study population) were recruited to the study; 138 and 142 in the control and intervention groups, respectively. As a planned sub-group analysis, the consistency of intervention effect on Māori was assessed on all smoking related outcomes and the IPAQ.

Overall, there was no significant intervention effect on any of the smoking outcomes with this sub-group of participants. There was also no significant treatment effect in MPSS score and physical activity measurements for Māori Participants.

For 7-day point prevalence, 32 (23.2%) and 36 (25.4%) of Māori participants self-reported quitting at 8 weeks in the control and intervention groups, respectively. The number of Māori participants who self-reported quitting reduced to 24 (17.4%) and 21 (14.8%) in the control and intervention groups, respectively, at 24 weeks. Less than 50% of participants who self-reported quitting at 24 weeks had their status validated with the salivary cotinine test. A total of 16 abstainers (8 per group) provided objectively verified point prevalence abstinence data.

For continuous abstinence, 27 (19.6%) and 33 (23.2%) Māori participants self-reported quitting at 8 weeks in the control and intervention groups. At 24 weeks, 16 (11.6%) and 17 (12.0%) Māori participants self-reported quitting in the two respective groups. Similarly, only about 50% of participants who self-reported quitting at 24 weeks had their status validated with the salivary cotinine test. A total of 11 abstainers (5 and 6 in the control and intervention groups) provided objectively verified continuous abstinence data.

5.3.8 COST-EFFECTIVENESS

The health-related quality of life (EQ-5D) results indicate that there were no significant differences at baseline, follow-up, or between groups, using both complete case (observed
.data) and ITT analyses. Between-group differences at follow-up were 0.0027 QALYs measured over 24 weeks.

The cost-effectiveness results suggest that an additional $269 on average is incurred per person for smoking cessation in the Fit2Quit exercise counseling programme for smoking cessation, compared with usual Quitline-delivered stop smoking support.

Given that there were no statistically significant differences for smoking abstinence and for QALYs within the 24-week timeframe of the trial, and the intervention is more costly, the Fit2Quit intervention was not cost-effective over 24 weeks.

However, when the data were examined for those participants who adhered to the intervention (i.e. received at least 70% of intervention calls), the ICERs for point prevalence and continuous abstinence were $2,783 and $4,004 respectively, per additional quitter abstaining, indicating that the intervention was cost-effective among those participants who adhered to it.

Running the Markov model for cohorts age 30 years old, the Fit2Quit intervention, compared with usual smoking cessation support and NRT, produced ICERs of $1,436 and $518 per QALY gained over the lifetime of the cohort, for males and females, respectively (see Table 19). These results suggest an ICER below the threshold of NZ$20,000 per QALY gained for both males and females, indicating that the intervention would be cost-effective over the lifetime of the cohort. The difference between males and females is most likely due to the longer life expectancy and the lower incidence of other diseases among females.
TABLE 19: SHORT AND LONG-TERM COST-EFFECTIVENESS OUTCOMES FOR INTERVENTION AND CONTROL GROUPS

<table>
<thead>
<tr>
<th>Short term (at end of 6-months)</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost for 1000 persons in each arm</td>
<td>$4,549,700</td>
<td>$2,353,400</td>
</tr>
<tr>
<td>Number of quitters at 6 months</td>
<td>171</td>
<td>177</td>
</tr>
<tr>
<td>ICER - per quitter at 6 months</td>
<td>-$36,605</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Long-term (lifetime)</th>
<th>Intervention (male)</th>
<th>Control (male)</th>
<th>Intervention (female)</th>
<th>Control (female)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean cost per person</td>
<td>$4248</td>
<td>$4023</td>
<td>$3938</td>
<td>$3719</td>
</tr>
<tr>
<td>QALYs gained per person</td>
<td>16.619</td>
<td>16.462</td>
<td>17.654</td>
<td>17.229</td>
</tr>
<tr>
<td>ICER - QALYs gained per person</td>
<td>$1436</td>
<td></td>
<td>$518</td>
<td></td>
</tr>
</tbody>
</table>
5.3.9 FACE-TO-FACE SUB-SAMPLE

Figure 34 shows the flow diagram for the participants in the face-to-face sub-sample. As with the full trial sample, there was a high loss to follow-up. Moreover, many participants opted to complete their 24-week follow-up assessment via telephone, reducing substantially the number of participants who completed the physiological measures. Two hundred and nineteen participants volunteered to complete a face-to-face assessment. Table 20 shows the baseline characteristics of participants in intervention and control groups in the sub-sample, with no observed differences between the two groups.

Randomised Participants (N=219)

- Intervention (N=110)
  - Study withdrawal (n=14)
  - 8-week follow-up
    - LSI (n = 96)
    - BE, Self-efficacy, LCE (n=84)

- Control (N = 109)
  - Study withdrawal (n=15)
  - 8-week follow-up
    - LSI (n=94)
    - BE, Self-efficacy, LCE (n=85)

- Study withdrawal (n=16)
  - 24-week follow-up
    - LSI, BE, Self-efficacy, LCE (n=70)
    - Weight, BMI (n=53)
    - Step test (n=45)

- Study withdrawal (n=21)
  - 24-week follow-up
    - LSI, BE, Self-efficacy, LCE (n=73)
    - Weight, BMI (n=46)
    - Step test (n=38)

FIGURE 34: FLOW DIAGRAM OF FIT2QUIT FACE-TO-FACE SUB-SAMPLE PARTICIPANTS
### TABLE 20: BASELINE FACE-TO-FACE PARTICIPANT DEMOGRAPHIC DATA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control (n=109)</th>
<th>Intervention (n=110)</th>
<th>Total (n=219)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>37.9 ± 10.2</td>
<td>39.3 ± 11.7</td>
<td>38.6 ± 10.95</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>55 (50.5)</td>
<td>54 (49.1)</td>
<td>109 (49.8)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>54 (49.5)</td>
<td>56 (50.9)</td>
<td>110 (50.2)</td>
</tr>
<tr>
<td>Prioritised ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Māori, n (%)</td>
<td>34 (31.2)</td>
<td>36 (32.7)</td>
<td>70 (32.0)</td>
</tr>
<tr>
<td>Pacific, n (%)</td>
<td>12 (11.0)</td>
<td>9 (8.2)</td>
<td>21 (9.6)</td>
</tr>
<tr>
<td>NZ European, n (%)</td>
<td>47 (43.1)</td>
<td>50 (45.5)</td>
<td>97 (44.3)</td>
</tr>
<tr>
<td>Asian, n (%)</td>
<td>5 (4.6)</td>
<td>6 (5.5)</td>
<td>11 (5)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>11 (10.1)</td>
<td>9 (8.2)</td>
<td>20 (9.1)</td>
</tr>
<tr>
<td>Smoking outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of cigarettes/day, mean ± SD</td>
<td>20.6 ± 9.2</td>
<td>19.1 ± 9.99</td>
<td>19.84 ± 9.63</td>
</tr>
<tr>
<td>Fagerström Test of Nicotine Dependence score, mean ± SD</td>
<td>5.79 ± 2.2</td>
<td>5.32 ± 2.04</td>
<td>5.56 ± 2.12</td>
</tr>
<tr>
<td>Strength of urge to smoke</td>
<td>2.57 ± 1.15</td>
<td>2.58 ± 1.14</td>
<td>2.58 ± 1.14</td>
</tr>
<tr>
<td>MPSS</td>
<td>10.78 ± 1.15</td>
<td>10.15 ± 1.18</td>
<td>10.47 ± 1.14</td>
</tr>
<tr>
<td>Exercise outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total physical activity (MET mins/week) - IPAQ</td>
<td>6903 ± 8230</td>
<td>7553 ± 8412</td>
<td>7229 ± 8309</td>
</tr>
<tr>
<td>Total leisure activity (MET mins/week) - IPAQ</td>
<td>119.3 ± 256.2</td>
<td>122.9 ± 213.9</td>
<td>121 ± 235.3</td>
</tr>
<tr>
<td>Weekly leisure exercise score (LSI)</td>
<td>20.7 ± 28.7</td>
<td>17.04 ± 18.65</td>
<td>18.87 ± 24.2</td>
</tr>
<tr>
<td>Psychological outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>59.05 ± 23.3</td>
<td>59.75 ± 26.4</td>
<td>59.4 ± 24.82</td>
</tr>
<tr>
<td>Barrier efficacy</td>
<td>52.83 ± 23.44</td>
<td>52.47 ± 25.64</td>
<td>52.65 ± 24.51</td>
</tr>
<tr>
<td>Locus causality of exercise</td>
<td>3.83 ± 1.35</td>
<td>4.12 ± 1.43</td>
<td>3.97 ± 1.40</td>
</tr>
<tr>
<td>Self-rated chance of quitting</td>
<td>4.23 ± 0.8</td>
<td>4.25 ± 0.9</td>
<td>4.24 ± .84</td>
</tr>
<tr>
<td>Anthropometric and fitness outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (n=108)</td>
<td>84.4 ± 20.5</td>
<td>85.0 ± 19.62</td>
<td>84.28 ± 20.79</td>
</tr>
<tr>
<td>BMI (n=108)</td>
<td>28.9 ± 6.6</td>
<td>29.12 ± 6.21</td>
<td>28.87 ± 6.66</td>
</tr>
<tr>
<td>Predicted VO₂max (n=96)</td>
<td>31.6 ± 5.6</td>
<td>31.4 ± 6.3</td>
<td>31.48 ± 5.9</td>
</tr>
</tbody>
</table>

Note: IPAQ = International Physical Activity Questionnaire; MPSS = Multidimensional Physiological Demand Scale; LSI = Leisure Sport Index; VO₂max = Maximum oxygen uptake; BMI = Body Mass Index.
5.3.9.1 *Smoking abstinence*

Seven day point prevalence abstinence rates were 33% and 36% at 8 weeks, and 22% and 22% at 24 weeks, in control and intervention groups, respectively. Continuous abstinence rates were 26% and 34% at 8 weeks, and 15% and 20% at 24 weeks, in control and intervention groups, respectively. There were no statistically significant differences between groups for either measure of smoking abstinence (Table 21).

5.3.9.2 *Psychological Measurements and physical activity*

There were no significant differences between groups for task self-efficacy, barrier efficacy, and LCE scales, and no trends were observed. However, as seen in Tables 20 and 21, weekly scores on the Leisure Time Index increased in both groups throughout the 24 weeks. The weekly leisure activity score had estimated mean scores of 38 (SE 3.42) and 47 (SE 3.36) in the control and intervention groups. The difference of 9.18 units (95% CI 1.12, 17.23) was statistically significant (p-value 0.0258).

5.3.9.3 *Physiological Measurements*

Average body weights were 84.4 kg (SD 20.5) and 85 kg (SD 19.6) at baseline in the control and intervention groups, respectively. At 24 weeks’ assessment, the mean body weight decreased to 80.2 kg (SD 17.3) and 82.0 kg (SD 16.8) in the two respective groups. However, the 24-week values are based on observed data from 99 participants only.

Using ITT analysis, there was no significant difference in body weight between the two groups at 24 weeks, with an average of 81.90 kg (SE 0.53) and 81.14 kg (SE 0.59) in control and intervention groups, respectively. The mean BMI score was 28 kg/m² (SE 0.2) in both groups.
TABLE 21: DESCRIPTIVE INFORMATION FOR ALL VARIABLES OF INTEREST AT 8 AND 24 WEEKS

<table>
<thead>
<tr>
<th>Outcome</th>
<th>8 weeks</th>
<th>24 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (n=109)</td>
<td>Intervention (n=110)</td>
</tr>
<tr>
<td>Smoking outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength of urge to smoke</td>
<td>1.95 ± 1.57</td>
<td>1.75 ± 1.45</td>
</tr>
<tr>
<td>MPSS</td>
<td>9.6 ± 5.95</td>
<td>9.01 ± 5.60</td>
</tr>
<tr>
<td>Single puff of a cigarette in the last 7 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>59 (54.1)</td>
<td>58 (52.7)</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>36 (33.0)</td>
<td>40 (36.4)</td>
</tr>
<tr>
<td>Missing, n (%)</td>
<td>14 (12.8)</td>
<td>12 (10.9)</td>
</tr>
<tr>
<td>Smoked more than 5 cigarettes since quit date</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>67 (61.5)</td>
<td>61 (55.5)</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>28 (25.7)</td>
<td>37 (33.6)</td>
</tr>
<tr>
<td>Missing, n (%)</td>
<td>14 (12.8)</td>
<td>12 (10.9)</td>
</tr>
<tr>
<td>Exercise outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total physical activity (min) - IPAQ</td>
<td>7679 ± 9814</td>
<td>7016 ± 8514</td>
</tr>
<tr>
<td>Total leisure activity (min) - IPAQ</td>
<td>163 ± 294</td>
<td>222.6 ± 314.9</td>
</tr>
<tr>
<td>Weekly leisure exercise score (LSI)</td>
<td>33.8 ± 26.03</td>
<td>44.19 ± 35.15</td>
</tr>
<tr>
<td>Psychological outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>63.9 ± 25.04</td>
<td>62.4 ± 22.75</td>
</tr>
<tr>
<td>Barrier efficacy</td>
<td>50.22 ± 25.27</td>
<td>56.9 ± 22.87</td>
</tr>
<tr>
<td>Locus causality of exercise</td>
<td>4.09 ± 1.44</td>
<td>4.30 ± 1.43</td>
</tr>
<tr>
<td>Self-rated chance of quitting</td>
<td>3.19 ± 1.69</td>
<td>3.69 ± 1.71</td>
</tr>
<tr>
<td>Anthropometric and fitness outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>80.2 ± 17.3</td>
<td>82.05 ± 16.8</td>
</tr>
<tr>
<td>BMI</td>
<td>28.1 ± 6.1</td>
<td>28.34 ± 5.0</td>
</tr>
<tr>
<td>Predicted VO(_{2})max</td>
<td>33.1 ± 7</td>
<td>31.4 ± 5.2</td>
</tr>
</tbody>
</table>
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The predicted VO$_{2\text{max}}$ at 24 weeks were 33.07 (SE 0.70) and 31.55 (SE 0.63) in the control and intervention groups, with a difference of -1.52 (95% CI, -3.32, 0.28) which was non-significant (p=0.097).

5.3.9.4 **Mediation analyses**

Mediation analyses were planned for the psychological measures, self-efficacy, barrier-efficacy, and motivation (LCE). However, as there were no statistically significant treatment effects for point prevalence abstinence or continuous abstinence in the sub-sample, and no statistically significant differences between groups for any of the psychological variables, mediation could not be tested.

5.4 **DISCUSSION**

5.4.1 **MAIN FINDINGS**

Overall, despite our efforts to address the methodological limitations of previous research into exercise and smoking cessation, such as a larger sample size, a longer duration and relatively intensive exercise intervention, we found no differences in smoking abstinence rates between intervention or control conditions.

These findings suggest that telephone delivered exercise counselling may not be sufficient to improve cessation rates over and above existing smoking cessation services such as the NZ Quitline. The quit rates observed in the present study in both arms are in fact similar to self-reported quit rates reported in Quitline evaluations of their service.

For such interventions to increase smoking abstinence, they must influence exercise or physical activity behaviour outcomes. In the present study, both groups reported an increase in their total physical activity levels from baseline, which may indicate a Hawthorne effect; but there were no statistical differences between conditions. However, it appears there was a greater allocation of time (difference of 220 minutes
per week or 31 minutes each day) to leisure-based exercise, which was the focus of the intervention. These findings suggest that while both groups increased overall activity, the intervention group spent more time being active in their leisure time. There was a non-significant difference between groups for domestic and garden domain activity in favour of the control group, which may partially explain why there was a statistically significant difference in favour of the intervention for the leisure domain, but no difference between groups for total physical activity.

Despite the null effect in the ITT analysis in the current study, we noted what appears to be a dose-response effect when we examined degree of adherence to the prescribed exercise regimen. For example, we found that participants who received at least 70% or more of the allocated intervention contacts were less likely to smoke at the end of the intervention and were 33% more likely to have quit compared to those in the control condition.

One of the proposed mechanisms for exercise aiding smoking cessation is mitigation of the negative effects of TWS. In the present trial, there was no intervention effect on TWS as measured with the Mood and Physical Symptoms Scale.\textsuperscript{84} This in turn may have contributed to the null effect of the intervention on quit rates. Alternatively, the null effect on TWS could be a problem of measurement. The magnitude of TWS would, most likely, have been strongest in the first week of a participant’s quit attempt, and if the exercise programme did have an effect on TWS, it would most likely be measured in the first week. We did not measure TWS until eight weeks after the quit day, which would have been too late to observe any exercise-induced mitigation of withdrawal symptoms.

There was a small, but statistically significant difference in number of cigarettes smoked per day between groups, in favour of the intervention group. Reduction prepares smokers for successful quit attempts, and has been shown to be at least as
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effective as abrupt quitting on long term (>6 months) quit rates.\textsuperscript{285} It may be that given the complexities of attempting to transform two behaviours (exercise and smoking) simultaneously, a smoking reduction approach may be more appropriate for exercise interventions for smoking cessation. However, the clinical relevance of a one cigarette difference between groups in cigarettes smoked per day is moot.

The complexity of initiating two behaviour change processes simultaneously is an important point. The majority of the previous studies to find an effect at the end of treatment all began the exercise programme at least one week before the quit date.\textsuperscript{178,183,189} In contrast, the Fit2Quit trial recruited smokers who had already phoned Quitline, so participants had either already started their quit attempt or were about to quit when they started the study; it was not ethical to delay their quit attempt. Although there is research to suggest that changing two health behaviours simultaneously can be at least as effective as a sequential approach to behaviour change,\textsuperscript{286} there is no evidence of it being a successful approach in trials of exercise interventions for smoking cessation when the health behaviour change processes for smoking cessation and exercise have commenced at the same time. As Ussher et al.\textsuperscript{68} recommended in their Cochrane review, beginning the exercise programme prior to the quit date is considered the best approach to enhance smoking cessation rates. Unfortunately, this was not possible in the Fit2Quit trial.

5.4.1.1 Cost-effectiveness

Findings from the cost-effectiveness analysis indicated that the Fit2Quit trial was not cost-effective in comparison to usual care. However, the numbers of quitters in both groups were small and therefore the results of the EQ-5D need to be interpreted with this in mind. Those who continued smoking in the Fit2Quit arm reported better improvements in health-related quality of life at 24-week follow-up than those who continued smoking in the control arm, which is primarily why the Fit2Quit intervention was cost-effective over the long term. It is possible that this could be an effect of the
intervention. The intervention may have caused participants to adopt a healthier lifestyle overall (e.g. increased leisure time physical activity, reduced number of cigarettes smoked per day if still smoking).

However, the Fit2Quit intervention was cost-effective (in the short term) over usual care among those participants who adhered to the intervention. The effect of adherence on cost-effectiveness is noteworthy, and mirrors the effect of adherence on the primary outcome. If rates of adherence to the intervention could be increased, then the intervention would not only be effective at increasing abstinence rates, but it would be a cost-effective treatment approach as well.

5.4.2 STRENGTHS
There were a number of strengths of this trial. First, we recruited a large sample size (despite not meeting the original target, it is still the largest study of its kind, excluding one Internet-based trial\textsuperscript{196}). Second, the trial was pragmatic in nature, using existing national delivery services for both smoking cessation and physical activity promotion. The use of a pragmatic approach, whereby the effectiveness of a programme in a ‘real-world’ setting is tested, has several advantages over explanatory studies. Results of such trials are generalisable to the wider population, and they provide a direct indication to policy makers to inform decisions about practice.\textsuperscript{287} This approach would have allowed for easy integration of these two services had the intervention proved effective.

Third, this was only the second study to provide an exercise intervention for smoking cessation of six months’ duration. Most previous studies have provided an exercise intervention of between 8 and 16 weeks in duration. These may not have been sustained long enough for participants to achieve exercise maintenance.

Fourth, a major strength of this study was the ethnically diverse sample, with Māori participants making up 31% of the sample. Most of the previous studies that have
reported ethnicity have reported percentages of study participants of Caucasian ethnicity over 80%\(^\text{184}\). Only Ciccolo et al.\(^\text{184}\) recruited an ethnically diverse sample representative of the population. Māori had greater rates of smoking than non-Māori. As the difference in smoking rates between Māori and non-Māori was common to both groups, it is not reflective of something specific to the exercise intervention. One explanation could be that the usual care intervention delivered by Quitline (which both groups received) is more appropriate for non-Māori than Māori smokers. This is unlikely, however, because the NZ Quitline has made a commitment to reducing smoking rates in priority populations (Māori, Pacific, and pregnant women), illustrated by increased rates of uptake of their services in the last few years.\(^\text{37}\) More research is required to explore culturally appropriate exercise interventions for smoking cessation in Māori, but also, given the lack of exercise intervention research worldwide on non-Caucasian smokers, other indigenous groups around the world.

Fifth, this was the first RCT of an exercise intervention for smoking cessation to present cost-effectiveness analysis data. It provides the first indication that, despite non-significant intervention effects for most previous trials, exercise interventions for smoking cessation may improve health-related quality of life, and as such prove cost-effective in comparison to usual care, over the long-term.

Sixth, although a number of serious adverse events were documented throughout the trial, none were related to the intervention. Moreover, there were no differences between groups in the number of reported adverse events, suggesting an exercise counselling intervention is well tolerated.

5.4.3 LIMITATIONS

Limitations of this trial include the relatively high loss to follow-up, which is not uncommon in smoking cessation trials,\(^\text{181}\) but has implications when interpreting
the findings. Using an ITT approach, we treated participants who did not provide follow-up data as smokers, thus higher loss to follow-up potentially attenuates any intervention effect. However, the sensitivity analysis also showed no intervention effect. There was also differential loss to follow-up between groups, such that loss to follow-up was higher in the intervention group. Differential loss to follow-up, also with higher rates in the exercise group, was reported in one previous trial, also conducted in NZ.\textsuperscript{196} We can only speculate as to the reasons for the high and differential loss to follow-up. However, we do know that participants did screen calls to avoid completing an assessment. It may be that the participant burden was too great. It is also possible that those participants who did not quit avoided answering calls or withdrew from the study because they did not want to be seen to have failed, and/or were frustrated that participating in the study had not helped them to quit, despite the amount of time spent answering questions on the phone. The fact that the intervention group also received intervention phone calls may have compounded this issue, and may explain the differential loss to follow-up.

Second, we did not recruit the initial target sample size of 1400 participants. The slow recruitment rate was identified early in the study, and numerous measures were put in place to counter the slow rate. These included introducing the telephone assessment option, recruiting more staff to help with recruitment and follow-up assessment phone calls, and reducing the number of measures. Increasing the pool of potential participants by recruiting outside of Quitline was discussed, but there were generally more than enough referrals from Quitline. The final sample (n=906) was well below the initial target, reducing the power to detect a statistically significant difference between groups in smoking abstinence. However, as there was no trend towards an effect, it is unlikely that recruiting an additional 494 participants would have resulted in a significant treatment effect.
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Third, smoking cessation outcomes were self-reported and, as assessments were conducted predominantly via telephone, we were unable to objectively verify abstinence for all self-reported abstainers, which introduced the potential for response bias. However, it is unlikely that this biased the results to favour the intervention group, as there is little evidence for statistically significant differences between intervention and control groups in false reporting of smoking abstinence.\textsuperscript{216}

Fourth, due to the nature of the intervention, it was not feasible to blind participants to their allocated study arm.

Fifth, exercise was assessed by self-report, which is associated with recall bias. Despite this, the IPAQ is a reliable and valid measure of physical activity and does permit international comparisons.\textsuperscript{289} Moreover, the long form of the IPAQ was used, which is appropriate for research and evaluation purposes.\textsuperscript{289} Our use of telephone assessments means it was impossible to know for certain if participants who adhered to the treatment (i.e. received a substantial proportion of the 10 scheduled calls) actually met the guideline recommendations of 30 minutes of moderate activity on at least 5 days a week. The results from the IPAQ show that the guideline recommendations were actually met for most participants regardless of study arm, and irrespective of whether they had adhered to the intervention or not (based on total physical activity scores). Thus, it appears that merely meeting the guidelines for total physical activity is not sufficient to aid smoking cessation. It also highlights the uncertainty around the dosage of activity that might be needed to realise benefits on cessation. However, given that the IPAQ measures activity across multiple domains, and 30 minutes of moderate activity per day can be achieved by most adults through activities they accumulate daily, such as work, housekeeping, and family care, one suggested approach is to analyse each domain separately.\textsuperscript{289} Of particular relevance are the leisure and transport domains, as these two domains seem to be the most relevant for public health interventions.\textsuperscript{289} Thus, of more importance with respect to
meeting physical activity guidelines are the changes in these domains, and the
statistically significant difference between groups for leisure time physical activity
observed in the present study. This difference in leisure time physical activity may
have more relevance than the non-significant difference between groups for total
physical activity. It is possible that the greater increase in leisure time physical
activity in the intervention group reflects increased knowledge of what one can class
as ‘leisure activity’ as a result of participation in the intervention. However the types
of activities under each domain were clearly explained by the research assistants
during each assessment, so it is unlikely that control participants were less aware of
what they could categorise as leisure time physical activity.

Sixth, funding constraints meant that it was not possible to follow-up participants at
12 months. This would have allowed comparison with other studies that have
followed participants through to 12 months post-quit date.\textsuperscript{178 181 186-189 191 193 198}

Seventh, Ussher et al.\textsuperscript{68} recommended in their Cochrane review to begin the
exercise programme prior to the quit date as the best approach to enhance smoking
cessation rates. This was not possible in the Fit2Quit trial because participants were
recruited through Quitline and were therefore potentially already engaging in a quit
attempt when they started the study. Future trials should, where possible, follow the
recommendations of Ussher et al.\textsuperscript{68}

Eighth, it is unclear whether the effect of adherence on smoking abstinence is a
result of increased physical activity or the increased social support they received
from adhering to the intervention calls. It is important that future research control for
social support by providing equal contact control conditions when possible. Moreover
the statistically significant effect of adherence on smoking abstinence should be
viewed with caution, considering the potential risk of bias of excluding participants
from analysis post-randomisation.\textsuperscript{290}
Ninth, for the cost-effectiveness analysis, it was not possible to produce separate results for Māori participants. These analyses were explored, but the sample of Māori participants that quit was too small to properly examine cost-effectiveness. Māori participants were included in the main analyses.

Tenth, due to time and funding constraints, only lung cancer and cardiovascular disease were included as outcomes in the Markov model. There are many other disease outcomes that could result from smoking, which could be incorporated into a more comprehensive model.

Finally, Fit2Quit incorporated two existing programmes with proven effectiveness for increasing physical activity (GRx\textsuperscript{285}) and smoking cessation (Quitline\textsuperscript{291}) rates. The assumption was that the GRx programme would be effective for increasing physical activity in smokers; however in retrospect it may have been useful to have conducted an efficacy trial of the Fit2Quit intervention to increase physical activity among smokers trying to quit.

5.4.4 MAIN STUDY FINDINGS WITH RESPECT TO PREVIOUS RESEARCH

Ussher et al.\textsuperscript{68} noted that only 3 of the 15 trials they reviewed showed significantly higher abstinence rates in the physically active (intervention) group compared with participants in the control group at the end of 8-12 weeks’ treatment, and only one study reported higher long-term abstinence rates (at 12 months) in the physically active group.

Findings from our meta-analyses in Chapter 4 suggest that, when these studies are combined, exercise does have an effect on point prevalence abstinence, at least up to six months. However, the meta-analysis of point prevalence abstinence at 12 months found no effect and there was no effect for continuous abstinence at end of
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treatment, 6 months, or 12 months. The weight of evidence from randomised trials therefore suggests that exercise interventions do not improve long-term smoking cessation outcomes compared to standard cessation support.

Lack of adherence to exercise treatment has been a limitation of many earlier studies, and as stated in Chapter 4, five previous studies also reported positive effects of exercise adherence on exercise group cessation rates. In the current study, adherence to the intervention had an effect on smoking cessation rates, but not physical activity. Given that a greater number of intervention contacts did not have an effect on Total IPAQ scores, the effect of adherence on quit rates could simply reflect the increased social support provided by the PSP rather than a dose-response relationship with exercise duration or intensity. However, there was no attention-control condition in the current study, so one could also interpret these findings as suggesting that adherence to the intervention increased the chances of stopping smoking, or that additional and sustained contact time may be needed to support smokers to quit.

This has implications for future research. In the present study we recruited people who had contacted Quitline to stop smoking, and asked them if they were interested in increasing their physical activity levels. This approach did not necessarily account for the participant’s readiness to initiate exercise. Identifying smokers that want to quit and screening them for readiness to exercise may be a more efficient way to maximise smoking cessation outcomes.

Taken together, these findings suggest that future trials should focus less on developing and testing new exercise interventions, and more on increasing adherence to existing programmes.

The current exercise intervention was delivered through GRx; however, in the present study there were two key differences from the usual delivery of GRx. First,
participants were recruited via Quitline and then referred by the research team directly to the GRx PSP, and second, the telephone counselling intervention aimed to be more intensive than standard GRx practice by delivering a total of 10 contacts. This may have accounted for the larger differences found in leisure time exercise found in our trial (31 minutes per day) compared to those reported in the original trial of GRx, which found that leisure time exercise increased by 2.7 kcal/kg/week (p=0.02) or 34 minutes/week more in the intervention group than the control group.

It is possible that the intensity of the telephone-delivered counselling intervention provided in the current study, although sufficient to increase leisure time exercise, was not sufficient to impact on smoking abstinence. Although introductory face-to-face meetings were encouraged for the first contact to help build rapport between the participant and the PSP, many participants opted to conduct this meeting over the telephone. The lack of face-to-face contact may have reduced the ability to build rapport, leading to a lack of accountability for these participants. However, previous studies have also found exercise counselling to be ineffective at increasing smoking abstinence rates. Ussher et al. concluded that the frequency and nature of their counselling was not sufficiently intensive to result in an effect. We had aimed to improve the intervention delivered by Ussher et al. by increasing the amount of support provided (the intervention was four months longer, and each session was of longer duration) but the lack of face-to-face contact may have hampered any additional effect.

Another important element of this trial that may have attenuated any effect of the exercise intervention is the use of NRT as part of standard smoking cessation care. Exercise has had its greatest effect as a smoking cessation aid in studies that have not provided NRT to both treatment groups. No study to date comparing exercise + NRT versus NRT alone has found a statistically significant effect of exercise on smoking abstinence. It may be that NRT attenuates any effect of exercise, although
there is no clear biological mechanism to explain why this might be the case. As NRT is part of usual cessation treatment in most developed countries, it is difficult ethically to conduct a trial of an exercise intervention without providing NRT, and it remains to be seen whether exercise can provide an additional effect over NRT. If NRT attenuates the effect of exercise on smoking cessation, then opportunities to test the effectiveness of exercise interventions for smoking cessation exist in countries where NRT is not currently provided as usual care, or in groups of people where the adverse effects of NRT are not known, such as pregnant women.

Few previous trials have measured or reported physical activity levels of the control group, which makes it difficult to compare the effect of exercise interventions for smoking cessation on physical activity levels. Of the studies that have reported this outcome, findings have been mixed. Three studies\textsuperscript{181, 184, 205} found a statistically significant effect on exercise levels in favour of the intervention group at the end of treatment, while three others found no differences.\textsuperscript{187, 196, 204} Of the studies that reported an effect at the end of treatment, only one found that this effect was maintained at one year of follow-up.\textsuperscript{181} As in our study, three trials reported increased levels of exercise in the control group from end of treatment to follow-up,\textsuperscript{184, 203, 205} which may have attenuated any effect of the intervention.

Previous studies that did show an effect on quit rates had more frequent or more prolonged exercise training,\textsuperscript{68, 178, 189} more supervised exercise,\textsuperscript{178} and higher exercise intensity.\textsuperscript{178} However, there has been a general reduction in exercise adherence following the end of treatment in all studies. Although we did not measure exercise adherence beyond treatment, the decline in leisure time exercise from 8 weeks (when the intervention contacts were relatively intensive) to 24 weeks (when contacts were monthly and designed to aid exercise maintenance), is consistent with declines observed post-treatment in other studies. Marcus et al.\textsuperscript{178} proposed that exercise
adherence beyond treatment may be increased if the intensity or frequency of exercise is lowered.

Recent studies\textsuperscript{180, 183, 184} have examined the feasibility of modalities of exercise other than cardiovascular exercise that involve exercising at low-to-moderate intensities. Al-Chalabi et al.\textsuperscript{180} tested the effects of isometric exercises and found that participants perceived the exercises to be slightly helpful for reducing urges to smoke. Ciccolo et al.\textsuperscript{184} conducted the first study to examine the efficacy of resistance exercise as an aid to smoking cessation. The sample size was too small to detect differences in smoking abstinence, but large effect size differences between groups for smoking abstinence at end of treatment and six months’ follow-up suggest that resistance training could be a viable adjunct to smoking cessation treatment. Bock et al.\textsuperscript{183} showed that women in an 8-week programme of Vinyasa yoga had a greater abstinence rate than a health and wellness programme control group at the end of the treatment.

Given that higher intensities of exercise appear to have the greatest effects on long-term quit rates, perhaps the solution is not to lower the intensity of the exercise, but the duration. Instead of asking participants to maintain levels of moderate-to-vigorous activity for at least 30 minutes per day, most days of the week, they could be encouraged to undertake short bouts of vigorous-intensity exercise instead. Participants may be more likely to adhere to an unsupervised exercise programme if they are less daunted by the duration of the exercise, particularly if the benefit is the same.

5.4.5 FACE-TO-FACE SUB-SAMPLE FINDINGS WITH RESPECT TO PREVIOUS RESEARCH

Of the outcomes measured in the face-to-face assessment sub-sample, the only statistically significant difference observed between groups was for the LSI. This was not surprising, given that the LSI focuses on leisure time physical activity, and a
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A statistically significant difference was observed in the main sample for the leisure domain of the IPAQ. Unfortunately, the LSI and other measures of solely leisure physical activity have not been used previously. It is therefore difficult to relate these findings back to previous research. Of those that reported findings for total physical activity (i.e. physical activity in all domains – leisure, work, home), only three\textsuperscript{181, 184, 205} reported statistically significant differences in favour of the exercise group at the end of treatment (between 9 and 12 weeks post-quit date), and only Bize et al.\textsuperscript{181} reported the effect lasting to follow-up (6 and 12 months). The lack of effect observed for total physical activity (measured with the IPAQ) in the main sample is consistent with findings in other studies that reported total physical activity.\textsuperscript{184, 204, 205}

There were no other statistically significant differences between groups for any of the other face-to-face sub-sample measures (BMI, physical fitness, self-efficacy, barrier-efficacy, and motivation). Given that the 95% confidence intervals for these variables were wide, it is possible that the lack of statistically significant differences between groups may have been due to the small sample size for these variables. As mentioned previously, the original study protocol was designed so that all 1400 of the targeted number of participants would complete face-to-face assessments. This would have provided enough statistical power to examine all of these outcomes. Despite this, most participants were unwilling to attend. The high level of participant burden also impacted on the loss to follow-up rate in the sub-sample. Approximately half of the 219 participants were unwilling to return for a face-to-face assessment at 24 weeks, and opted instead to complete the assessment over the phone or were lost to follow-up.

While acknowledging these issues, the lack of effect on physical fitness is in contrast to most previous studies, which have found a statistically significant difference between groups in physical fitness at the end of treatment.\textsuperscript{178, 184, 188, 189, 191, 198, 202}
However, all of these previous studies incorporated supervised structured exercise programmes, and the greater level of face-to-face support and supervision may have resulted in participants exercising at greater intensities.

The non-significant findings for weight gain and BMI were consistent with the majority of previous studies. Of the trials with enough statistical power to examine differences in anthropometric outcomes, only two showed statistically significant difference between groups in favour of exercise, neither of which incorporated NRT into their programmes. This study is similar to the other three studies, in that NRT was provided to both groups, which provides further support to the summation by Ussher et al., that studies incorporating NRT in both groups are unlikely to see an effect of exercise on weight or BMI because of the attenuation effect of NRT on post-cessation weight gain.

A greater number of participants were able to complete the psychological measures (self-efficacy, barrier-efficacy, and motivation) at six months. One hundred and forty-three of the 219 participants (65%) completed these measures at follow-up. Given the theoretical basis of the intervention, the lack of effect on these variables was surprising.

Possible explanations for the lack of intervention effect on self-efficacy include the following. The telephone counselling intervention may not have been sufficient to impart the key constructs. For example, the lack of face-to-face contact, a buddy system, and support groups may have limited the opportunity to enhance vicarious experiences. If participants were sedentary or insufficiently active at baseline, they may not have fully understood what is required to complete 30 minutes of moderate-intensity activity most days in the following week, and subsequently overestimated their ability at baseline. As those participants began to exercise they may have gained a better understanding of their exercise capabilities, and subsequently
answered the self-efficacy questions after 8 and 24 weeks of exercise with a more realistic understanding. Finally, task self-efficacy increased in both groups, whilst there were no changes in either group for barrier efficacy. The increase in self-efficacy in both groups reflects the increase in total physical activity in both groups. Mastery experience is considered the most powerful means to build self-efficacy. It is possible that the increased self-efficacy in both groups resulted from the mastery experience gained from increased physical activity, which may have had a greater impact on self-efficacy than anything offered in the intervention.

5.5 CONCLUSIONS

The findings from the Fit2Quit trial were that:

- An individually tailored telephone-delivered exercise counselling intervention, when delivered in combination with usual care smoking cessation support, did not increase smoking abstinence rates over and above usual care alone.
- There were no differences between groups for overall physical activity, but differences were observed between groups for leisure time physical activity, which was the target of the intervention.
- Participants who received at least 70% of intervention calls were more likely to be abstinent from smoking at 24 weeks compared with those who received less than 70% of calls.
- There were no effects of the intervention on any psychological or anthropometric outcomes measured in the sub-sample of face-to-face assessment participants.
- The intervention was not cost-effective in comparison to usual care (in the short term), but was cost-effective among participants who adhered to the intervention.
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It was hypothesised that an effect of the intervention on smoking abstinence rates would be observed. Although this was not the case, the non-significant findings are consistent with the majority of previous studies that have not found an effect of exercise on smoking cessation rates, and raise a number of questions about the role of exercise as a smoking cessation aid. The review in Chapter 4 concluded that more trials were needed with larger sample sizes and more intense exercise interventions. Fit2Quit is the largest trial of its kind (with the exception of one internet-based trial\textsuperscript{196}), and more intense than most studies in terms of the number of contacts delivered and the duration of the intervention. However, it was also less intense due to the telephone counselling nature of the intervention. The studies that have been effective to date\textsuperscript{178 183 188 193} have provided structured supervised exercise and it is possible that smokers making a quit attempt need to have at least that level of support to adhere to an exercise programme long enough to sustain cessation. However, the effect of intervention adherence on smoking abstinence suggests that telephone counselling is a sufficiently intense mode of delivery. Such adherence effects have been observed in previous studies regardless of the intensity of the delivery of the exercise programme.\textsuperscript{178 179 187 191 202} Thus, the lack of effect of this and previous exercise interventions for smoking cessation may have little to do with how the exercise programme is delivered, and more to do with the personal characteristics of the individual and the likelihood of that individual participating in an exercise programme. The importance of intrinsic motivation to exercise, attitude, enjoyment, competence, and autonomous regulation has been observed previously in many studies of exercise participation,\textsuperscript{285 292 293} and weight control.\textsuperscript{156 158 294} It would not be surprising for a previously sedentary smoker to score low on these variables, impacting their ability to increase their exercise behaviour.

If exercise works for some individuals and not others, perhaps interventions for smoking cessation should include exercise as one intervention component for those
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individuals who are motivated and have a positive attitude towards exercise. Suggestions for future research regarding this point are discussed below.

...
CHAPTER 6  QUALITATIVE EVALUATION OF THE FIT2QUIT STUDY INTERVENTION

6.1  INTRODUCTION
The qualitative sub-study was conducted with participants from the intervention group of the Fit2Quit trial to determine their thoughts and perceptions regarding the acceptability of the intervention, to determine which, if any, components of the intervention were considered beneficial, and to inform future adaptations of the intervention. Intervention group participants were interviewed after they had completed the intervention, using qualitative research methods (described below).

6.1.1  AIM
To investigate participants’ thoughts and perceptions of the Fit2Quit intervention.

6.2  METHODS
6.2.1  STUDY POPULATION
The study population included Fit2Quit intervention group participants who had completed their time in the trial. Participants were eligible for the study if they were able to provide informed consent, able to participate in a phone interview, and had received the exercise intervention during the Fit2Quit trial and therefore met all eligibility criteria of the trial (see Chapter 5).

6.2.2  RECRUITMENT
Participants in the Fit2Quit study intervention group (n=455) were identified from the electronic data capture system at the NIHI. As this qualitative study was conducted towards the end of the 2-year data collection period, only those that completed the study in the final 5 months (September 2011 to January 2012, n=119) were
contacted. Participants who completed the Fit2Quit trial within the timeframe of this sub-study were informed via a mailed letter of invitation containing the study Participant Information Sheet (Appendix 23) and Consent Form (Appendix 24).

Interested participants were asked to contact the NIHI after receiving the letter of invitation. Participants who did not respond were contacted via telephone within two weeks to ask if they had received the letter and were willing to participate. Purposive sampling was used to obtain a mix of demographics and smoking status in order to establish a broad range of participant perspectives. Participants meeting that description were phoned in order of date of registration for the main trial. Interested participants were asked to provide oral informed consent over the telephone. Oral consent was the process used for the majority of participants in the Fit2Quit trial, and was therefore considered appropriate for the exit interviews also. As per the main trial, a hard copy of the signed informed consent form was posted to each participant following the phone call. All participants were reimbursed for the time spent completing the interview with a $20 supermarket voucher.

6.2.3 INTERVIEW

One-on-one semi-structured telephone interviews were conducted by the candidate. Leila Pfaeffli (LP), an experienced qualitative researcher, provided interviewing training and monitored the first two interviews to ensure they were conducted appropriately. The interviewer used open-ended questions to allow for a reflexive discussion to take place and unscripted themes to surface. The discussion revolved around reasons for participating in the study, expectations of the programme, likes/dislikes regarding the intervention, potential improvements to the intervention, feedback on the delivery of the intervention, and other lifestyle changes that may have taken place as a result of the intervention. See Appendix 25 for the semi-structured interview guidelines. With participant consent, all interviews were digitally recorded and transcribed verbatim. The candidate checked for consistency of
transcription by listening to two of the digital recordings and checking the transcription was accurate.

6.2.4 SAMPLE SIZE AND ANALYSIS

Twenty intervention participants took part in the study. This was the proposed sample size at outset, and was considered sufficient to reach data saturation (where no new themes emerged from new participants).

A general inductive approach was followed, which allows research findings to emerge from the themes in the raw data. The transcripts were read several times by the candidate to identify themes and categories. The computer software programme NVivo9 was used to manage the transcripts and facilitate the analysis process. After a peer debriefing of potential themes and categories with a second reviewer (LP), the candidate coded the transcripts. General categories were initially derived from the sub-study’s aims, followed by more specific categories, which were developed from numerous readings of the transcripts. A second reviewer (LP) read and coded a subsample of transcripts to enhance the trustworthiness of the data analysis. A check of the clarity of the categories was conducted by a peer debriefing process with the second reviewer. No discrepancies were found between the two coders. Following this discussion, the categories were conceptualised into themes.

A table was used to group segments of text from different transcripts by theme. A rigorous and systematic coding approach identified the major themes. Towards the end of the study no new themes emerged, suggesting saturation had been reached. Relationships between themes were identified using a tree diagram and similarities and differences across sub-groups (e.g. quitters vs non-quitters, exercisers vs non-exercisers) were explored. Differences in responses by sex, age, and ethnicity were examined, but the numbers in each of these groups were too small to comment on specifically.
6.2.5 STUDY ORGANISATION
The candidate led the design of the qualitative sub-study, the ethics application, the
development of the interview guidelines, contacted participants, conducted the
interviews, coded the transcripts, and undertook the thematic analysis. LP provided
consultation throughout all of the above processes. Ms Enid Dorey (ED), an
experienced qualitative researcher, completed the transcription of all interviews, and
provided feedback throughout the thematic analysis process.

6.2.6 ETHICS APPROVAL
Ethical Approval for this sub-study was obtained from the NZ Multi-region Ethics
Committee [MEC/11/EXP/102].

6.3 RESULTS
6.3.1 PARTICIPANT CHARACTERISTICS
Letters were mailed to 119 participants in the Fit2Quit study intervention group. Of
these, attempts were made to contact 42 via telephone. Of the 42, 5 declined to
participate, and 17 others were unable to be contacted. A sub-sample of 20 Fit2Quit
study intervention group participants volunteered to participate in the exit interviews.
The 20 participants were representative of the main intervention group with regard to
age, sex, and ethnicity. See Table 22 for participant characteristics. Demographic
information for the total intervention group sample is also presented for comparison.
TABLE 22: BASELINE DEMOGRAPHIC DATA FOR QUALITATIVE STUDY PARTICIPANTS AND TOTAL INTERVENTION GROUP

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exit Interview sub-study (n=20)</th>
<th>Total Intervention group (n=451)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>39.6 ± 12.9</td>
<td>37.6 ± 12.2</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>7 (35)</td>
<td>208 (45.7)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>13 (65)</td>
<td>247 (54.3)</td>
</tr>
<tr>
<td>Prioritised ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Māori, n (%)</td>
<td>9 (45)</td>
<td>142 (31.2)</td>
</tr>
<tr>
<td>Pacific, n (%)</td>
<td>1 (5)</td>
<td>47 (10.3)</td>
</tr>
<tr>
<td>NZ European, n (%)</td>
<td>8 (40)</td>
<td>218 (47.9)</td>
</tr>
<tr>
<td>Asian, n (%)</td>
<td>1 (5)</td>
<td>13 (2.9)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>1 (5)</td>
<td>35 (7.7)</td>
</tr>
<tr>
<td>Quit, n (%)</td>
<td>10 (50)*</td>
<td>105 (23.1)**</td>
</tr>
</tbody>
</table>

*Self-reported quit status at time of interview,
**Self-reported 7-day point prevalence abstinence at 24 weeks

Of the 20 participants, 10 self-reported not smoking at the time they were interviewed, 9 of which had quit during the intervention period, and stated that the intervention contributed to the success of their quit attempt. One stated that he had quit following the end of the intervention after spending some time in hospital. Of the 10 participants still smoking at the time of the interview, 7 stated that they had quit for a brief period (up to 2 weeks) but had relapsed to smoking during the programme.

6.3.2 THEMATIC ANALYSIS

The analysis of the interview data produced the following themes: 1) A genuine interest: Tailored and meaningful support, 2) New Awareness, new attitude, new lifestyle: I could see the benefits, 3) Timing, willpower, weather, cost: Barriers to change, and 4) A bit more hands on: The potential for more support. Reference to the theoretical underpinnings of the intervention is made within these four themes, and discussed later. All quotes are presented with demographic information (age, sex, ethnicity), and quit status at time of interview (“quit” or “smoking”).
### FIGURE 35: SCHEMATIC CHART OF KEY THEMES AND SUB THEMES

<table>
<thead>
<tr>
<th>Key themes</th>
<th>Sub-themes</th>
<th>Related participant beliefs and perceptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>A genuine interest: Tailored and meaningful support</td>
<td>Type of support provided</td>
<td>PSPs were genuinely interested in behaviour change processes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PSPs provided unwavering encouragement</td>
</tr>
<tr>
<td></td>
<td>Level of individual tailoring</td>
<td>Intervention focused on unique barriers specific to the individual</td>
</tr>
<tr>
<td>New awareness, new attitude, new lifestyle: I could see the benefits</td>
<td>Exercise</td>
<td>Increased knowledge of benefit of exercise for smoking cessation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Making exercise part of routine</td>
</tr>
<tr>
<td></td>
<td>Smoking behaviour</td>
<td>Programme helped alter smoking behaviour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Experienced relief from cravings following exercise</td>
</tr>
<tr>
<td></td>
<td>Diet and alcohol</td>
<td>Substituted exercise for more healthy behaviours</td>
</tr>
<tr>
<td>Timing, willpower, weather, cost: Barriers to change</td>
<td>Internal motivation</td>
<td>Improved diet to avoid weight gain when quitting</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduced alcohol intake as a result of quitting</td>
</tr>
<tr>
<td></td>
<td>External stressors</td>
<td>Lack of intrinsic motivation to exercise</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lack of time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Financial barriers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bad weather</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Injuries</td>
</tr>
<tr>
<td>A bit more hands on: The potential for more support</td>
<td>Greater Face-to-face contact</td>
<td>To increase accountability, build greater rapport, and allow for greater monitoring</td>
</tr>
<tr>
<td></td>
<td>Individually tailored call</td>
<td>Increased frequency of contact at specific times around the quit attempt</td>
</tr>
<tr>
<td></td>
<td>Facilitating the support</td>
<td>A support group or buddy system approach would have been beneficial</td>
</tr>
</tbody>
</table>
6.3.3 THEME 1 – A GENUINE INTEREST: TAILORED AND MEANINGFUL SUPPORT

Theme 1 describes the type and nature of the support provided in the intervention. Comments highlighted the supportiveness of the PSP who delivered the intervention and the level of individual tailoring provided throughout. All participants talked favourably of the PSPs and their genuine interest in their behaviour change processes, as well as their unwavering encouragement throughout the intervention. The following comments reflect this.

"It sounded like they had a genuine interest in what I was doing, as opposed to just a [standard] reaction to everybody. It felt as if it was a personal thing." – 66-year-old male, European, quit

“"I liked that …for the hardest part of giving up, [name of PSP] was ringing me every single week. I liked that there was someone there to actually talk to, to get you through it, rather than just the Quitline itself. She was absolutely awesome.” – 31-year-old female, NZ Māori, quit

“It gave us who were trying to quit the impression that people cared.” – 45-year-old female, NZ Māori, smoking

Having personalised support from the PSP throughout the intervention instilled a sense of responsibility and accountability among some participants. Many commented that they liked having someone to report to, and found that their motivation to exercise increased knowing that someone they were accountable to would be checking up on their progress.

“It was as if you needed to achieve something, rather than if you were just doing it for yourself you’d say ‘ah well nobody’s watching.’ It’s good to have someone to report to. And the people you were talking to sounded genuinely interested in what you were achieving” – 66-year-old male, other European, quit
“I liked the phone calls cause, it’s like, you know, someone’s watching you. You know, it’s like, oh OK; you can’t weasel out of stuff. And I actually liked talking to someone about it” – 46-year-old female, NZ Māori, quit

Participants also appreciated that the intervention was individually tailored, which was different to their initial expectations. Individual tailoring aspects included establishing what physical activities participants enjoyed and encouraging those activities by seeking out opportunities to participate in those activities in their local community. Exercise prescription was also based on the individual’s exercise level at baseline. Although PSPs were required to cover specific topics at each contact, the content of each call varied depending on the progress of the participant, both in terms of exercise and smoking behaviour.

“It was a lot more personal... I thought it would be across the board sort of questions… I was really encouraged by the questions I was asked and they provoked a bit of thought some of them.” – 66-year-old male, other European, quit

“Because we are individuals ….we are all smokers, but each individual, they have a personality and different circumstances surrounding them.” – 58-year-old male, Japanese, smoking

Five participants commented that the pedometer they received as part of the intervention helped them meet their exercise prescription.

“I liked the fact that you guys sent out pedometers….that really helped, helped me to reach my goals”

There were also specific comments relating to feeling supported when facing specific and personal barriers to exercise as identified by the individual. Discussions around these specific barriers appeared to enhance their confidence to perform exercise in the face of certain barriers (barrier efficacy).261
“I found that really helpful, just coming up with some of the issues that I faced um and then perhaps getting some ideas on how to mitigate those issues that I came across.” – 46-year-old female, NZ Māori, quit.

There were very few suggested improvements for the content of the exercise programme with respect to individual tailoring and exercise prescription. Most participants simply appreciated that the exercise was prescribed specifically for them.

6.3.4 THEME 2 – NEW AWARENESS, NEW ATTITUDE, NEW LIFESTYLE: I COULD SEE THE BENEFITS

Theme 2 describes the positive lifestyle changes that resulted from participating in the intervention. The positive lifestyle changes explored during the interviews included changes to smoking behaviour, exercise, and other lifestyle changes such as improvements to diet, and drinking (alcohol) behaviours.

6.3.4.1 Smoking behaviour

As stated above, half of the 20 participants self-reported having quit smoking, and some felt that the support provided helped them to alter their smoking behaviour. Two participants commented that they had repeatedly tried to quit throughout the six months.

“Oh what I did, I kept repeatedly quitting and starting. During the study.” - 46-year-old female, NZ European, quit

Others talked about substituting their usual smoking time with other more healthy behaviours such as walking or eating breakfast.

“I don’t really smoke so much at work now. I sorta don’t smoke in the morning cause I wasn’t having breakfast and now I have breakfast and it sort of takes up that smoking time before I go to work.” – 28-year-old male, NZ Māori, smoking
“If anything it motivated me to do other things. It made me get out of my car. Away from my car and actually walk it. It helped at points where it would have been easy, easy to just pick up a cigarette I suppose.” - 33-year-old female, NZ Māori, quit

Participants were also asked whether exercise relieved their cravings for a cigarette. Many of the participants said that they experienced relief from cravings both during and immediately after exercise. Some described the craving relief as a physiological mechanism, whereas others talked about exercise as a distraction from smoking-related thoughts.

“Put it this way, if you are walking around the block or anything, you don't actually feel like stopping for a cigarette.” – 54-year-old male, NZ European, smoking

“Most of the time that I was thinking about cigarette smoking was when I was sitting around absolutely doing nothing. When I had an activity like walking down the hill to the park and walking back up the hill and that I wasn't thinking about cigarette smoking I was just thinking about getting up the hill, basically… and yeah so of course when I did get up the hill I was a bit puffed anyway so I wasn't in any condition to smoke.” - 66-year-old male, other European, quit

6.3.4.2 Exercise

In addition to changes to smoking behaviour, participants also commented that the support and reminders to exercise did actually increase the amount of exercise they undertook.

“I started getting myself into a routine mainly I’m not into over exertion, I’m past the days of going to the gym all the time so I chose to start walking again and get myself into a routine” – 49-year-old female, NZ Māori, quit

“Yes they encouraged me to exercise more. There were times when I was sort of slacking off a bit and they said well you know, “do you think you could actually do
more”. And you know you ask yourself the question and inevitably you have to say yes well I probably could do more. So yeah it did encourage you to do a bit more than I may have done.” - 66-year-old male, other European, quit

For those participants that increased their exercise levels, it was evident that the scheduling efficacy component of the programme was positively received. Participants reported that they had been encouraged to fit exercise into their day, and make time for exercise.

“I sort of got out of the mindframe… like in the mill where I am working, I’ll drive from point A to point B, and yeah, you know, so instead of driving I would walk. So It gave me a 10 min that way and a 10min back. Instead of just being lazy and hopping in the ute.” – 49-year-old male, NZ European, quit

An additional benefit of the programme was the increased level of awareness of the importance of exercise and the body’s physiological responses to exercise. For many participants, the intervention phone calls served as a reminder that they should be exercising.

“It made me more conscious of getting out there and doing something, um so it brought more light to me, getting out there and being more active, opposed to me not, and I knew someone was going to check up on me, so it was just that consciousness of getting out there and being active” – 46-year-old female, NZ Māori, quit

“I was probably going out once or twice a week but with a bit of encouragement I started to enjoy going out more. Maybe 3 or 4 times a week, and albeit it was only for half an hour because of my breathing problems and that, and but that’s alright it was very beneficial to me and it was good for my muscles, you know it gave them a work out…. As I exercised more I actually started to enjoy it more… And I could see
the benefits too as opposed to when I used to smoke.” – 66-year-old male, other European, quit

One of the goals of the programme was to guide participants through the behaviour change process so that at the end of the intervention participants were armed with the knowledge, skills, self-efficacy, and self-motivation to continue to exercise in the long term. Although there were some that struggled to initiate an exercise regimen, a few commented that they had maintained their behaviour beyond the intervention timeframe. Making exercise part of the routine and fitting it into their schedule were mentioned, suggesting that the intervention was successful in increasing scheduling efficacy for these participants.

“It did get me motivated, now exercise is a part of my daily [routine]….. So like for instance I pay 120 bucks for a treadmill in my house but I use it, where I never would have ever looked at hiring something like that.” – 28-year-old female, NZ Māori, smoking

“More time with my boys. My boys are into riding their bikes and going for walks and going to the park and stuff. Like I used to take my car to the park and we are only a couple of kms away. ….So now a couple of times a week we go down to the park….. And I make time for that because it’s for me as well as them. So that was really cool. Cause that came about from “oh how do I fit this in”, I’ve got so much going on, but like I’m spending time at the same time with them, which they appreciate.” – 28-year-old female, NZ Māori, smoking

6.3.4.3 Other lifestyle changes

Although the intervention focussed primarily on smoking cessation and exercise, PSPs were also encouraged to discuss other healthy lifestyle changes with participants as they arose. The most common additional lifestyle change mentioned in the interviews was a healthy diet. A few participants commented that they had
improved their diet to avoid gaining weight when they quit smoking. Also, as a consequence of quitting smoking, taste buds changed and healthy food was appreciated more.

“And yeah, as for the diet, yeah, well the takeaways are completely just wiped out… I tend to like cooking more than the take-outs… I can’t remember the last time I had KFC. One of my biggest things when I started this was the fact that I loved KFC. I may be a small person but I can really pack it away. I found that it’s gotten easier. Cause where we live, it’s everywhere, it’s not just KFC, its every takeaway, whatever, I find myself quite resilient to it now.” – 33-year-old female, NZ Māori, quit

“Ever since I stopped smoking I can taste things better, smell better, um and things taste different to me now. And now I’m focussing on eating healthy, more healthy than ever before, it keeps me busy just thinking about what is good food plans for me, like what is the five different food groups I should be having and things like that.” – 49-year-old female, NZ Māori, quit

Two participants also expressed that they had reduced their alcohol intake as a result of quitting smoking. They commented that smoking and drinking used to go hand in hand, and that it was difficult trying to avoid smoking when they had a few drinks. One participant said that he initially had to avoid drinking to quit smoking, while another said that he did not drink anymore, because it did not taste as good now that he did not smoke.

“Yeah I sort of don’t drink so much…. That was a big thing with smoking for myself….. Like a whole packet would last me a weekend and then I would go get drunk and it would be gone by the next morning” – 28-year-old male, NZ Māori, smoking

“Less drinking you know… Just doesn’t taste as good anymore” – 24-year-old male, NZ European, quit
6.3.5 THEME 3 – TIMING, WILLPOWER, WEATHER, COST: BARRIERS TO CHANGE

Throughout the interviews, participants also highlighted some aspects of the programme that had not worked for them. These included a range of obstacles or barriers, some of which were internal (they simply lacked the motivation to exercise or to quit smoking), whilst others were external (such as life stressors and bad weather).

6.3.5.1 Internal

A core component of the intervention was to enhance participant’s motivation to exercise. The PSPs were trained in motivational interviewing, and instructed to use such techniques throughout the intervention. These techniques included: identifying the participant’s intrinsic values and goals to help stimulate self-motivation for behaviour change, highlighting the key sources of self-efficacy (mastery experiences, social persuasion, physiological responses, and vicarious experiences) when encouraging behaviour change, resolving ambivalence around behaviour change, avoiding direct persuasion, and using a quiet-eliciting counselling style. The OARS approach (Open-ended questions, Affirmations, Reflective listening, Summaries) was used to elicit these techniques.\(^{295}\) Despite the emphasis of the intervention to enhance these constructs, a number of participants stated that they did not have the motivation required to get out and exercise.

“I’d probably say, if I did the exercise like they said I should, it probably would have been more successful, but I didn’t do it so I don’t know. I just couldn’t be bothered.” – 52-year-old female, NZ European, smoking

“What it really came down to was my willpower really.” – 43-year-old female, NZ Māori, smoking
6.3.5.2 External

Based on participant’s comments, it was apparent that the intervention was unsuccessful for some in aiding them to overcome external barriers to exercise. Barriers discussed included life stressors, lack of time, injuries, bad weather and financial hardship. Two participants also mentioned that external life stressors had impacted on their ability to quit smoking, which included emotional events, and having a busy lifestyle.

“I’ve had a really stressful time, I’ve had a couple of deaths in my family… we’ve also been robbed as well in the time… and I haven’t given up smoking, I’ve returned to it full blown. My problem is I have an extremely busy job that’s 10-12 hours a day and Sundays and it was really hard for me to fit in the exercise, but you know, you always can, it’s just that I didn’t, so yeah that was my personal problem with the whole thing.”

– 28-year-old female, NZ Māori, smoking

Three participants complained that the bad weather made it difficult to exercise. The intervention tried to specifically target bad weather as a potential barrier to address.

“The only trouble was that it was right in the middle of winter. So um the trouble is we’ve got two little house dogs, so you take those out for a walk and that and they are wet through and you need to bath them and clean them up and dry them when you get home. So it was just really the timing with the weather that wasn’t really right for me, unfortunately.” – 54-year-old male, NZ European, smoking

“Unfortunately it was sort of at the wrong time of the year…. like you know, it was pouring with rain or blowing a gail, or, you know what I mean? You couldn’t really get out and do stuff.” – 54-year-old male, NZ European, smoking

“My exercise regime, went up and down depending on the season.” – 46-year-old female, NZ Māori, quit
The PSPs were trained to encourage participation in pre-existing free physical activity community-based programmes such as GRx. Despite this, two participants expressed that they would have exercised more if there wasn’t a financial barrier, and the intervention could have included free or subsidised access to local exercise facilities.

“Maybe helping people going to the gym or something like that… Yeah like get into the gym or something, you know, like they can’t afford it… I was sort of hoping that there would be a green card to go to gyms and all that. For cheaper.” – 24-year-old male, NZ European, quit

The other commonly mentioned barrier to exercise was injury. Three participants mentioned that injuries had halted or disrupted their exercise regimen. Although the exercise programme was designed to prevent injuries by starting at low intensities and duration and slowly building up the body’s tolerance for exercise, injuries did occur throughout the programme. In response to the question, ‘how often do you exercise now?’ to explore whether exercise levels were maintained beyond the programme, one participant said:

“Not as often as what I was doing sort of in the peak of it all. Um because I hurt my Achilles, sort of overdid it a bit.” - 44-year-old female, NZ Māori, quit

One participant commented that they would have preferred a PSP with slightly more knowledge of specific injuries, who could provide advice on appropriate modalities of exercise for the injury concerned.

“I have a knee injury that limited the type of exercises I can do, um I thought perhaps I would have had more sort of a coaching person on the phone that could have suggested certain kinda exercises for me to do.” – 46-year-old female, NZ Māori, quit
6.3.6 THEME 4 – A BIT MORE HANDS ON: THE POTENTIAL FOR MORE SUPPORT

During the course of the interviews participants offered suggestions about how the intervention could be improved, including greater face-to-face contact, greater tailoring of the call schedule, and greater facilitation of social support. These suggestions came predominantly from participants who did not quit smoking, or did not increase their exercise levels.

6.3.6.1 Greater F2F contact

When the intervention was originally designed it included an initial face-to-face meeting between the participant and the PSP in the first session. The face-to-face meeting was included in the programme to help build rapport between the PSP and the participant. Unfortunately, there were a number of participants that, for various reasons (e.g. logistical reasons around transport and timing of potential meetings), were unable to attend a face-to-face meeting, and this session was conducted over the telephone instead. Although it was usually the participant who opted to conduct the first session over the phone, many of the participants (n=5) interviewed suggested that the intervention would have been more effective with greater face-to-face contact.

“Yeah that would have been really cool. Like they were very helpful but it was more advice over the phone. And it is kinda easy to ignore that, or easier to ignore that than, even though I really wanted to do it, than actually having someone there going “right I’m going to check up on you in two days and see if you’ve carried on” or something like that.” – 46-year-old female, NZ European, quit

“Um, maybe just made it a bit more hands on with actual people. … Like to visit them. Doesn’t have to be every week but you know once a month or something. Just to say “Yep you are doing well” and give them a little pat on their back, physical contact or something.” – 31-year-old female, NZ Māori, quit
“I thought that that there was a big gap between having a conversation with the person as to what goals I could set and when I could do my exercise, and actually doing it. And um I guess the ideal, in an ideal world with heaps of money would be actually having them there, like having them do personal training with you once a week or something to keep you motivated would have been really cool. Cause it was really easy not to do it” -- 46-year-old female, NZ European, quit

These few participants commented that the lack of face-to-face contact made them feel less accountable. It was easier to ignore the advice than it otherwise would have been if contact had been face-to-face. They also suggested that face-to-face contact would have allowed for greater monitoring of the intervention, as it would have enabled activity logs and pedometer step counts to be checked regularly throughout the intervention. This is in contrast to the previous participants’ comments, who felt that the phone support from the PSP held them accountable.

“Even with the checking and seeing my progress…I could have just made up, and most of the time I just made up lies that I had done. And they weren’t able to see any evidence of me doing exercise. ... I only said what I wanted them to hear but in actual fact I wasn’t really doing it and so they couldn’t see that side of it.....” -- 27-year-old female, Samoan, smoking

“I would recommend … a meeting, an actual meeting with this person. And the actual charts that they have sent out, the actual charts to be filled out and some proof of it and they also sent out, oh what’s that little [pedometer] thing, where you check your steps. ... And for that for the person to bring it and they can actually see how many steps they had done on that day or whatever.” -- 27-year-old female, Samoan, smoking
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“Even if they just went to the gym with you once a week and you did the rest and they checked up on you and you know made sure you had done it. That would have been really good for me.” – 46-year-old female, NZ European, quit

6.3.6.2 Individually tailored call schedule

As mentioned in Theme 1, the PSPs were encouraged to personally tailor the intervention to each participant as much as possible. About half of the participants found the call schedule (weekly calls for one month, fortnightly calls for one month, and monthly calls for four months) worked well and liked that calls were more frequent at the beginning of the programme and then became less frequent as the intervention progressed.

“Well she used to ring me I think it was every week to start with, then it was two weeks, then it went to a month. And it was quite good. ... It wasn’t like you were getting bugged and it wasn’t like too far apart that you don’t give a damn. So it was quite good in that respect.” – 49-year-old male, NZ European, quit

“I liked the frequency of the phone calls initially and like how it petered out was really good… ... Especially in those early days it was good to have that constant contact cause you know, it was like a day by day process. Knowing that she was going to ring in a few days’ time, you know, as the week went along, helped you hang on a bit longer.” – 44-year-old female, NZ Māori, quit

However, there were a number of comments suggesting even more tailoring would have been helpful. Some (n=4) participants who did not quit at the start of the programme, but quit in the last 4 months (when they were receiving monthly calls), expressed that they would have liked more frequent contacts around the time they quit. Such participants had to wait up to a month to talk to the PSP about their quit attempt, and may have already relapsed to smoking again before the next phone call.
“I thought it would be better to ring more often. Because when I did give up, I gave up for the two weeks and I sort of felt like talking to someone about it.” – 24-year-old female, NZ European, smoking

One participant suggested that it would have been useful to provide a service where participants could phone the PSPs themselves, instead of having to wait for their next call.

“Well sometimes I wished I could have called someone to say ‘ah my god what a terrible week I’ve had,’ you know, instead of like at the end of the month because sometimes you’ve like forgotten … or some of the times you were just like ‘oh my gosh I don’t know what to do’ or I wish I could have rung up someone and spoke to them about the issues you faced just for that week.” – 46-year-old female, NZ Māori, quit

Alternatively, another participant suggested that more frequent (weekly) contact throughout the programme would have helped to address this issue.

“I think it would have been good weekly the whole way through. .... You know, the more the better really. I think it helps with the motivation. Cause you are dealing with people that have smoked and aren’t fit in general you know. So it takes quite a lot to get those people going. I’m sure you can but it’s not easy……. you know, people say “it only takes ‘x’ amount of time to form a habit” but I actually think you need a bit more than that. I think stopping smoking and exercising, both of those things are quite hard to keep doing. Yeah so I reckon weekly, personally... Weekly the whole way through,” – 46-year-old female, NZ European, quit

6.3.6.3 Facilitating the support network

According to self-efficacy theory, vicarious experience is a key source of self-efficacy. Throughout the intervention PSPs encouraged participants to exercise with a peer who had successfully engaged in the behaviour. Beyond this suggestion, the ability
to increase vicarious experiences through self-efficacy was limited, particularly as the PSPs were all non-smokers (who had never smoked).

“You wonder the people that do it have ever smoked. Cause if they haven’t, they have no idea how hard it is. But that’s not their fault.” – 52-year-old female, NZ European, smoking

Two participants commented that they would have benefited from exercising as part of a group, and suggested that this could have been organised by the PSPs rather than simply suggesting they find an exercise buddy themselves.

“Cause when you are on your own you find it hard to motivate yourself. Like even though [Name] rung once a week, or once every two weeks and that was good, I think I only met her once. ...It does kind of help when you have someone with you. .... Buddy system is better than a group thing cause you know most people don’t want to advertise or be around a whole heap of people but at least with one person they have the similar, you know, they can bounce off each other, yeah.” – 33-year-old female, NZ Māori, quit

“Um might have been helpful to possibly be part of a support group. If there were others participating on that as well. It would have been quite neat to have a session and such together. As it is always good to see other people that are struggling or making their way through a new process as well.” – 44-year-old female, NZ Māori, quit

6.4 DISCUSSION
This qualitative study sought to elicit more in-depth information on participants’ beliefs and perceptions of the intervention, which may have provided insight into why
the Fit2Quit trial was unsuccessful at improving abstinence rates over and above usual care.

Overall, participants found the intervention to be acceptable in terms of delivery, frequency and duration. This was largely due to the supportiveness of the PSPs, and the tailoring of the intervention to meet participants’ needs. The telephone counselling approach was chosen because it built on an existing delivery infrastructure offered by Sport Auckland; however this was augmented with a more intensive approach and strong theoretical grounding. Despite this, and as highlighted by participant feedback, this approach did not suit all people, all the time. Some participants felt that the intervention could have been enhanced with greater opportunity for face-to-face contact, more tailoring of the intervention schedule and greater facilitation of a support network.

Participants liked the supportiveness of the PSPs. However, participants who didn’t quit smoking early in the programme but quit later on lacked the frequency of support necessary to sustain their quit attempt, suggesting the provision of a reactive service (where participants could telephone for support as they need it) could be a useful addition to future interventions. Moreover, the lack of face-to-face support reduced the motivation and accountability levels of some participants.

The lack of motivation expressed by some participants is an important point. These findings demonstrate differences between highly motivated and less motivated individuals. Although there were a number of good suggestions to improve the intervention, those participants who do not have the motivation to quit and/or exercise are unlikely to successfully change these behaviours, regardless of the delivery, frequency, intensity and duration of the intervention. Therefore, as discussed in Chapter 5, perhaps exercise interventions for smoking cessation only work for highly motivated individuals, or at least those motivated to change their
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exercise behaviour. Although participants were asked during initial screening whether they were willing to engage in regular physical activity, a few participants in this sub-study stated that they did not have the motivation or willpower required to exercise. One suggestion for future research could be to only recruit those individuals who screen high on motivation to exercise. This would increase adherence rates, reduce loss to follow-up, and, although the results would not be generalisable to less motivated smokers, it would enable accurate assessment of the effect of exercise on smoking abstinence.

6.4.1.1 Support for theoretical basis of intervention

As mentioned previously, the intervention was grounded in self-efficacy theory. Therefore, particular components of the intervention were designed to target the sources of self-efficacy (mastery experiences, social persuasion, vicarious experiences, and physiological responses). There were a number of comments to suggest that the intervention successfully enhanced efficacious beliefs via these sources. The most prominent source of self-efficacy mentioned by participants was verbal (social) persuasion. Many participants were appreciative of the support provided, not only encouraging them to exercise, but also supporting them through their quit attempt. This is consistent with the findings of a qualitative evaluation of a mobile phone based intervention for smoking cessation, which also found the provision of support to be the most appreciated aspect of the programme.

Mastery experiences were improved by encouraging participants to partake in activities that they had previously enjoyed and/or felt confident to participate in, and also through the provision of pedometers, which enabled participants to monitor their progress throughout the programme, keep track of their step counts, and set future goals. Although not every participant used the pedometer regularly, the comments from those that did suggested it was a useful tool for building self-efficacy and goal setting. A number of participants also stated that the more they understood and
realised the benefits of exercise, the greater their confidence, which enhanced adherence to the behaviour.

There were also a few comments that suggested that participants experienced positive physiological responses, which encouraged them to continue to exercise. None of the interviewed participants reported that they had not exercised because they disliked the physiological responses they experienced during and after exercise, which suggests that this aspect of the intervention was covered adequately.

The intervention aimed to increase vicarious experiences by suggesting that participants exercise with a friend. Beyond this, it was difficult to increase vicarious experiences. One of the common suggestions to improve the programme was the provision of an exercise support group, buddy system, or a role model (a previous smoker to whom the participant could identify with who had successfully quit smoking with exercise).

### 6.4.1.2 Limitations of the qualitative sub-study

The above findings should be interpreted with the following limitations in mind:

These results are from a small sample and are not generalisable to a larger population. Although this is the nature of qualitative research and the purpose is not to generalise, the sub-sample does reflect the demographics of the large RCT, increasing transferability.

Only those people that were contactable throughout the Fit2Quit intervention were approached to participate in this study, which may have biased the results; however, it was important for participants to have experienced the intervention in order to determine their response to it.

Researcher bias: The interviewer for this sub-study (the candidate) had a vested interest in the study. The candidate was not a PSP, but was involved heavily in the
intervention design. This may have introduced researcher bias, whereby the candidate may have asked questions in a certain way to obtain favourable responses, and/or analyse and interpret the findings differently from someone external to the study. However, a number of approaches were used to avoid this. First, the candidate designed the interview questions with Associate Professor Ralph Maddison, Associate Professor Chris Bullen, and LP. Second, a peer-debriefing process was conducted, whereby LP and ED both looked over the themes independently, and questioned the candidate’s findings to ensure the themes were sound.

Participants were interviewed between one and six weeks after they had completed the study. This may have affected memory recall of various aspects of the intervention. Four of the ten participants that stated that they were not smoking at the time of the interview, self-reported smoking at least a single puff of a cigarette in the seven days prior to their 24-week assessment. It is unclear whether they quit during the period between the 24-week assessment and the interview, misreported their smoking status at one or both interviews, or considered themselves smoke-free but had one cigarette prior to the 24-week assessment. Regardless, this may have affected their perspectives of the intervention.

Finally, on reflection, it would have been useful to include a question within the semi-structured interview to explore participant perceptions of the advantages and disadvantages of changing two behaviours (exercise and smoking cessation) simultaneously rather than sequentially. This did not emerge from the thematic analysis as an issue, but a specific question around this may have increased the likelihood of it surfacing.
6.5 CONCLUSIONS

To the best of my knowledge, this is the first trial of an exercise intervention for smoking cessation to conduct a qualitative analysis of the intervention. These findings are crucial to our understanding of the role of exercise as a smoking cessation aid, and provide important information that could not have been obtained by quantitative means. Overall, the Fit2Quit intervention appears to have been appreciated by most of the participants in this sub-study. However, it appears that future interventions need to be even more individually tailored to ensure participants receive the support required at the time they require it.

Moreover, establishing a support network for participants to share their experiences and obtain social support could also be a useful addition. This could be provided via an online website, or via the provision of face-to-face support groups and/or buddy systems. Future research should also explore the use of role models in this context to enhance vicarious experiences and social support, as has been suggested in previous qualitative studies of interventions for smoking cessation (without exercise)\textsuperscript{296} and depression.\textsuperscript{297}

Finally, the qualitative study findings provide further support to the notion that exercise is an appropriate intervention tool for some individuals, but not others, and that it should be offered as one treatment option to those individuals who are motivated to exercise.
CHAPTER 7  GENERAL DISCUSSION

7.1 AIM AND OUTLINE

In summary, this thesis presents a group of research studies, which were conducted to better understand the relationship between exercise and cigarette cravings, TWS and smoking cessation. Two systematic reviews of the literature, that included meta-analyses of primary outcomes, informed the development of the two RCTs and three sub-studies described in this thesis.

This closing chapter provides an overall summary and synthesis of this programme of research. The wider implications of the results for practice and policy, together with a consideration of future directions and priorities for research, are discussed.

7.2 KEY FINDINGS

The key findings of the systematic review of studies of the acute effects of exercise on cigarette cravings and TWS were:

- Exercise is more effective than passive control conditions for reducing cravings for a cigarette during temporary smoking abstinence.
- There are only small differences in the magnitude of effect for light, moderate or vigorous exercise.
- Further research is required to a) examine potential mechanisms underlying the relationship between exercise and cravings, and b) establish the intensity and modality of exercise that provides the greatest reduction in cravings.

The key findings of the crossover RCT were:

- Vigorous exercise reduces cravings relative to light- and moderate-intensity exercise.
• There were no statistically significant differences between light- and moderate-intensity exercise for cravings, withdrawal symptoms, affect, arousal, and food cravings. The lack of difference between the two conditions is also reflected in all of the measured peripheral biomarkers of neurobiology.

• There were statistically significant differences between light and vigorous conditions for all measures of HRV. It is possible that HRV could explain the link between exercise and cigarette cravings.

• Noradrenaline and cortisol both increased following vigorous exercise. These increases may explain greater reductions in cravings in comparison with light and moderate exercise.

The key findings of the systematic review of studies of exercise interventions for smoking cessation were:

• Meta-analyses results suggest that exercise is effective for point prevalence smoking abstinence up to 6 months, but effects are not sustained to 12 months.

• The most effective modality, intensity, frequency, and duration of exercise, method of intervention delivery, and exercise setting, remain unclear.

• Most trials to date have provided structured exercise as a supervised programme but have been too small and therefore underpowered, and/or too low in intensity or duration to conclude that there is an effect of intervention.

• Further trials are needed with larger sample sizes, sufficiently intense exercise interventions, and measures of exercise adherence.

The findings from the Fit2Quit trial were that:

• The individually tailored telephone-delivered exercise counselling
intervention, when delivered in combination with usual care smoking cessation support, did not increase smoking abstinence rates, over and above usual care alone.

- Participants who adhered to the intervention (i.e. received at least the median number [7 out of 10] intervention calls) were more likely to be abstinent from smoking at 24 weeks compared with those who received less than 70% of calls.

- There were no differences between groups for overall physical activity levels, but differences were observed between groups for leisure time physical activity in the total sample (n = 906), and in the face-to-face sub-group, (n = 219)), which was the target of the intervention.

- The face-to-face sub-study found no effect of the Fit2Quit intervention on anthropometric (BMI, weight), fitness, or psychological (self-efficacy, barrier-efficacy, motivation) outcomes.

- The cost-effectiveness analysis indicated that the Fit2Quit trial was not cost-effective in comparison to usual care. However, the Fit2Quit intervention was cost-effective (in the short term) over usual care among those participants who adhered to the intervention.

- The qualitative sub-study findings indicate that the Fit2Quit intervention was well received, and that parts of the intervention, particularly the provision of support and encouragement from the PSP, were useful to aid exercise initiation and smoking cessation.

- Suggested improvements to the Fit2Quit intervention included greater tailoring of the call schedule, greater face-to-face contact, and the provision of an exercise buddy-system or support group.
7.3 DISCUSSION OF MAIN FINDINGS

The crossover trial extended previous research\(^64\) by exploring the effects of three different intensities of exercise on cigarette cravings, and demonstrated that an acute bout of vigorous intensity exercise causes a greater reduction in cigarette cravings during temporary smoking abstinence compared with either light- or moderate-intensity exercise. This is consistent with findings from the first systematic review (Chapter 2) and a recently published review\(^69\) that vigorous exercise results in the greatest reduction in cravings in the short term, and may be a viable strategy to help people deal with cravings when trying to quit. Despite this, other research supports the use of moderate- and/or light-intensity exercise because they have less impact on negative mood,\(^96\) and reductions in cravings last longer than for vigorous exercise.\(^102\)\(^\hspace{1em}^{103}\) Therefore the most effective intensity to relieve cravings is still unclear.

The crossover trial builds on existing research by examining a number of previously untested potential mechanisms to explain the exercise and cigarette cravings relationship. The observed effects of vigorous-intensity exercise on HRV, noradrenaline and cortisol provide preliminary support for a physiological mechanism underlying the relationship, not evident for the lighter intensity activities. In summary, this is the first study to examine these peripheral markers in smokers after overnight smoking abstinence and the findings support the use of vigorous exercise to reduce cravings. However, more research with larger sample sizes is needed to determine whether these variables mediate the exercise-cravings relationship.

The research paradigm used in this acute study was consistent with many previous studies in this context, in that participants were asked to abstain from smoking temporarily prior to attending each treatment session. A limitation of this approach is that it does not replicate the environment and experience of an actual quit attempt. While many of the previous studies have attempted to increase ecological validity by
presenting smoking-related cues in the study laboratory, the situation is not the same as the participant’s usual environment, where smoking-related cues may be more common. Thus, the participant’s cravings post-exercise may be less frequent or intense simply because of the environment in which the study is conducted. Moreover, temporarily abstinent smokers may experience cravings differently to those undergoing a quit attempt simply because they know they will be able to smoke again after the treatment session. These factors may explain why, in general, studies of the acute effects of exercise on cigarette cravings and TWS in temporarily abstinent smokers have found significant reductions in cravings following exercise, but trials of exercise interventions for smoking cessation have largely shown no effect.

The Fit2Quit trial was a large pragmatic RCT to determine the effectiveness of a telephone counselling intervention in addition to usual smoking cessation support to augment quit rates compared to usual care alone. Despite addressing a number of methodological limitations highlighted in previous reviews and the systematic review presented in this thesis (Chapter 4), the Fit2Quit trial had a null effect. Consistent with the majority of previous studies, there was no statistically significant effect of the exercise intervention on abstinence rates in comparison with usual care. Based on these findings and from findings from previous research, the weight of evidence suggests that exercise interventions do not improve long-term smoking cessation outcomes compared to standard cessation support.

An important finding from the Fit2Quit trial was that participants who received at least 70% of the intervention contacts were more likely to be abstinent from smoking at 24 weeks compared with those who received less than 70% of calls. This finding is consistent with previous studies, which have found an effect of adherence on smoking abstinence, and suggests that exercise interventions are effective for those that adhere to them. Moreover, there was also an effect of
adherence on cost-effectiveness, indicating that the Fit2Quit intervention was cost-effective over usual care among the participants that adhered to it.

There were no differences between groups for overall physical activity, however differences were observed for leisure time physical activity, which was the target of the intervention. Physical activity outcomes have not always been reported in previous trials, but the Fit2Quit trial results are consistent with three trials that also did not show an intervention effect on total physical activity. Only one RCT showed a statistically significant difference in total physical activity between groups in favour of the intervention that lasted to at least six months. However, as stated previously, physical activity in the leisure-time domain may be a more appropriate measure of the effectiveness of a physical activity intervention than total physical activity, so the observed difference between groups for leisure-time in the Fit2Quit trial is an important finding, and future studies should also include domain-based measurement of physical activity.

Findings from the Fit2Quit qualitative sub-study suggest that participants appreciated the support provided, the individual nature of the support, and having someone to be held accountable to. They also reported positive lifestyle changes as a result of the intervention. Altering the intervention to include greater tailoring of the call schedule, greater face-to-face contact, and an exercise buddy-system/support group may enhance the effectiveness of future programmes. Collectively, the five studies presented in this thesis increase our understanding of the role of exercise as a smoking cessation aid. The aim of these studies was to investigate the acute and chronic effects of exercise on cigarette cravings and smoking abstinence, and the potential mechanisms underlying these relationships. Whilst exercise has an acute effect on cigarette cravings in the laboratory, its chronic effect on smoking abstinence rates is less clear. One of the underlying assumptions for why exercise might be expected to aid smoking cessation is the similarities between the effects of nicotine
and exercise on neurobiological processes in the brain,\textsuperscript{53, 54} and that exercise can therefore offset the negative effects of withdrawal from nicotine dependence. Results for noradrenaline and cortisol in the crossover trial provide preliminary support for this assumption. However, such effects are short-term, and the crossover trial findings suggest that vigorous intensity exercise is required. Therefore, the inability of exercise interventions to significantly reduce smoking cessation rates is potentially due to how exercise has been prescribed in interventions to date. The effect of vigorous exercise on cravings is acute, so the exercise intervention should be designed to target acute cravings. Rather than promoting increases in daily physical activity, short bouts of vigorous intensity exercise need to be marketed as an aid for acute craving relief at the specific time-points when one experiences a craving.

However, exercise interventions have been shown to be effective at increasing abstinence rates among participants who adhere to the intervention,\textsuperscript{178, 179, 187, 191, 202} suggesting that if one is ready for exercise behaviour change and motivated enough to adhere to exercise then the current exercise intervention approach of prescribing increases in daily total physical activity can be a useful aid for smoking cessation. Whilst it is preferable to find smoking cessation solutions that are effective for everyone, there are a number of psychological factors that determine whether an individual will likely partake in an exercise programme,\textsuperscript{285, 292, 293, 156, 158, 294} and as stated above, it is likely that many previously sedentary smokers would have low levels of motivation, exercise readiness, and perceived enjoyment. Offering support to increase daily physical activity could be a useful addition to current usual care smoking cessation support for those ready and motivated to exercise. These findings have implications for both research and policy that are discussed below.
7.4 STRENGTHS OF THIS THESIS

A major strength of this thesis is the use of a mixture of study designs, which provides a broad perspective on the relationship between exercise and smoking cessation. The exercise and smoking cessation literature has two distinct, but linked streams of research: one on the acute effects of exercise on TWS and cravings, and one on the long-term effects of exercise on smoking cessation. By combining in one thesis, a systematic review for each stream of research, a crossover trial of the acute effects of exercise on cigarette cravings, and an RCT of an exercise intervention for smoking cessation (both of which were the largest of their kind), it was possible to synthesise and summarise all findings regarding the acute and long-term effects of exercise on smoking cessation. Moreover, qualitative research was conducted to enhance the quantitative findings from the Fit2Quit trial.

The benefit of an RCT design is that it is the most efficient design for investigating causality because one can ensure the ‘cause’ precedes the ‘effect’, and it minimises bias and confounding in ascertaining treatment effects.298

Throughout the conduct of the trial all efforts were made to reduce threats to internal validity, including:

- Adherence to CONSORT guidelines299 and the guidelines for Good Clinical Practice.300
- The use of a computer generated random allocation sequence, and allocation concealment up to the point of randomisation.
- The application of the ITT principle to analyse the primary outcome.
- The use of a crossover trial design to increase statistical power.
- Stratification by key variables in the Fit2Quit trial (sex, ethnicity and geographic area).
Controlling for covariates (e.g. age, sex, ethnicity, baseline strength of urge to smoke) in the analyses in both studies.

Other methodological strengths of this research included its examination of mechanisms, the use of pragmatic design features and inclusion of a cost-effectiveness analysis. Many previously untested potential mechanisms were explored including HRV, noradrenaline, adrenaline, glucose, insulin, food cravings, self-efficacy, barrier efficacy, and motivation. Fit2Quit used currently available national delivery services for both smoking cessation (Quitline) and physical activity promotion (GRx). This enabled the effectiveness of the intervention to be tested in a ‘real-world’ setting. This adds to the applicability of the results to the wider NZ population, and also provides a direct indication to policy makers to inform decisions about practice.\(^{287}\) It’s setting in the NZ context was also a strength. Before this research, little was known about the effects of exercise on TWS, cravings, and smoking cessation among a NZ population, with only one previous trial conducted.\(^{198}\)

Both trials recruited an ethnically diverse sample representative of the NZ population, with greater than 30% of participants who self-identified as being of Māori ethnicity. This is a major strength of this research, as most previous studies recruited predominantly Caucasian samples. This research therefore provides valuable contextual information on the relationship between exercise and smoking.

The Fit2Quit trial was the first RCT of an exercise intervention for smoking cessation to include an analysis of cost-effectiveness, and the first to indicate that, despite non-significant effects on smoking abstinence in the short term, exercise interventions for smoking cessation can be cost-effective in the long term and have positive effects on health-related quality of life, compared to usual care.
Chapter 7: General Discussion

7.5 LIMITATIONS

The limitations of each component of this thesis have been discussed in previous chapters. This section highlights the general limitations of this research.

Limitations of the systematic reviews:

Both reviews included meta-analyses using group level data, which differs from the more recent approach by Haasova et al., who used individual participant data (IPD) in their meta-analysis of studies of the acute effects of exercise on cigarette cravings, and also included additional studies not included in my first review (Chapter 2). IPD meta-analyses are considered the gold-standard approach; they facilitate standardisation of the analyses across studies, and are potentially more reliable than aggregate data approaches. However, they are also resource intensive and budget constraints did not allow for such an approach in the current review. Nevertheless, the findings in my review are consistent with Haasova et al., that exercise is effective to reduce cravings when compared with passive control conditions.

Limitations to both empirical studies:

Both trials failed to meet their target sample sizes, which had an impact on the available power to detect any differences. The Fit2Quit trial also had high and differential loss to follow-up, which is a potential source of bias and needs to be considered when interpreting the results. It may be that participants in the intervention group experienced greater participant burden (from intervention phone calls) than control participants and were therefore more likely to avoid assessment calls. All those lost to follow-up were considered smokers, so the differential loss to follow-up reduced the chances of detecting a difference between groups in favour of the intervention.
Due to the nature of both studies we were unable to blind participants to the intervention. We did not have the financial resources to blind assessors to treatment allocation.

Self-selection bias: as in most pragmatic studies, participants volunteered to take part. The sample of volunteer smokers in both trials may not necessarily be generalisable to non-volunteers who may differ significantly from volunteers in terms of participant characteristics such as motivation and self-confidence.

7.6 FUTURE RESEARCH AND IMPLICATIONS

The following sections present key suggestions for future research and implications.

7.6.1.1 Laboratory studies

The mechanisms underlying the relationship between acute exercise and cigarette cravings remain unclear, requiring additional research. Future studies should focus on including a passive control condition to determine how vigorous exercise affects variables such as noradrenaline, cortisol, and HRV in abstaining smokers. Studies with large participant numbers are required to provide sufficient power to explore mediating effects of the peripheral markers of neurobiological changes.

The crossover trial was the first study to examine HRV as a potential mediator of the relationship between exercise and cigarette cravings, and the preliminary findings suggest future research is warranted. The effects of exercise on HRV in abstaining smokers need to be compared with a non-smoking control group to accurately determine differences in the autonomic response to exercise among smokers. Moreover, for further studies of HRV in this context, it would be helpful to have a more accurate measure of physical fitness (i.e. VO\textsubscript{2}max) to ensure the heart rates reached during each condition accurately depict light, moderate, and vigorous
intensity for each participant. This would enable a more precise assessment of HRV response during exercise.

7.6.1.2 Translational Research

Laboratory-based studies on the effects of exercise on cravings in temporarily abstinent smokers have generally found positive effects on cigarette cravings, but studies of exercise interventions have largely been unsuccessful at increasing smoking abstinence rates. Therefore, it is imperative that the findings from the laboratory setting are translated to the real world by examining the acute effects of exercise in more ecologically valid settings. To date, only one study has attempted to do this.\(^\text{103}\)

More research is needed to explore the acute effects of exercise over the course of a quit attempt, which would better reflect the real world. This would also help to link the two streams of research within the exercise and smoking cessation literature. For example, as discussed above, one recommendation could be to encourage participants to use brief bouts of vigorous exercise to manage cravings when trying to quit. This approach may have advantages over more traditional approaches including: 1) it may improve relief from cravings, and 2) participants may be more likely to adhere to an unsupervised exercise programme if they are less daunted by the duration of the exercise bout.

7.6.1.3 Methodological considerations

A number of methodological considerations for future research are required. For exercise interventions to work on smoking cessation outcomes, they must have an effect on exercise or physical activity behaviour. Thus future research is required to enhance the impact of the intervention on exercise behaviour, and to enhance adherence to the intervention.
To improve impact of the intervention on behaviour it may be that using bouts of exercise as a strategy to relieve cravings may have more utility than trying to increase overall levels of exercise or physical activity. Qualitative study findings from Fit2Quit suggest that greater individually tailoring may be beneficial, but could be resource intensive and cost-prohibitive. Identifying participants that want to quit but who are also motivationally ready to exercise may be a better approach. This may also enhance adherence to the behaviour in the long term.

Future research might also want to consider using technology such as mobile phones to deliver short message service (SMS) messages for both smoking cessation and exercise behavioural support. SMS interventions have successfully been used to enhance quit rates in NZ\textsuperscript{302} and the UK.\textsuperscript{303} These interventions could be augmented with strategies to improve exercise behaviour. As highlighted in previous research,\textsuperscript{68} future exercise interventions should start prior to the participants setting a quit date.

The meta-analyses presented in Chapter 4 suggest that whilst exercise may have an effect on smoking abstinence up to 6 months, the effect is not sustained at 12 months. It is therefore important to determine whether effects of exercise last at least 12 months.

Loss to follow-up might be decreased by reducing participant burden. Screening of telephone calls was a common practice among participants in the Fit2Quit trial, and this may have been avoided if the number of assessments and/or the number of questions in each assessment were reduced. It also may be beneficial to conduct assessments via a different medium to the intervention delivery medium. By screening calls to avoid assessments participants also failed to adhere to the intervention. Likewise, participants who screened calls for the intervention also avoided assessment calls. If the Fit2Quit trial was to be conducted again, perhaps the development of web-, mobile application- or text- (SMS messaging) based
assessments would be necessary to distinguish between the assessment and the telephone-delivered intervention.

More research is also required to explore culturally appropriate exercise interventions for smoking cessation for Māori, but also, given the lack of exercise intervention research worldwide among non-Caucasian smokers, other indigenous groups, and ethnically diverse samples.

Future trials would also benefit from the measurement of the following variables. 1) Exercise or physical activity outcomes in both conditions. Of those studies that measured physical activity, many only reported the physical activity rates of the exercise group. 2) Exercise adherence should be measured as accurately and as objectively as possible, and the effects of exercise adherence on smoking abstinence should be reported. 3) TWS should be measured at the time they are most likely to be experienced (i.e. within the first week of smoking abstinence). Future trials need to incorporate a measure of TWS within this time period.

7.6.2 IMPLICATIONS FOR POLICY AND PRACTICE

Increasing smoking cessation rates is a public health priority in NZ. The NZ Government has committed to the goal of becoming a smoke-free nation by 2025, and to achieve this we need to continue to develop new strategies to augment existing methods of smoking cessation. Research around such strategies not only broadens the knowledge base and strengthens our understanding as researchers; it also serves to raise awareness of the issue.

If the intervention had been shown to be effective we had planned to encourage the integration of two national services to increase national quit rates. Nevertheless, the conduct of the research presented in this thesis has raised awareness of the benefits of exercise to overall health. Despite the lack of an effect of exercise on smoking cessation outcomes, physical activity is beneficial for a wide range of other health
risks and outcomes such as depression, cardiovascular disease and Type 2 diabetes, as well as for offsetting weight gain post quitting. Therefore it is important that physically inactive or insufficiently active smokers are encouraged to be physically active and are referred to programmes to increase activity levels.

While the Fit2Quit intervention content has potential, more focus is needed on increasing the uptake of the intervention. The Fit2Quit trial was considered effective for increasing abstinence rates and cost-effective for those that adhered to the intervention. This has implications for future policy and practice. Identifying those who want to quit and exercise via the Quitline and ensuring they are referred to exercise programmes such as GRx, may have positive effects on health outcomes in the long-term.

However, if behavioural interventions for smoking cessation, such as the exercise intervention reviewed here, as well as other intervention methods (e.g. NRT, other pharmacotherapies, intensive behavioural counseling) are ineffective, future interventions might focus more on policy and environmental changes. Such moves are afoot, including banning smoking in public places, and changes to government policy to raise the tax on tobacco and implement plain packaging on all tobacco products. Fiscal strategies to encourage people to exercise and quit might also be considered. Reward programmes or vouchers to promote healthy behaviour (exercise) over and above the taxation and banning strategies currently used may also be useful.

Nevertheless, there is still a place for both intervention approaches. Policy interventions take a long time to implement, and individuals will require help to quit in the meantime before such policies come into effect. Moreover, such environmental policies don’t actually help the smoker cope with the psychological and physiological effects of nicotine withdrawal. Therefore, general recommendations and
encouragement for people to exercise and be active are imperative to realise the associated health (physical and psychological) benefits.

7.7 CONCLUSION

Findings suggest that vigorous-intensity exercise, rather than moderate- or light-intensity exercise, should be recommended as a tool to reduce cigarette cravings in the short term and in the acute setting. Further research is needed to determine whether there is a physiological basis for this recommendation involving HRV, noradrenaline, and cortisol.

In the long term, the effects of exercise on smoking cessation outcomes are far less convincing. The Fit2Quit intervention showed no effect on smoking abstinence rates over usual care, consistent with most previous studies. However, the findings of the cost-effectiveness analysis do suggest that such interventions are cost-effective in the long term, particularly for those who adhere. It is important to improve adherence to the intervention and improve the effect of the intervention on the target behaviour. The incongruity between the acute effects and long-term effects of exercise on smoking cessation remains a concern. The lack of statistically significant effects in exercise intervention for smoking cessation studies is perplexing considering the positive effect of exercise on cravings observed in acute studies. Further work is needed to determine if:

1) Exercise only reduces cigarette cravings and TWS in the laboratory environment, and is ineffective as a smoking cessation aid in the real world.

2) Exercise reduces cravings and TWS and is therefore a useful aid to smoking cessation, but only works as an intervention for those that are motivated to change their exercise behaviour.
3) Exercise does work, but we have not found an effective method of intervention delivery.

Regardless, exercise has a multitude of health benefits aside from its potential effect on smoking cessation, and as such, should be recommended to insufficiently active smokers as much as possible.
## APPENDIX 1: ORGANISATIONAL AFFILIATIONS OF OTHER CONTRIBUTORS

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APPENDIX 2: CROSSOVER TRIAL PARTICIPANT INFORMATION SHEET – MAIN SAMPLE
APPENDIX 3: CROSSOVER TRIAL CONSENT FORM – MAIN SAMPLE
APPENDIX 4: CROSSOVER TRIAL PARTICIPANT INFORMATION SHEET – SUBSAMPLE
APPENDIX 5: CROSSOVER TRIAL CONSENT FORM – SUB-SAMPLE
**APPENDIX 6: CROSSOVER TRIAL INCREMENTAL FITNESS TEST DATA ANALYSIS SHEET (EXAMPLE)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Weight (g)</th>
<th>Last minute average HR</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 mins</td>
<td>0</td>
<td>85</td>
<td>10-20% 75 - 86</td>
</tr>
<tr>
<td>4-8 mins</td>
<td>300</td>
<td>99</td>
<td>40-60% 110 - 133</td>
</tr>
<tr>
<td>8-12 mins</td>
<td>600</td>
<td>104</td>
<td>70-85% 145 - 162</td>
</tr>
<tr>
<td>12-16 mins</td>
<td>900</td>
<td>118</td>
<td></td>
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<tr>
<th></th>
<th>Age: 40</th>
<th>Resting HR: 63</th>
<th>Max HR: 180</th>
</tr>
</thead>
</table>

Heart rate formula example (10%)

10% HR = (Maximum HR - Resting HR) x 10% + Resting HR

Weight formula example (10%)

10% Weight = (10% HR - c)/m

Rounded weight formula example (10-20%)

10-20% Rounded Weight = ROUND(((10% Weight + 20% Weight)/2), -2)
APPENDIX 7: CROSSOVER TRIAL FORM B – BASELINE DEMOGRAPHICS QUESTIONNAIRE
APPENDIX 8: CROSSTRIAL FORM A2 – SCREENING FORM
APPENDIX 9: CROSSOVER TRIAL FORM S – SMOKING OUTCOMES FORM
APPENDIX 10: CROSSOVER TRIAL 1 PLASMA CORTISOL ASSAY PROTOCOL
APPENDIX 11: CROSSOVER TRIAL SALIVARY CORTISOL ASSAY PROTOCOL
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APPENDIX 13: FIT2QUIT PARTICIPANT INFORMATION SHEET – TELEPHONE ASSESSMENT
APPENDIX 14: FIT2QUIT CONSENT FORM – TELEPHONE ASSESSMENT
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APPENDIX 21: FIT2QUIT FORM P
APPENDIX 22: EXAMPLE OF LINEAR REGRESSION GRAPH OF PAI AND HRAR VALUES

Note: The y-axis represents heart rate in beats per minute.

The three regression lines represent the rest, exercise, and recovery phases.
APPENDIX 23: FIT2QUIT QUALITATIVE STUDY PARTICIPANT INFORMATION SHEET
APPENDIX 24: FIT2QUIT QUALITATIVE STUDY CONSENT FORM
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APPENDIX 2: CROSSED TRIAL PARTICIPANT INFORMATION SHEET – MAIN SAMPLE
Effects of Exercise on Tobacco Withdrawal Symptoms
and Neurobiological Factors During Temporary
Smoking Abstinence: A Cross-over Trial.

PARTICIPANT INFORMATION SHEET

You are invited to take part in a clinical trial about smoking and exercise. To help you make a decision about participating in the study, we ask that you read this information sheet.

Please let us know if you wish to have an interpreter.

Who is co-ordinating this study?
The study is co-ordinated by the Clinical Trials Research Unit (The University of Auckland).

What are my legal rights?
Your participation in this study is entirely voluntary (your choice). You do not have to take part. If you choose not to take part in this study you will not be affected in any way. You may withdraw from the study at any time, without having to give a reason. Your withdrawal from the study will not affect your future health care from the smoking cessation programme or any other health service.

What is the aim of this study?
The aim of the study is to see if smokers who abstain from smoking overnight experience less tobacco withdrawal symptoms and nicotine and food cravings when they complete a small bout of exercise compared to when they do not perform any exercise.

Why have I been selected?
- You have been selected to take part in this study because you have contacted the Clinical Trials Research Unit and indicated you are willing to participate in this research. You also meet the requirements below:
  - You currently smoke more than 15 cigarettes per day and have done so for the past year
  - You are 18-70 years of age
  - You have your first cigarette within 30 minutes of waking up
  - You are in good health
  - You are able to perform a bout of exercise
  - You are able to attend the study site for the duration of the study

You cannot take part in this study if you have any of the following conditions:
- You have had a stroke or heart attack or angina pectoris in the last six months
- You have diabetes mellitus, or another serious medical condition
- You currently have a chemical dependence other than nicotine
- You have a psychiatric disorder
- You are pregnant or breast feeding
- You have blood pressure greater than 150mmHg systolic and/or 100mmHg diastolic

Brief bouts of exercise on TWS Study PiS – non-PK_Version 2
© Clinical Trials Research Unit, The University of Auckland, 2010

Date: 30/11/2010
• You have a history of severe depression
• You are currently using smoking cessation medications
• You are unwilling to abstain from smoking from 8pm the day before each study day until the end of each study day.
• You want to quit smoking during the study period

Where will the study take place?
All study procedures will take place in the Department of Sport and Exercise Science building at the Tamaki Campus of the University of Auckland.

How long will the study take?
You're involvement in the study will take 2 weeks. The entire study will run for approximately three months, from December 2010 to March 2011.

How many people will be recruited into the study?
We are looking to recruit approximately 48 smokers for this study.

What is involved if I take part?
If after reading this information sheet, you decide that you would like to take part in the study, we will need you to give us your permission in writing. To do this we ask that you read and sign the consent form. Once the consent form has been signed, we will ask you to attend your first assessment session (you probably will have already agreed on a date and time for this session during a recent phone call with a study researcher). In this assessment session you will be asked to complete some measures: blood pressure, heart rate, a fitness test, height, weight, and a questionnaire on your smoking and exercise habits. This session will take approximately one hour of your time.

After this session, if you are eligible for the study you will be asked to attend three study days. Prior to each of these study days you will need to abstain from smoking cigarettes (tailor-made and roll-your-own) and not eat or drink anything (except water) from 8pm the previous evening, until the end of the assessment session. In order to ensure you do not have to fast for too long, each of the three sessions will take place early in the morning (7.30am). In each of these sessions you will be asked to perform a 15-minute bout of exercise on a stationary bicycle. The intensity of the exercise (easy, moderate, and hard) will be different in each session. You will be asked to wear a heart rate monitor to measure your heart rate throughout each session, and you will be asked to complete some questionnaires on how you feel during each session. Each of these sessions will take approximately two and a half hours of your time.

Will there be any costs involved?
Taking part in the study will not cost you any money apart from the cost of travel to the four sessions. However, we will reimburse you for your travel costs with a $50 petrol voucher.

What are the risks and benefits of this study?
Possible benefits
Your involvement in this study will help researchers and health services to better understand the opinions of smokers, and may indirectly benefit people who want to stop smoking in the future.
Possible risks

There are a number of side effects associated with abstaining from smoking. You may temporarily experience nicotine withdrawal symptoms such as agitation, anxiety, and disturbed sleep. As a result of overnight fasting, you may also experience some discomfort associated with being hungry. A snack will be provided for you immediately after the testing session. There are also certain risks associated in participating in exercise, however, we will ask you some questions to make sure you are capable of performing an exercise bout for 15 minutes (you may have already been asked these questions during a recent telephone call).

Compensation

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by the Accident Compensation Corporation (ACC) legislation. ACC cover is not automatic and each case is assessed by ACC, according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are a wage earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. If you have any questions about ACC, please contact your nearest ACC office or ask us for more information before you agree to take part.

Will the information about me be kept confidential?

The study files and all information that you provide will remain strictly confidential. No material that could personally identify you will be used in any reports on this study. The information will be kept securely at the Clinical Trials Research Unit, The University of Auckland and destroyed after 15 years according to national research guidelines. All computer records will be password protected. All future use of the information collected will be strictly controlled in accordance with the Privacy Act, 1994.

During the study, ethics committee representatives, study personnel, members of the research team and possibly representatives of the study sponsor may check your records. This will only be done to check the accuracy of the information collected for the study and the information will remain confidential.

When will the results be available?

This study will take three months to conduct, so results will be available by April 2011. You will be asked if you would like to be sent a copy of the overall results.

Has the study received ethical approval?

Yes, this study has received ethics approval from the Northern Y Ethics Committee. NTY/10/10/079

Who do I contact?

You are encouraged to ask questions at any time during the study. If you have any questions please ask a study researcher at an assessment session or contact:

Vaughan Roberts, study co-ordinator, Clinical Trials Research Unit, Faculty of Medical and Health Sciences, The University of Auckland, Private Bag 92019, Auckland. Ph: (09) 373-7599 extn 84718. Fax: (09) 373-1710. Email: v.roberts@ctr.u.auckland.ac.nz

Brief bouts of exercise on TWS Study PIS – non-PK_Version 2
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Date: 30/11/2010
If you have any questions or concerns regarding your rights as a participant in this study you may wish to contact a Health and Disability Advocate at the Health Advocates Trust: Northland to Franklin ph 0800 555 050

Study Investigators
- Dr Ralph Maddison, Vaughan Roberts, Dr Chris Bullen, Dr Yannan Jiang, Clinical Trials Research Unit, Faculty of Medical and Health Sciences, University of Auckland
- Dr Nick Gant, Department of Sport and Exercise Science, Faculty of Science, University of Auckland

Thank you for taking the time to read about this study.
Please keep this sheet for your information.
Effects of Exercise on Tobacco Withdrawal Symptoms and Neurobiological Factors During Temporary Smoking Abstinence: A Cross-over Trial.

CONSENT FORM

<table>
<thead>
<tr>
<th>Request for an Interpreter</th>
<th>English</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>English</td>
<td>I wish to have an interpreter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori</td>
<td>E hiaha ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero</td>
<td>Ae</td>
<td>Kao</td>
</tr>
<tr>
<td>Samoan</td>
<td>Oute mana 'o ia iai se fa 'amatala upu</td>
<td>loe</td>
<td>Leai</td>
</tr>
<tr>
<td>Tongan</td>
<td>'Oku ou fiema 'u ha fakatonulea</td>
<td>'Io</td>
<td>'Ikai</td>
</tr>
<tr>
<td>Cook Island</td>
<td>Ka inangaro au I tetai tangata uri reo</td>
<td>Ae</td>
<td>Kare</td>
</tr>
<tr>
<td>Niuean</td>
<td>Fia manako au ke fakaaoaga e taha tagata fakahokohoko kupu</td>
<td>E</td>
<td>Nakai</td>
</tr>
</tbody>
</table>

- I understand the information sheet for volunteers taking part in this study, which has been read and discussed with study researchers. The study is designed to determine whether a short bout of exercise is more likely to reduce tobacco withdrawal symptoms and cravings after overnight smoking abstinence compared to performing no exercise.
- I have had the opportunity to discuss this study with study researchers and I am satisfied with the answers I have been given.
- I have had the opportunity to use whanaufamily support or a friend to help me ask questions and understand the study.
- I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my future health care/continuing health care from smoking cessation programmes or other health providers.
- I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.
- I understand that I will be asked to breathe into a carbon monoxide monitor on arrival at each testing session to verify that I have been abstinent from smoking overnight.
- I understand that I will be required to undertake a screening fitness test during the first session to determine my fitness level.
- I understand that I will be required to undertake a 15-minute bout of exercise on each of the three study days.
- I understand the compensation provisions for this study.
- I have had time to consider whether to take part.
- I know whom to contact if I have any questions about the study.

Date: 29/11/2010
I understand that there will be no personal details that identify me (such as my name, address) on the questionnaires.

I understand that any data collected as part of this study will be stored securely for 15 years at the Clinical Trials Research Unit, The University of Auckland, in accordance with the Privacy Act, 1994. After this time the information will be safely destroyed.

I understand that any information collected, as part of this study will not be used for any other purpose, without my permission and ethical approval, nor given to any other third party outside of the research team.

I understand that there may be a significant delay between data collection and publication of the results.

I wish to receive a copy of the results

YES/NO

I ________________________________ (print full name)
of ________________________________ (print address)

herewith consent to take part in this study.

Signature: ________________________________

Date: ___/___/___

day/month/year

Project explained by: ________________________________

Project role: ________________________________

Signature: ________________________________

Date: ___/___/___

day/month/year

Ethical Approval

This study has received ethical approval from the Northern Y Regional Ethics Committee. NTY/10/10/079

Brief bouts of exercise on TWS Study Consent form – non-PK_Version 2
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Date: 29/11/2010
Appendices

APPENDIX 4: CROSSOVER TRIAL PARTICIPANT INFORMATION SHEET – SUB-SAMPLE
Effects of Exercise on Tobacco Withdrawal Symptoms and Neurobiological Factors During Temporary Smoking Abstinence: A Cross-over Trial.

PARTICIPANT INFORMATION SHEET - substudy

You are invited to take part in a clinical trial about smoking and exercise. To help you make a decision about participating in the study, we ask that you read this information sheet.

Please let us know if you wish to have an interpreter.

Who is co-ordinating this study?
The study is co-ordinated by the Clinical Trials Research Unit (The University of Auckland).

What are my legal rights?
Your participation in this study is entirely voluntary (your choice). You do not have to take part. If you choose not to take part in this study you will not be affected in any way. You may withdraw from the study at any time, without having to give a reason. Your withdrawal from the study will not affect your future health care from the smoking cessation programme or any other health service.

What is the aim of this study?
The aim of the study is to see if smokers who abstain from smoking overnight experience less tobacco withdrawal symptoms and nicotine and food cravings when they complete a small bout of exercise compared to when they do not perform any exercise.

Why have I been selected?
- You have been selected to take part in this study because you have contacted the Clinical Trials Research Unit and indicated you are willing to participate in this research. You also meet the requirements below:
  - You currently smoke more than 15 cigarettes per day and have done so for the past year
  - You are 18-70 years of age
  - You have your first cigarette within 30 minutes of waking up
  - You are in good health
  - You are able to perform a bout of exercise
  - You are able to attend the study site for the duration of the study

You cannot take part in this study if you have any of the following conditions:

- You have had a stroke or heart attack or angina pectoris in the last six months
- You have diabetes mellitus, or another serious medical condition
- You currently have a chemical dependence other than nicotine
- You have a psychiatric disorder
- You are pregnant or breast feeding
- You have blood pressure greater than 150mmHg systolic and/or 100mmHg diastolic
- You have a history of severe depression

Date: 30/11/2010

Brief bouts of exercise on TWS Study PiS – PK Version 2
© Clinical Trials Research Unit, The University of Auckland, 2010
• You are currently using smoking cessation medications
• You are unwilling to abstain from smoking from 8pm the day before each study day until the end of each study day.
• You want to quit smoking during the study period

Where will the study take place?
All study procedures will take place in the Department of Sport and Exercise Science building at the Tamaki Campus of the University of Auckland.

How long will the study take?
You’re involvement in the study will take 2 weeks. The entire study will run for approximately three months, from December 2010 to March 2011

How many people will be recruited into the study?
We are looking to recruit approximately 48 smokers for this study.

What is involved if I take part?
If after reading this information sheet, you decide that you would like to take part in the study, we will need you to give us your permission in writing. To do this we ask that you read and sign the consent form. Once the consent form has been signed, we will ask you to attend your first assessment session (you probably will have already agreed on a date and time for this session during a recent phone call with a study researcher). In this assessment session you will be asked to complete some measures: blood pressure, heart rate, a fitness test, height, weight, and a questionnaire on your smoking and exercise habits. This session will take approximately one hour of your time.

After this session, if you are eligible for the study you will be asked to attend three study days. Prior to each of these study days you will need to abstain from smoking cigarettes (tailor-made and roll-your-own) and not eat or drink anything (except water) from 8pm the previous evening, until the end of the assessment session. In order to ensure you do not have to fast for too long, each of the three sessions will take place early in the morning (7.30am). In each of these sessions you will be asked to perform a 15-minute bout of exercise on a stationary bicycle. The intensity of the exercise (easy, moderate, and hard) will be different in each session. You will be asked to wear a heart rate monitor to measure your heart rate throughout each session, and you will be asked to complete some questionnaires on how you feel during each session. Each of these sessions will take approximately two and a half hours of your time.

If you agree to participate in the additional component of the study involving the collection of blood and saliva samples, these samples will be taken at certain time points throughout each of the three sessions. You will have an intravenous cannula inserted in your arm and 20ml blood samples will be collected prior to your bout of exercise and then 5, 10, 15, 30 and 60 minutes after exercise. A total of 18 samples will be collected (six per day over the three study days). There will be a brief sharp sensation as the cannula is positioned, but after this you shouldn’t experience any discomfort. This is a similar sensation to having a blood test or receiving a vaccination. If you do experience any ongoing discomfort, please notify the experimenter. The catheter will be removed after the last sample is collected each day. As with all blood tests, there is a very small risk of infection. However, this risk is minimised by having appropriately certified experimenters taking the samples, and following approved hygiene protocols. The samples will be used to measure concentrations of glucose, insulin, ghrelin, cortisol, epinephrine, and
norepinephrine in your blood. Your samples will be analysed, and stored for 6 years in accordance with University of Auckland guidelines for handling and the disposal of body fluids. If at any stage we would like to re-analyse your blood during this six year period we will not do so without contacting you and obtaining your ethical consent. The additional blood and saliva component of the study is a preliminary investigation. While we understand the physiological responses of these variables during and after exercise, we need to determine what happens to these variables after exercise in temporarily abstinent smokers.

Will there be any costs involved?
Taking part in the study will not cost you any money apart from the cost of travel to the four sessions. However, we will reimburse you for your travel costs with a $100 petrol voucher.

What are the risks and benefits of this study?
Possible benefits
Your involvement in this study will help researchers and health services to better understand the opinions of smokers, and may indirectly benefit people who want to stop smoking in the future.

Possible risks
There are a number of side effects associated with abstaining from smoking. You may temporarily experience nicotine withdrawal symptoms such as agitation, anxiety, and disturbed sleep. As a result of overnight fasting, you may also experience some discomfort associated with being hungry. A snack will be provided for you immediately after the testing session. There are also certain risks associated in participating in exercise, however, we will ask you some questions to make sure you are capable of performing an exercise bout for 15 minutes (you may have already been asked these questions during a recent telephone call). As with all blood tests, there is a very small risk of infection. However, as stated above, this risk is minimised by having appropriately certified experimenters taking the samples, and following approved hygiene protocols.

Compensation
In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by the Accident Compensation Corporation (ACC) legislation. ACC cover is not automatic and each case is assessed by ACC, according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are a wage earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. If you have any questions about ACC, please contact your nearest ACC office or ask us for more information before you agree to take part.

Will the information about me be kept confidential?
The study files and all information that you provide will remain strictly confidential. No material that could personally identify you will be used in any reports on this study. The information will be kept securely at the Clinical Trials Research Unit, The University of Auckland and destroyed after 15 years according to national research guidelines. All computer records will be password protected. All future use of the
Information collected will be strictly controlled in accordance with the Privacy Act, 1994. During the study, ethics committee representatives, study personnel, members of the research team and possibly representatives of the study sponsor may check your records. This will only be done to check the accuracy of the information collected for the study and the information will remain confidential.

**When will the results be available?**
This study will take three months to conduct, so results will be available by April 2011. You will be asked if you would like to be sent a copy of the overall results.

**Has the study received ethical approval?**
Yes, this study has received ethics approval from the Northern Y Ethics Committee. NTY/10/10/079

**Who do I contact?**
You are encouraged to ask questions at any time during the study. If you have any questions please ask a study researcher at an assessment session or contact:

Vaughan Roberts, study co-ordinator, Clinical Trials Research Unit, Faculty of Medical and Health Sciences, The University of Auckland, Private Bag 92019, Auckland. Ph: (09) 373-7599 extn 84718. Fax: (09) 373-1710. Email: v.roberts@ctru.auckland.ac.nz
If you have any questions or concerns regarding your rights as a participant in this study you may wish to contact a Health and Disability Advocate at the Health Advocates Trust: Northland to Franklin ph 0800 555 050

**Study Investigators**
- Dr Ralph Maddison, Vaughan Roberts, Dr Chris Bullen, Dr Yannan Jiang, Clinical Trials Research Unit, Faculty of Medical and Health Sciences, University of Auckland
- Dr Nick Gant, Department of Sport and Exercise Science, Faculty of Science, University of Auckland

Thank you for taking the time to read about this study. Please keep this sheet for your information.
Appendices

APPENDIX 5: CROSSOVER TRIAL CONSENT FORM – SUB-SAMPLE
CONSENT FORM – sub-study

<table>
<thead>
<tr>
<th>Request for an interpreter</th>
<th>English</th>
<th>Maori</th>
<th>Samoan</th>
<th>Tongan</th>
<th>Cook Island</th>
<th>Niuean</th>
</tr>
</thead>
<tbody>
<tr>
<td>I wish to have an interpreter</td>
<td>Yes</td>
<td>E hiaha ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero</td>
<td>Oute mana 'o ia iai se fa 'amatala upu</td>
<td>'Oku ou fiema 'u ha fakatonulea</td>
<td>Ka inangaro au I tetai tangata uru reo</td>
<td>Fia manako au ke fakaaroa e taha tagata fakahokohoko kupu</td>
</tr>
<tr>
<td>Ae</td>
<td>Kao</td>
<td>loe</td>
<td>Leai</td>
<td>'Io</td>
<td>'Ikai</td>
<td>E</td>
</tr>
</tbody>
</table>

- I understand the information sheet for volunteers taking part in this study, which has been read and discussed with study researchers. The study is designed to determine whether a short bout of exercise is more likely to reduce tobacco withdrawal symptoms and cravings after overnight smoking abstinence compared to performing no exercise.

- I have had the opportunity to discuss this study with study researchers and I am satisfied with the answers I have been given.

- I have had the opportunity to use whanau/family support or a friend to help me ask questions and understand the study.

- I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my future health care/continuing health care from smoking cessation programmes or other health providers.

- I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.

- I understand that I will be asked to breathe into a carbon monoxide monitor on arrival at each testing session to verify that I have been abstinent from smoking overnight.

- I understand that I will be required to undertake a screening fitness test during the first session to determine my fitness level.

- I understand that I will be required to undertake a 15-minute bout of exercise on each of the three study days.

- I understand that I will be asked to provide blood and saliva samples on each of the three study days.

- I understand the compensation provisions for this study.

- I have had time to consider whether to take part.
• I know whom to contact if I have any questions about the study.

• I understand that there will be no personal details that identify me (such as my name, address) on the questionnaires.

• I understand that any data collected as part of this study will be stored securely for 15 years at the Clinical Trials Research Unit, The University of Auckland, in accordance with the Privacy Act, 1994. After this time the information will be safely destroyed.

• I understand that any information collected, as part of this study will not be used for any other purpose, without my permission and ethical approval, nor given to any other third party outside of the research team.

• I understand that there may be a significant delay between data collection and publication of the results.

• I wish to receive a copy of the results

[YES/NO]

I __________________________________________ (print full name)

of ______________________________________ (print address)

_________________________________________

_________________________________________

hereby consent to take part in this study.

Signature: __________________________________

Date: __/___/____

day/month/year

Project explained by: __________________________________

Project role: _________________________________________

Signature: _________________________________________

Date: __/___/____

day/month/year

Ethical Approval

This study has received ethical approval from the Northern Y Regional Ethics Committee. NTY/10/10/079
APPENDIX 6: CROSSOVER TRIAL INCREMENTAL FITNESS TEST DATA ANALYSIS SHEET (EXAMPLE)

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>10-xxx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cadence (rpm)</td>
<td>60</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>Weight (g)</th>
<th>Last minute average HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 mins</td>
<td>0</td>
<td>85</td>
</tr>
<tr>
<td>4-8 mins</td>
<td>300</td>
<td>99</td>
</tr>
<tr>
<td>8-12 mins</td>
<td>600</td>
<td>104</td>
</tr>
<tr>
<td>12-16 mins</td>
<td>900</td>
<td>118</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HR</th>
<th>10-20%</th>
<th>75 - 86</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-60%</td>
<td>110 - 133</td>
<td></td>
</tr>
<tr>
<td>70-85%</td>
<td>145 - 162</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight</th>
<th>10-20%</th>
<th>-322.8 - 14.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-60%</td>
<td>688.8 - 1363.0</td>
<td></td>
</tr>
<tr>
<td>70-85%</td>
<td>1700.3 - 2206.0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age: 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting HR: 63</td>
</tr>
<tr>
<td>Max HR: 180</td>
</tr>
</tbody>
</table>

| m= | 0.0347 |
| c= | 85.9  |

<table>
<thead>
<tr>
<th>y = mx + c</th>
</tr>
</thead>
</table>

Heart rate formula example (10%)
10% HR = (Maximum HR - Resting HR) x 10% + Resting HR

Weight formula example (10%)
10% Weight = (10% HR - c)/m

Rounded weight formula example (10-20%)
10-20% Rounded Weight = ROUND(((10% Weight + 20% Weight)/2),-2)
APPENDIX 7: CROSSOVER TRIAL FORM B – BASELINE DEMOGRAPHICS QUESTIONNAIRE
Brief Bouts of Exercise on TWS
Form B: Baseline Demographics

Survey Information Sheet

The purpose of this questionnaire is to collect some background information about you. This survey will take about 5-10 minutes to complete. If you have any questions then you can ask one of the researchers.

Please answer ALL questions. DO NOT LEAVE BLANK SPACES. Tick circles and write numbers in boxes.

The answers that you write are private and will not be shared with anyone other than the researchers. You do not need to tell anyone else what you write on this questionnaire.

If you are worried about anything, or have any questions let the researcher know.

Study Manager's contact details:
Vaughan Roberts CTRU, University of Auckland
Phone: 09 3737599 ext. 84718
e-mail: v.roberts@ctru.auckland.ac.nz

<table>
<thead>
<tr>
<th>1 Assessment Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.01 Date</td>
</tr>
<tr>
<td>(dd/mm/yyyy)</td>
</tr>
<tr>
<td>__________/_____/2010</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2 About you</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.01 Sex</td>
</tr>
<tr>
<td>☐ Male</td>
</tr>
<tr>
<td>☐ Female</td>
</tr>
</tbody>
</table>

Which ethnic group or groups do you belong to?
Please indicate Yes or No to every option.

<table>
<thead>
<tr>
<th>2.02 NZ Maori</th>
<th>☐ Yes</th>
<th>☐ No</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.03 NZ European</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>2.04 Other European</td>
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<td>☐ No</td>
</tr>
<tr>
<td>2.05 Samoan</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>2.06 Cook Island Maori</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>2.07 Tongan</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>2.08 Niuean</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>2.09 Chinese</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
<tr>
<td>2.10 Indian</td>
<td>☐ Yes</td>
<td>☐ No</td>
</tr>
</tbody>
</table>
2.11 Other (please specify) □ Yes □ No
2.12 Other

Code (Office use) _________________________

3 Work and Education

3.01 At present are you? (select one only)

☐ Self-employed
☐ Full time salary or wage earner
☐ Part-time salary or wage earner (less than 30 hrs/week)
☐ Retired
☐ Full-time home-maker
☐ Student
☐ Unemployed
☐ Other beneficiary
☐ Refuse to answer

If you answered 'full-time home-maker', 'student', 'unemployed', 'other beneficiary', or 'refuse to answer', go to Q 3.04.
For all other answers, go to Q 3.02

3.02 What is your current occupation?
Or if retired, what was your previous occupation? (select one only)

☐ Clerical or sales employee
☐ Semi-skilled worker
☐ Technical or skilled worker
☐ Business manager or executive
☐ Business owner or self-employed
☐ Teacher, nurse, police, other trained service worker
☐ Professional or senior government official
☐ Labourer, manual, agricultural or domestic worker
☐ Farmer owner or manager
☐ Other
☐ Refuse to answer

3.03 If Other, please specify
3.04 What is your highest educational qualification? (select one only)
   If None, select 'No school examinations'
   □  5th form qualification (School Certificate, NCEA)
   □  6th form qualification (6th Form Cert., University Entrance, NCEA)
   □  School qualification higher than 6th form (Higher School Certificate, Bursary)
   □  Other school qualification (e.g. overseas school, Cambridge examination, A levels)
   □  Polytechnic/university course below Bachelors degree
   □  Bachelors degree
   □  Degree higher than Bachelor (Bachelors with honours, Masters, PhD)
   □  Other tertiary
   □  Refuse to answer
   □  No school examinations

3.05 If other tertiary, please specify the qualification

3.06 Which of these categories best describes you? (select one only)
   □  Married/living with partner
   □  Separated, divorced, widowed
   □  Never married
   □  Refuse to answer

3.07 Please indicate which of these categories best matches your household’s income (select one only)
   □  Under $20,000
   □  $20,001 to $30,000
   □  $30,001 to $40,000
   □  $40,001 to $50,000
   □  $50,001 to $60,000
   □  $60,001 to $70,000
   □  $70,001 to $80,000
   □  $80,001 to $90,000
   □  Over $90,000
   □  Don’t know
   □  Refuse to answer
4.01 Which types of tobacco do you usually smoke?
   Factory Made □ Yes □ No

4.02 If YES, how many on average do you smoke per day?
   ___ ___ number smoked/day

4.03 Which types of tobacco do you usually smoke?
   Roll your own/loose □ Yes □ No
   If NO, go to Q 4.07

4.04 If YES, how many grams on average do you smoke per week?
   ___ ___ grams/week

4.05 What sized package or pouch do you normally buy?
   ___ ___ grams (rounding up any decimal places)

4.06 About how many days does it take you to smoke the contents of this size
   of pouch or package?
   ___ ___ days

4.07 Do you smoke a pipe? □ Yes □ No

4.08 If YES, how many grams do you smoke per week?
   ___ ___ grams/week

4.09 Do you smoke Cigars? □ Yes □ No

4.10 If YES, how many on average do you smoke per week?
   ___ ___ number smoked/week

4.11 How many cigarettes and/or roll your own do you smoke each day, on
   average?
   ___ ___ number smoked/day

4.12 At what age did you start smoking?
4.13 How many years have you been smoking continuously?  

4.14 Have you made any attempts to stop smoking?  
□ Yes  □ No

If NO, go to Q 5.01.

4.15 In the last 12 months have you made any attempts to stop smoking completely? If YES, how many times?  
□ Yes – 1 attempt  
□ Yes – 2 attempts  
□ Yes – 3 attempts  
□ Yes – 4 or more attempts  
□ No attempts  
□ Don’t know

If you answered ‘No attempts’ or ‘Don’t know’, go to Q 4.01. Otherwise go to Q 4.16

4.16 How long did you quit smoking for (in the last 12 months)?  

[ ] [ ] days

What method(s) did you use to help you stop smoking that time?  
(Please answer all questions)

4.17 NRT products, such as patches, gum, or lozenge  
□ Yes  □ No

4.18 Medication, such as zyban, nortriptyline or varenicline  
□ Yes  □ No

4.19 Nothing  
□ Yes  □ No

4.20 Other  
□ Yes  □ No

4.21 If other, please specify

---

5. Nicotine Dependency

5.01 How many cigarettes do you smoke per day? (select one only)

□ 31 or more  
□ 21-30  
□ 11-20  
□ 10 or less
5.02 How soon after you wake up do you smoke your first cigarette? (select one only)

☐ Within 5 minutes
☐ 6-30 minutes
☐ 31-60 minutes
☐ More than 60 minutes

5.03 Do you find it difficult to stop smoking in smokefree areas, e.g. in cafes, bars, at the movies etc?  
☐ Yes ☐ No

5.04 Which cigarette would you most hate to give up? (select one only)

☐ The first one in the morning
☐ All others

5.05 Do you smoke more frequently during the first hours after waking than during the rest of the day?  
☐ Yes ☐ No

5.06 Do you smoke if you are so ill that you are in bed most of the day?  
☐ Yes ☐ No

6 Exercise

During a typical 7 day period (a week), how many times on the average do you do the following kinds of exercise for more than 15 minutes during your free time?

6.01 Vigorous exercise (heart beats rapidly) (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)

☐☐☐☐ times per week

6.02 Moderate exercise (not exhausting) (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)

☐☐☐☐ times per week

6.03 Mild exercise (minimal effort) (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking)

☐☐☐☐ times per week
8 Signature of Study Researcher

8.01 Signature

Printed Name

Date 1_1_1 / 1_1_1 / 1_2_0 / 1_1_1
APPENDIX 8: CROSSTRIAL FORM A2 – SCREENING FORM
Brief Bouts of Exercise on TWS
Form A2: Clinical Screening

The purpose of this form is to assess the potential participant's eligibility for and interest in participating in the study and to record the participant's baseline measurements.

Study Researcher: Complete Form A2 at the baseline assessment session for all potential participants who have been assessed as eligible from the phone session.

FOR PAPER FORMS ONLY
- Answer all questions. DO NOT LEAVE BLANK SPACES
- Tick boxes. Write text in spaces provided.
- If the data are unavailable, put an asterisk "*".
- If the data are not applicable, put a dash "-".
- Refer to the Manual of Procedures for complete instructions

1 Assessment Details

1.01 Date  __________/________/________ (dd/mm/yyyy)

2 Clinical Criteria

2.01 Blood Pressure (mmHg)
   Systolic  __________
   Diastolic  __________

2.02 Carbon Monoxide
   Carbon monoxide monitor number: ______________________
   Carbon monoxide measurement (ppm):  __________

3 Exclusion Criteria

3.01 Have you had a stroke or heart related condition in the last 6 months?  □ Yes  □ No

3.02 Have you had severe angina in the last 6 months?  □ Yes  □ No
3.03 Blood pressure > 150mmHg systolic or > 100mmHg diastolic

☐ Yes    ☐ No

If YES to any exclusion criteria then they are not eligible. Thank the participant for their interest and time and explain that their circumstances do not meet the criteria for being in the study.

4 Written Consent

4.01 Participant attended initial screening

☐ Yes    ☐ No

4.02 Date of consent  

☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ (dd/mm/yyyy)

5 Clinical Data

5.01 Weight

☐☐☐☐☐☐☐☐kg

☐☐☐☐☐☐☐☐kg

☐☐☐☐☐☐☐☐kg

5.02 Height

☐☐☐☐☐☐☐☐cm

☐☐☐☐☐☐☐☐cm

☐☐☐☐☐☐☐☐cm

5.03 Do you take any regular medication?

☐ Yes    ☐ No

If YES, complete form M

5.04 Intensities from fitness test

(Seat height ______)

<table>
<thead>
<tr>
<th>Intensity</th>
<th>Weight</th>
<th>HR range</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vigorous</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6 Signature of Study Researcher

6.01 Signature

________________________________________

6.02 Printed Name

________________________________________

6.03 Date

☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ (dd/mm/yyyy)

Brief bouts of exercise on TWS Form A2 _version 2
30/11/2010
APPENDIX 9: CROSSOVER TRIAL FORM S – SMOKING OUTCOMES FORM
Participant Initials  

Participant DOB  

Registration Number  

Day/Month/Year  

**Brief Bouts of Exercise on TWS**  
**Form S: Participant Questionnaires**  

**Survey Information Sheet**

The purpose of these questionnaires is to collect information about how you are feeling during the study. If you have any questions then you can ask one of the researchers.

Please answer ALL questions by ticking the square that best fits how you feel. Only tick one square for each question. DO NOT LEAVE BLANK SPACES.

The answers that you write are private and will not be shared with anyone other than the researchers. You do not need to tell anyone else what you write on this questionnaire.

If you are worried about anything, or have any questions let the researcher know.

**Study Manager’s contact details:**  
Vaughan Roberts CTRU, University of Auckland  
Phone: 09 3737599 ext. 84718  
e-mail: v.roberts@ctr.u.auckland.ac.nz

---

**Date of Assessment:**  
___ / ___ / 20___

**Assessment session:**  
☐ One  
☐ Two  
☐ Three
### Desire to Smoke

1.01 I have a desire for a cigarette right now?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>strongly disagree</td>
<td>neither agree nor disagree</td>
<td>strongly agree</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.02 The strength of my desire to smoke right now is…

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>very weak</td>
<td>neither weak nor strong</td>
<td>very strong</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### How are you feeling right now?

1.03 Right now, how irritable do you feel?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not at all</td>
<td>Somewhat</td>
<td>Extremely</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.04 Right now, how depressed do you feel?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not at all</td>
<td>Somewhat</td>
<td>Extremely</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.05 Right now, how difficult are you finding it to concentrate?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not at all</td>
<td>Somewhat</td>
<td>Extremely</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.06 Right now, how restless do you feel?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not at all</td>
<td>Somewhat</td>
<td>Extremely</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.07 Right now, how tense do you feel?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not at all</td>
<td>Somewhat</td>
<td>Extremely</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1.08  Right now, how **hungry** do you feel?  
1  [ ]  2  [ ]  3  [ ]  4  [ ]  5  [ ]  6  [ ]  7  [ ]  
Not at all  [ ]  Somewhat  [ ]  Extremely  [ ]

1.09  Right now, how **stressed** do you feel?  
1  [ ]  2  [ ]  3  [ ]  4  [ ]  5  [ ]  6  [ ]  7  [ ]  
Not at all  [ ]  Somewhat  [ ]  Extremely  [ ]

1.10  Do you have an urge to smoke right now?  
[ ] Yes  [ ] No

1.11  If YES, how strong is the urge to smoke?  
1  [ ]  2  [ ]  3  [ ]  4  [ ]  5  [ ]  6  [ ]  7  [ ]  
Slight  [ ]  Moderate  [ ]  Strong  [ ]  Very Strong  [ ]  Extremely Strong  [ ]

1.12  Estimate here how aroused you actually feel. Do this by ticking the appropriate square. By "arousal" we mean how "worked-up" you feel. You might experience **high arousal** in one of a variety of ways, for example as **excitement** or **anxiety** or **anger**. **Low arousal** might also be experienced by you in one of a number of different ways, for example as **relaxation** or **boredom** or **calmness**.  
1  [ ]  2  [ ]  3  [ ]  4  [ ]  5  [ ]  6  [ ]  7  [ ]  
Low arousal  [ ]  high arousal  [ ]

1.13  While participating in exercise, it is common to experience changes in mood. Some individuals find exercise pleasurable, whereas others find it to be unpleasant. Additionally, feeling may fluctuate across time. That is, one might feel good and bad a number of times during exercise. Scientists have developed this scale to measure such responses.  
+5  [ ]  +4  [ ]  +3  [ ]  +2  [ ]  +1  [ ]  0  [ ]  -1  [ ]  -2  [ ]  -3  [ ]  -4  [ ]  -5  [ ]  
very good  [ ]  good  [ ]  neutral  [ ]  bad  [ ]  very bad  [ ]
Appetite

For each of the questions in this section please indicate how much you agree or disagree with each of the following statements:

1.14 I’m craving tasty food.
   ![Rating Scale]
   1. strongly disagree
   2. 3. 4. 5. strongly agree

1.15 I have an urge for tasty food
   ![Rating Scale]
   1. strongly disagree
   2. 3. 4. 5. strongly agree

1.16 I have an intense desire to eat something tasty
   ![Rating Scale]
   1. strongly disagree
   2. 3. 4. 5. strongly agree

1.17 If I ate something, I wouldn’t feel so sluggish and lethargic
   ![Rating Scale]
   1. strongly disagree
   2. 3. 4. 5. strongly agree

1.18 Satisfying my appetite would make me feel less grouchy and irritable
   ![Rating Scale]
   1. strongly disagree
   2. 3. 4. 5. strongly agree

1.19 I would feel more alert if I could satisfy my appetite
   ![Rating Scale]
   1. strongly disagree
   2. 3. 4. 5. strongly agree

1.20 If I ate right now, my stomach wouldn’t feel as empty
   ![Rating Scale]
   1. strongly disagree
   2. 3. 4. 5. strongly agree

1.21 I am hungry
   ![Rating Scale]
   1. strongly disagree
   2. 3. 4. 5. strongly agree

1.22 I feel weak because of not eating
   ![Rating Scale]
   1. strongly disagree
   2. 3. 4. 5. strongly agree

Brief bouts of exercise on TWS Form S_version 2
30/11/2010
1.23  My desire to eat something tasty seems overpowering

1  2  3  4  5

☐ ☐ ☐ ☐ ☐

strongly disagree

☐ ☐ ☐ ☐ ☐

strongly agree

1.24  I know I’m going to keep on thinking about tasty food until I actually have it.

1  2  3  4  5

☐ ☐ ☐ ☐ ☐

strongly disagree

☐ ☐ ☐ ☐ ☐

strongly agree

1.25  If I had something tasty to eat, I could not stop eating it

1  2  3  4  5

☐ ☐ ☐ ☐ ☐

strongly disagree

☐ ☐ ☐ ☐ ☐

strongly agree

1.26  If I were to eat what I’m desiring, I am sure my mood would improve

1  2  3  4  5

☐ ☐ ☐ ☐ ☐

strongly disagree

☐ ☐ ☐ ☐ ☐

strongly agree

1.27  Eating something tasty would feel wonderful

1  2  3  4  5

☐ ☐ ☐ ☐ ☐

strongly disagree

☐ ☐ ☐ ☐ ☐

strongly agree

1.28  Eating something tasty would make things just perfect

1  2  3  4  5

☐ ☐ ☐ ☐ ☐

strongly disagree

☐ ☐ ☐ ☐ ☐

strongly agree
APPENDIX 10: CROSOVER TRIAL 1 PLASMA CORTISOL ASSAY PROTOCOL
Pre-assay preparation

Buffer preparation

Dilute the contents of one vial of EIA Buffer Concentrate with 90ml of UltraPure (UP) water. Rinse the vial to remove any salts that may have precipitated.

Assay Protocol

Preparation of Assay-specific reagents

Cortisol EIA Standard

1. Equilibrate a pipette tip in ethanol
2. Using the equilibrated pipette tip, transfer 100μl of the Cortisol EIA standard into a clean test tube, then dilute with 900μl of UP water. This is the bulk standard.
3. Obtain eight clean test tubes and number them #1 through #8.
4. Aliquot 900μl EIA buffer to tube #1
5. Aliquot 600μl EIA buffer to tubes #2 - 8
6. Transfer 100μl of the bulk standard to tube #1 and mix thoroughly.
7. Serially dilute the standard by removing 400μl from tube #1 and placing in tube #2; mix thoroughly.
8. Next remove 400μl from tube #2 and place it into tube #3; mix thoroughly.
9. Repeat this process for tubes #4-8

Cortisol AChE Tracer

Reconstitute the Cortisol AChE Tracer as follows:
100 dtn Cortisol AChE Tracer: Reconstitute with 6ml EIA Buffer
- Optional Tracer Dye Instructions
  - Add 60μl of dye to 6ml of tracer

Cortisol EIA Monoclonal Antibody

Reconstitute the Cortisol EIA Monoclonal Antibody as follows:
100 dtn Cortisol EIA Monoclonal Antibody: Reconstitute with 6ml EIA buffer
- Optional Antibody dye instructions
  - Add 60μl of dye to 6ml of antibody

Performing the Assay

Pipetting tips:

Before pipetting each reagent, equilibrate the pipette tip in that reagent.

Do not expose the pipette tip to the reagent already in the well

Assay tips:

Tick off each sample on plate set up template as you go

Addition of the reagents

1. Samples
   Using Gilson 200ml pipette, add 50μl of sample per well.

2. Standards
   Using Gilson 200ml pipette, add 50μl from tube #8 to both of the wells labelled S8.
Add 50μl from tube #7 to both of the wells labelled S7
Continue with this procedure until all standards are aliquoted.

3. Cortisol AChE Tracer
   Using the 8-channel pipette, add 50μl to all wells containing either standard or sample

4. Cortisol EIA Monoclonal Antibody
   Using the 8-channel pipette, add 50μl to all wells containing either standard or sample

5. EIA Buffer
   Using Gilson 200ml pipette, add 100μl EIA Buffer to NSB wells
   Add 50μl EIA Buffer to Bo wells.

6. Cortisol AChE Tracer
   Using the Gilson 200ml pipette, add 50μl to the NSB and Bo wells

7. Cortisol EIA Monoclonal Antibody
   Using the Gilson 200ml pipette, add 50μl to the Bo wells

**Incubation of the plate**

Cover plate with a plastic film and incubate overnight at 4°C

Store all buffers, standards, reagents in fridge at 4°C

**Day 2**

**Preparation for development of the plate**

1. Wash Buffer preparation
   Dilute 2ml Wash Buffer Concentrate with 800ml UP water. Add Polysorbate 20 (0.4ml).

   Note: Polysorbate 20 is a viscous liquid and cannot be measured by a regular pipette.

2. Reconstitute Ellmans reagent immediately before use (20ml of reagent is sufficient to develop 100 wells)
   100 dtm vial Ellman’s Reagent: Reconstitute with 20ml of UP water

**Development of the plate**

1. Empty the wells and rinse 5 times with Wash Buffer. Use 200μl per well per wash
2. Add 200μl of Ellman’s reagent to each well
3. Add 5μl of Cortisol AChE Tracer to the Total Activity well
4. Cover the plate with a plastic film.
5. Place plate on orbital shaker. Cover with large flat cover to allow the plate to develop in the dark. This assay typically develops in 90-120 minutes
Reading the plate

1. Wipe the bottom of the plate with a clean tissue to remove fingerprints, dirt etc.
2. Remove the plate cover, being careful to keep Ellman’s reagent from splashing on the cover.
3. Read the plate at a wavelength between 405 and 420nm. The absorbance may be checked periodically until the Bo wells have reached a minimum of 0.3 A.U. (blank subtracted). The plate should be read when the absorbance of the Bo wells are in the range of 0.3-1.0 A.U. (blank subtracted). If the absorbance of the wells exceeds 2.0, wash the plate, add fresh Ellman’s reagent and let it develop again.

Analysis

The data should be plotted as either %B/Bo versus log concentration using a four-parameter logistic fit, or as logit B/Bo versus log concentration using a linear fit. Refer to Cayman data analysis Microsoft Excel spread sheet.

Average the absorbance readings from the NSB wells.

Average the absorbance readings from the Bo wells

Subtract the NSB average from the Bo average. This is the corrected Bo or corrected maximum binding

Calculate the B/Bo (Sample or standard bound/maximum bound) for the remaining wells. To do this, subtract the average NSB absorbance from the S1 absorbance and divide by the corrected Bo (from Step 3). Repeat for S2-S8 and all sample wells. To obtain %B/Bo for a logistic four-parameter fit, multiply these values by 100.

NB: The total activity (TA) value is not used in the standard curve calculations. Rather, they are used as a diagnostic tool; the corrected Bo divided by the actual TA (10x measured absorbance) will give the % bound. This value should closely approximate the % bound that can be calculated from the Sample Data (see page 27 of manual). Erratic absorbance values and a low (or no) % Bound could indicate the presence of organic solvents in the buffer or other technical problems (see page 31 of manual).

Plot the Standard Curve

Plot %B/Bo for standards S1-S8 vs cortisol concentration using linear (y) and log (x) axes and perform a 4-parameter logistic fit.

Determine Sample Concentration

Calculate the %B/Bo value for each sample. Determine the concentration of each sample using the equation obtained from the standard curve plot.
APPENDIX 11: CROSSOVER TRIAL SALIVARY CORTISOL ASSAY PROTOCOL
Salivary Cortisol assay protocol

General Kit use advice

This kit uses break-apart microtitre strips. You may run less than a full plate. Unused wells must be stored at 2-8°C

The quantity of reagent provided with a single kit is sufficient for 3 partial runs. The volumes of wash buffer and conjugate prepared for assays using less than a full plate should be scaled down accordingly, keeping the same dilution ratio. Do not mix components from different lots of kits.

When using a multichannel pipette, reagents should be added to duplicate wells at the same time. Follow the same sequence when adding additional reagents so that incubation time is the same for all wells.

Pipetting of samples and reagents must be done as quickly as possible across the plate. Ideally the process should be completed within 20 minutes or less.

Room temperature must be 20-23°C

Use opened reagents within one month

Pre-assay preparation

Reagent, buffer, and sample preparation

Bring all reagents to room temperature and mix before use. A minimum of 1.5 hours is necessary for the 24ml of assay diluent used in Step 5 to come to room temperature.

Bring microtitre plate to room temperature before use. Keep ziplock pouch closed until warmed to room temperature as humidity may have an effect on the coated wells.

Prepare 1X wash buffer by diluting wash buffer concentrate 10-fold with room temperature deionized water (100ml of 10X wash buffer to 900mL of deionized H2O). Dilute only enough for current day's use, and discard any leftover reagent. If precipitate has formed in the concentrated wash buffer, it may be heated to 40°C for 15 minutes. Cool to room temperature before use in assay.

Thaw samples completely, vortex, and centrifuge at 1500 x g (@3000rpm) for 15 minutes. Samples should be at room temperature before adding to assay plate.

Assay Protocol

Step 1: Determine plate layout

Step 2: Break off 2 NSB wells from the strip of NSB wells included in the foil pouch. Break off the two wells in the plate where you plan to put the NSB wells. Place NSB wells on the plate. Reseal the zip-lock foil pouch containing unused wells and desiccant. Store at 2-8°C

Do not use NSB wells from one plate in a different plate.
Step 3: Pipette 24mL of assay diluent into a disposable tube. Set aside for Step 5

Step 4: Pipette 25μl of standards, controls, and unknowns into appropriate wells. Assayed in duplicate

Pipette 25μl of assay diluent into 2 wells to serve as the zero value

Pipette 25μl of assay diluent into each NSB well

Step 5: Make a 1:1600 dilution of the conjugate by adding 15μl of the conjugate to the 24mL of assay diluent prepared in Step 3. Immediately mix the diluted conjugate solution and pipette 200μl into each well using a multichannel pipette. Make note of any wells with dark yellow (acidic) or purple (alkaline) pH indicator changes. Dark yellow or purple indicate that a pH value for that sample should be obtained using pH strips. Cortisol values from samples with a pH ≤ 3.5 or ≥ 9.0 may be artificially inflated or lowered.

Step 6: Mix plate on rotator for 5 minutes at 500rpm and incubate at room temperature for an additional 55 minutes

Step 7: Wash the plate 4 times with 1X wash buffer. Pipette 300μl of wash buffer into each well. Discard liquid by inverting the plate over the sink. Plate should be thoroughly blotted before turning up right

Step 8: Add 200μl of TMB solution to each well with a multichannel pipette

Step 9: Mix on a plate rotator for 5 minutes at 500rpm and incubate the plate in the dark at room temperature for an additional 25 minutes

Step 10: Add 50μL of stop solution with a multichannel pipette

Step 11: Mix on a plate rotator for 3 minutes at 500 rpm

Wipe off bottom of plate with a water-moistened, lint-free cloth and wipe dry

Read in a plate reader at 250nm. Read plate within 10 minutes of adding stop solution. Correction at 490 to 630 is desirable

<table>
<thead>
<tr>
<th>Steps</th>
<th>Reagent</th>
<th>Zero</th>
<th>NSB</th>
<th>Std/Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prepare plate</td>
<td>Break off 2 NSB wells and add to plate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Add reagents</td>
<td>Standard/Sample</td>
<td>25μl</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assay diluent</td>
<td>25μl</td>
<td>25μl</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Conjugate/assay diluent dilution</td>
<td>200μl</td>
<td>200μl</td>
<td>200μl</td>
</tr>
<tr>
<td>Mix</td>
<td>Mix on rotator for 5 minutes at 500rpm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incubate</td>
<td>Incubate at room temperature for 55 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wash</td>
<td>Wash all wells 4 times with 300μl wash buffer (1X)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Add reagents</td>
<td>TMB solution</td>
<td>200μl</td>
<td>200μl</td>
<td>200μl</td>
</tr>
<tr>
<td>Mix</td>
<td>Mix on rotator for 5 minutes at 500rpm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incubate</td>
<td>Incubate in the dark at room temperature for an additional 25 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Add reagents</td>
<td>Stop solution</td>
<td>50μl</td>
<td>50μl</td>
<td>50μl</td>
</tr>
<tr>
<td>Mix</td>
<td>Mix on rotator for 3 minutes at 500rpm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Read</td>
<td>Read plate at wavelength 250nm within 10 minutes of adding stop solution</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX 12: CROSSTRIAL CATECHOLAMINES ASSAY PROTOCOL
**Pre-assay preparation – 2 hours**

Allow reagents and samples to reach room temperature. Duplicate determinations are recommended. - 2 hours thawing process

<table>
<thead>
<tr>
<th>Wash Buffer</th>
<th>Distilled water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilute the 20 mL Wash Buffer Concentrate with distilled water to a final volume of 1000 mL. – 10 min</td>
<td></td>
</tr>
<tr>
<td>Storage: up to 6 months 2–8°C</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Wash Buffer</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilute the 20 mL Wash Buffer Concentrate with distilled water to a final volume of 1000 mL. – 10 min</td>
<td></td>
</tr>
<tr>
<td>Storage: up to 6 months 2–8°C</td>
<td></td>
</tr>
</tbody>
</table>

**Assay Protocol**

<table>
<thead>
<tr>
<th>Adrenaline</th>
<th>Noradrenaline</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Sample volume 500 – 750 µL: Pipette into the respective wells of the Extraction Plate: 10 µL of Standards, 10 µL of controls and 500 – 750 µL of sample. Fill up each well with distilled water to a final volume of 750µL (e.g. 10 µL standard plus 740µL dist. water). - 50 min</td>
<td></td>
</tr>
<tr>
<td>2. Pipette 25 µL of TE Buffer into all wells. – 10 min</td>
<td></td>
</tr>
<tr>
<td>4. Cover the plate with adhesive foil. Shake 60 min at RT (20-25°C) on a shaker (approx. 600 rpm).</td>
<td></td>
</tr>
</tbody>
</table>

| 1. Sample volume 500 – 750 µL: Pipette into the respective wells of the Extraction Plate: 10 µL of Standards, 10 µL of controls and 500 – 750 µL of sample. Fill up each well with distilled water to a final volume of 750µL (e.g. 10 µL standard plus 740µL dist. water). - 50 min |
| 2. Pipette 25 µL of TE Buffer into all wells. – 10 min |
| 4. Cover the plate with adhesive foil. Shake 60 min at RT (2-25°C) on a shaker (approx. 600 rpm). |

| 5. Remove the foil and empty the plate. Blot dry by tapping the inverted plate on absorbent material. - 2 min |
| 6. Pipette 1 mL of Wash Buffer into all wells. Cover the plate with adhesive foil. – 10 min |
| 7. Shake 5 min at RT (20-25°C) on a shaker (approx. 600 rpm). – 5 min |
| 8. Remove the foil and empty the plate. Blot dry by tapping the inverted plate on absorbent material. – 2 min |
| 6. Pipette 1 mL of Wash Buffer into all wells. Cover the plate with adhesive foil. – 10 min |
| 7. Shake 5 min at RT (20-25°C) on a shaker (approx. 600 rpm). – 5 min |
| 8. Remove the foil and empty the plate. Blot dry by tapping the inverted plate on absorbent material. – 2 min |
| 10. Pipette 150 µL of Acylation Buffer into all wells. – 10 min |
| 11. Pipette 25 µL of Acylation Reagent into all wells. – 10 min |
| 12. Shake 20 min at RT (20-25°C) on a shaker (approx. 600 rpm). |
13. Empty the plate and blot dry by tapping the inverted plate on absorbent material. – 2 min

| 9a. Pipette 1 mL of Wash Buffer into all wells. Cover the plate with adhesive foil. – 10 min |
| 9b. Shake 5 min at RT (20-25°C) on a shaker (approx. 600 rpm). – 5 min |

14. Pipette 1 mL of Wash Buffer into all wells. Cover plate with adhesive foil. – 5 min

15. Shake 5 min at RT (20-25°C) on a shaker (approx. 600 rpm). – 5 min

| 9c. Remove the foil and empty the plate. Blot dry by tapping the inverted plate on absorbent material. – 2 min |
| 10. Pipette 150 µL of Acylation Buffer into all wells. – 5 min |

16. Remove the foil and empty the plate. Blot dry by tapping the inverted plate on absorbent material. – 2 min

| 11. Pipette 25 µL of Acylation Reagent into all wells. – 5 min |
| 12. Shake 20 min at RT (20-25°C) on a shaker (approx. 600 rpm). – 20 min |

17. Wash one more time as described (step 14, 15, 16). – 12 min

18. Pipette 100 µL of Hydrochloric Acid into all wells. – 8 min

19. Cover plate with adhesive foil. Shake 10 min at RT (20-25°C) on an o shaker (approx. 600 rpm).

| 13. Empty the plate and blot dry by tapping the inverted plate on absorbent material. – 2 min |
| 14. Pipette 1 mL of Wash Buffer into all wells. Cover plate with adhesive foil. – 5 min |
| 15. Shake 5 min at RT (20-25°C) on a shaker (approx. 600 rpm). – 5 min |
| 16. Remove the foil and empty the plate. Blot dry by tapping the inverted plate on absorbent material. – 2 min |

Do not decant the supernatant thereafter! 90 µL of the supernatant is needed for the subsequent enzymatic conversion

Enzymatic Conversion = 45 minutes plus 2 hour incubation. Pipette 90 µL of the extracted standards, controls and samples into the respective wells of the Microtiter Plate. – 30 min

Enzyme Solution

Reconstitute the content of the vial labelled ‘Enzyme’ with 1 mL distilled water and mix thoroughly. Add 0.3 mL of Coenzyme followed by 0.7 mL of Adjustment Buffer. The total volume of the Enzyme Solution is 2.0 mL. The Enzyme Solution has to be prepared freshly prior to the assay (not longer than 10 - 15 minutes in advance). Discard after use! – 5 min

2. Add 25 µL of Enzyme Solution (refer to 6.1) to all wells. – 5 min

3. Cover plate with Adhesive Foil. Shake 1 min at RT (20-25°C) on a shaker to mix. – 1 min
4. Incubate for 2 hours at 37°C. The following volumes of the supernatants are needed for the subsequent ELISA: Adrenaline 100 µL – 2 hours

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>17.</td>
<td>Wash one more time as described (step 14, 15, 16). – 10 min</td>
</tr>
<tr>
<td>18.</td>
<td>Pipette 100 µL of Hydrochloric Acid into all wells. – 8 min</td>
</tr>
<tr>
<td>19.</td>
<td>Cover plate with adhesive foil. Shake 10 min at RT (20-25°C) on an o shaker (approx. 600 rpm). – 10 min</td>
</tr>
<tr>
<td></td>
<td>Do not decant the supernatant thereafter!</td>
</tr>
<tr>
<td></td>
<td>90 µL of the supernatant is needed for the subsequent enzymatic conversion</td>
</tr>
</tbody>
</table>

**Enzymatic Conversion – 45 minutes plus 2 hour incubation**

1. Pipette 90 µL of the extracted standards, controls and samples into the respective wells of the Microtiter Plate. – 20 min

**Enzyme Solution**

Reconstitute the content of the vial labelled ‘Enzyme’ with 1 mL distilled water and mix thoroughly. Add 0.3 mL of Coenzyme followed by 0.7 mL of Adjustment Buffer. The total volume of the Enzyme Solution is 2.0 mL. The Enzyme Solution has to be prepared freshly prior to the assay (not longer than 10 - 15 minutes in advance). Discard after use! - 5 min

2. Add 25 µL of Enzyme Solution (refer to 6.1) to all wells. – 5 min

3. Cover plate with Adhesive Foil. Shake 1 min at RT (2025°C) on a shaker to mix. 1 min

4. Incubate for 2 hours at 37°C. The following volumes of the supernatants are needed for the subsequent ELISA: Noradrenaline 100 µL – 2 hours

Approx 1 hour break.

### Adrenaline ELISA – 45 minutes plus overnight incubation

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Pipette 100 µL of standards, controls and samples from the Microtiter Plate (refer to 6.4) into the respective pre-coated Adrenaline Microtiter Strips. – 40 min</td>
</tr>
<tr>
<td>2.</td>
<td>Pipette 50 µL of the Adrenaline Antiserum into all wells. – 5 min</td>
</tr>
<tr>
<td>3.</td>
<td>Cover the plate with Adhesive Foil. Incubate for 1 min at RT (20-25°C) on a shaker. – 1 min</td>
</tr>
<tr>
<td>4.</td>
<td>Incubate for 15 – 20 hours (overnight) at 2 – 8 °C.</td>
</tr>
</tbody>
</table>

### Noradrenaline ELISA – 45 minutes plus overnight incubation

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Pipette 100 µL of standards, controls and samples from the Microtiter Plate (refer to 6.4) into the respective pre-coated Noradrenaline Microtiter Strips. – 40 min</td>
</tr>
<tr>
<td>2.</td>
<td>Pipette 50 µL of the Noradrenaline Antiserum into all wells. – 5 min</td>
</tr>
<tr>
<td>3.</td>
<td>Cover the plate with Adhesive Foil. Incubate for 1 min at RT (20-25°C) on a shaker. – 1 min</td>
</tr>
<tr>
<td>4.</td>
<td>Incubate for 15 – 20 hours (overnight) at 2 – 8 °C.</td>
</tr>
<tr>
<td></td>
<td>Adrenaline ELISA day 2 – two and a half hours</td>
</tr>
<tr>
<td>---</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>5. Remove the foil and discard or aspirate the contents of the wells and wash each well 4 times thoroughly with 300 µL Wash Buffer. Blot dry by tapping the inverted plate on absorbent material. – 20 min</td>
</tr>
<tr>
<td></td>
<td>6. Pipette 100 µL of Enzyme Conjugate into all wells – 10 min</td>
</tr>
<tr>
<td></td>
<td>7. Cover the plate with Adhesive Foil and incubate 30 min at RT (20-25°C) on a shaker (approx. 600 rpm).</td>
</tr>
<tr>
<td></td>
<td>Noradrenaline ELISA day 2 – two and a half hours</td>
</tr>
<tr>
<td></td>
<td>5. Remove the foil and discard or aspirate the contents of the wells and wash each well 4 times thoroughly with 300 µL Wash Buffer. Blot dry by tapping the inverted plate on absorbent material. – 20 min</td>
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<td>6. Pipette 100 µL of Enzyme Conjugate into all wells. – 10 min</td>
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<tr>
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<td>7. Cover the plate with Adhesive Foil and incubate 30 min at RT (20-25°C) on a shaker (approx. 600 rpm).</td>
</tr>
<tr>
<td></td>
<td>8. Remove the foil and discard or aspirate the contents of the wells and wash each well 4 times thoroughly with 300 µL Wash Buffer. Blot dry by tapping the inverted plate on absorbent material. – 20 min</td>
</tr>
<tr>
<td></td>
<td>9. Pipette 100 µL of Substrate into all wells. – 10 min</td>
</tr>
<tr>
<td></td>
<td>10. Incubate 20-30 min at RT (20-25°C) on a shaker (approx. 600 rpm). Avoid exposure to direct sun light!</td>
</tr>
<tr>
<td></td>
<td>11. Pipette 100 µL of Stop Solution into all wells. -10 min</td>
</tr>
<tr>
<td></td>
<td>12. Read the absorbance of the solution in the wells within 10 minutes, using a microplate reader set to 450 nm and a reference wavelength between 620 nm and 650 nm.</td>
</tr>
<tr>
<td></td>
<td>11. Pipette 100 µL of Stop Solution into all wells. – 10 min</td>
</tr>
<tr>
<td></td>
<td>12. Read the absorbance of the solution in the wells within 10 minutes, using a microplate reader set to 450 nm and a reference wavelength between 620 nm and 650 nm.</td>
</tr>
</tbody>
</table>
Appendices

APPENDIX 13: FIT2QUIT PARTICIPANT INFORMATION SHEET – TELEPHONE ASSESSMENT
Fit2Quit study: Exercise to Enhance Smoking Cessation Outcomes

An invitation...

You are invited to take part in a clinical trial about stopping smoking and exercise. To help you make a decision about participating in the study, we ask that you read this information sheet. Please let us know if you wish to have an interpreter.

Who is co-ordinating this study?

The study is co-ordinated by the Clinical Trials Research Unit (The University of Auckland).

What is the aim of this study?

The aim of the study is to see if smokers who use a combination of an exercise programme and nicotine replacement therapy (NRT) to help stop smoking, are more likely to have quit smoking at six months than smokers who only used NRT.

Why have I been selected?

- You have been selected to take part in this study because you have contacted Quitline; a smoking cessation service provider, and said that you were willing to participate in research. You also meet the requirements below:
- You are currently smoking and are interested in quitting smoking in the next two weeks
- You are 18 years of age or older
- You have access to a phone (land line or mobile)
• You have your first cigarette within 30 minutes of waking up
• You want to be physically active

You cannot take part in this study if you have any of the following conditions:
• You have had a stroke or heart attack or severe angina in the last two weeks
• You enrolled in the “Text2Quit” or “NRT Online” programmes
• You have a medical condition which may limit your ability to exercise safely
• You currently participate in moderate to vigorous physical activity for 30 minutes or more on 5 days per week or more
• You currently have a Green Prescription

Where will the study take place?

Participants for this study will be identified through the Quitline smoking cessation service, and will be from throughout the Auckland and Waikato regions.

How long will the study take?

You’re involvement in the study will take 6 months. You will be contacted at least 3 times during the 6 months for information about your smoking habits and your quit attempt. This will be in addition to the contact you receive from Quitline. The entire study will run for approximately two years, from February 2010 to February 2012.

How many people will be recruited into the study?

We are looking to recruit approximately 1,400 smokers who wish to quit.

What is involved if I take part?

If you are eligible to take part, a trained researcher will seek your permission over the phone. If you agree to take part (that is, you said “yes” or “I agree”) this will be recorded on a form and you will be asked a few more questions. You do not have to answer all the questions, and you may stop the interview at any time. The form showing your agreement to take part in the study will be posted to you (along with this information sheet about the study) as well as details of a person to contact if you have any more questions or concerns about the study.

If you agree to take part in the study, you will be randomly allocated (like the toss of a coin) to one of two groups:

• **Usual Care Group:** Everyone in this group will receive subsidised (low cost) NRT patches and/or gum or lozenges for eight weeks, to help them with their quit attempt. People in this group will be asked to stop smoking cigarettes and start using the NRT provided.

• **Exercise Group:** As above, everyone in this group will receive subsidised (low cost) NRT patches and/or gum or lozenges for eight weeks, to help them with their quit attempt. However, this group will also receive a comprehensive exercise programme to help them with their quit attempt. The exercise programme will be individually tailored and will include face-to-face and telephone support, goal setting, scheduling and planning of exercise, mood management, and referral to existing community based physical activity programmes, and will be provided over a six month period by trained Green Prescription (GRx) Patient Support Person(s) (PSP’s). The GRx PSP’s will obtain permission from your general practitioner (GP) if you decide to attend a community exercise programme.

If you decide to join this study you will be asked to complete questionnaires over the phone approximately eight weeks after your first assessment session. You will also be asked to complete questionnaires over the phone 6 months after your first assessment session. In this session you will be asked to complete the same questionnaires as your first session. If you quit smoking you may also be asked to give a sample of spit.

Clinical Trials Research Unit • The University of Auckland • Level 4 • School of Population Health Building
Tamaki Campus • Morris Road • Glen Innes • Auckland • Private Bag 92019 • Auckland • NEW ZEALAND
Telephone: 64 9 373 7999 • Facsimile: 64 9 373 1710 • Email: ctru@ctru.auckland.ac.nz • www.ctru.auckland.ac.nz

*Fit2Quit Study: Exercise to Enhance Smoking Cessation Outcomes*
(saliva) at six months, so we can measure the level of cotinine (a by-product of nicotine) in your system and/or to confirm that you have managed to quit. We will need to arrange a time to meet with you to collect this sample. The sample will be destroyed at the end of the study unless you indicate that you would like it returned. We anticipate that participation in the study will take approximately 20 minutes at each assessment session.

**Will there be any costs involved?**

Taking part in the study will not cost you any additional money than you would normally pay when enrolling in a quit smoking programme (e.g. $10-15).

**What are the risks and benefits of this study?**

**Possible benefits**

The different treatments we are looking at in this study may or may not help you with your quit attempt. Your responses will help researchers and health services to better understand the opinions of smokers, and may indirectly benefit people who want to stop smoking in the future.

**Possible risks**

When you give up smoking you may experience nicotine withdrawal symptoms such as agitation, anxiety, depression and disturbed sleep. Taking NRT when you stop smoking may reduce these symptoms. NRT is a safe medication and is associated with few side effects. However, some people can experience mild symptoms such as discomfort in the stomach (gastrointestinal discomfort), hiccups, and throat irritation when using products such as the nicotine gum, tablet, and inhalator. Jaw ache can also be a side effect of chewing gum. Patches may occasionally cause redness and itching. These side effects will be fully explained by your smoking cessation provider or study researchers at the time you begin the study, and in written or video material provided in the selection box. Like all medication, NRT should be stored safely out of reach of children and animals.

There are no other anticipated physical risks over and above the risks associated with engaging in everyday physical activity.

**Compensation**

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by the Accident Compensation Corporation (ACC) legislation. ACC cover is not automatic and each case is assessed by ACC, according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are a wage earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. If you have any questions about ACC, please contact your nearest ACC office or ask us for more information before you agree to take part.

**Will the information about me be kept confidential?**

The study files and all information that you provide will remain strictly confidential. No material that could personally identify you will be used in any reports on this study. The information will be kept securely at the Clinical Trials Research Unit, The University of Auckland and destroyed after 15 years according to national research guidelines. All computer records will be password protected. All future use of the information collected will be strictly controlled in accordance with the Privacy Act, 1994.

During the study, ethics committee representatives, study personnel, members of the research team and possibly representatives of the study sponsor may check your records. This will only be done to check the accuracy of the information collected for the study and the information will remain confidential.
When will the results be available?

This study will take three years to conduct, so results will not be available until 2012. You will be asked if you would like to be sent a copy of the overall results.

Has the study received ethical approval?

Yes, this study has received ethics approval from the National Multi-region Ethics Committee, which reviews National and Multi-regional studies.

What are my legal rights?

Your participation in this study is entirely voluntary (your choice). You do not have to take part. If you choose not to take part in this study you will not be affected in any way. You may withdraw from the study at any time, without having to give a reason. Your withdrawal from the study will not affect your future health care from the smoking cessation programme or any other health service. You are encouraged to ask questions at any time during the study. If you have any questions please ask a Fit2Quit study researcher or GRx Patient Support Provider at an assessment session or contact:

**Midi Tsai,**
Study Co-ordinator,
Clinical Trials Research Unit,
Faculty of Medical and Health Sciences,
The University of Auckland,
Private Bag 92019,
Auckland.
**Ph:** (09) 373-7599 extn 84741
**Fax:** (09) 373-1710
**Email:** m.tsai@ctru.auckland.ac.nz

**Vaughan Roberts,**
Research Fellow,
Clinical Trials Research Unit,
Faculty of Medical and Health Sciences,
The University of Auckland,
Private Bag 92019,
Auckland.
**Ph:** (09) 373-7599 extn 84718
**Fax:** (09) 373-1710
**Email:** v.roberts@ctru.auckland.ac.nz

If you have any questions or concerns regarding your rights as a participant in this study you may wish to contact a Health and Disability Advocate at the Health Advocates Trust:

Northland to Franklin ph 0800 555 050
Mid and Lower North Island ph 0800 423 638 (4 ADNET)

Study Investigators

- Dr Ralph Maddison, Dr Chris Bullen, Dr Yannan Jiang, Clinical Trials Research Unit, Faculty of Medical and Health Sciences, University of Auckland
- Dr Marewa Glover, Auckland Tobacco Control Research Centre, Social & Community Health, University of Auckland
- Marilyn Stephens, The Quit Group, Wellington
- Sue Brewster, Sport Auckland, Auckland
- Matthew Cooper, Sport Waikato, Hamilton
- Dr Hayden McRobbie, Inspiring Ltd., Auckland
- Sue Taylor, T & T consulting, Levin
- Paul Brown, Health Systems, Faculty of Medical and Health Sciences, University of Auckland
- Professor Harry Prapavessis, Exercise and Health Psychology Laboratory, University of Western Ontario, Canada

Please keep this sheet for your information.

Thank you for taking the time to read about this study.
Consent Form – Telephone Assessments

Fit2Quit Study: Exercise to Enhance Smoking Cessation Outcomes

Request for an interpreter

<table>
<thead>
<tr>
<th>Language</th>
<th>Request</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>English</td>
<td>I wish to have an interpreter</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Maori</td>
<td>E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero</td>
<td>Ae</td>
<td>Kao</td>
</tr>
<tr>
<td>Samoan</td>
<td>Oute mana'o ia iai se fa'amatala upu</td>
<td>Ioe</td>
<td>Leai</td>
</tr>
<tr>
<td>Tongan</td>
<td>Oku ou fiema'u ha fakatonulea</td>
<td>Io</td>
<td>Ikai</td>
</tr>
<tr>
<td>Cook Island</td>
<td>Ka inangaro au i tetai tangata uri reo</td>
<td>Ae</td>
<td>Kare</td>
</tr>
<tr>
<td>Niuean</td>
<td>Fia manako au ke fakaaoega e taha tagata fakahokohoko kupo</td>
<td>E</td>
<td>Nakai</td>
</tr>
</tbody>
</table>

- I understand the information sheet for volunteers taking part in this study, which has been read and discussed with study researchers. The study is designed to determine whether using a combination of exercise and NRT, to help you stop smoking, is more likely to have you quit smoking at 6 months compared to smokers using usual methods (with NRT available by patch and/or gum or lozenge).

- I have had the opportunity to discuss this study with study researchers and I am satisfied with the answers I have been given.

- I have had the opportunity to use whanau/family support or a friend to help me ask questions and understand the study.

- I understand that I may be asked to provide a spit (saliva) sample to measure nicotine levels.

- I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my future health care/continuing health care from smoking cessation programmes or other health providers.

- I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.

- I understand that information provided by me to the smoking cessation provider (Quitline) may be shared with the researchers where relevant.

- I understand that the GRx Patient Support Person(s) will need to obtain permission from my general practitioner (GP) if I decide to attend a community exercise programme.

- I understand the compensation provisions for this study.

- I have had time to consider whether to take part.
Consent Form Page 2

- I know whom to contact if I have any questions about the study.

- I understand that there will be no personal details that identify me (such as my name, address) on the questionnaires.

- I understand that any data collected as part of this study will be stored securely for 15 years at the Clinical Trials Research Unit, The University of Auckland, in accordance with the Privacy Act, 1994. After this time the information will be safely destroyed.

- I understand that any information collected, as part of this study will not be used for any other purpose, without my permission and ethical approval, nor given to any other third party outside of the research team.

- I understand that there may be a significant delay between data collection and publication of the results.

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| ○   | ○  | I wish to receive a copy of the results
|     |    |
| ○   | ○  | I wish my saliva sample to be returned to me

---

I [full name] (print full name)

of [print address]

hereby consent to take part in this study.

Verbal consent of participant received? [Yes / No] (circle response)

Date: [day month year]

---

Full name of Researcher: [Insert name]

Phone no: [Insert phone number]

Project explained by: [Insert name]

Project role: [Insert role]

Signature: [Signature]

Date: [day month year]

---

This study has received ethical approval from the National Multi-region Ethics Committee, which reviews National and Multi regional studies.

FitzQuit Study: Exercise to Enhance Smoking Cessation Outcomes
PARTICIPANT INFORMATION SHEET

Face-to-Face Assessments

FIT2QUIT

Fit2Quit study: Exercise to Enhance Smoking Cessation Outcomes

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tamaki Makaurau

An invitation...

You are invited to take part in a clinical trial about stopping smoking and exercise. To help you make a decision about participating in the study, we ask that you read this information sheet.

Please let us know if you wish to have an interpreter.

Who is co-ordinating this study?

The study is co-ordinated by the Clinical Trials Research Unit (The University of Auckland).

What is the aim of this study?

The aim of the study is to see if smokers who use a combination of an exercise programme and nicotine replacement therapy (NRT) to help stop smoking, are more likely to have quit smoking at six months than smokers who only used NRT.

Why have I been selected?

- You have been selected to take part in this study because you have contacted Quitline; a smoking cessation service provider, and said that you were willing to participate in research. You also meet the requirements below:

- You are currently smoking and are interested in quitting smoking in the next two weeks
- You are 18 years of age or older
- You have access to a phone (land line or mobile)
• You have your first cigarette within 30 minutes of waking up
• You want to be physically active

You cannot take part in this study if you have any of the following conditions:
• You have had a stroke or heart attack or severe angina in the last two weeks
• You enrolled in the “Text2Quit” or “NRT Online” programmes
• You have a medical condition which may limit your ability to exercise safely
• You currently participate in moderate to vigorous physical activity for 30 minutes or more on 5 days per week or more
• You currently have a Green Prescription

Where will the study take place?

Participants for this study will be identified through the Quitline smoking cessation service, and will be from throughout the Auckland and Waikato regions.

How long will the study take?

You’re involvement in the study will take 6 months. You will be contacted at least 3 times during the 6 months for information about your smoking habits and your quit attempt. This will be in addition to the contact you receive from Quitline. The entire study will run for approximately two years, from February 2010 to February 2012

How many people will be recruited into the study?

We are looking to recruit approximately 1,400 smokers who wish to quit.

What is involved if I take part?

If after reading this information sheet, you decide that you would like to take part in the study, we will need you to give us your permission in writing. To do this we ask that you read and sign the consent form. Once the consent form has been signed, we will ask you to attend your first assessment session (you probably will have already agreed on a date and time for this session during a recent phone call with a study researcher). In this assessment session you will be asked to complete some measures: height, weight, a physical activity questionnaire, a questionnaire about your smoking habits, and a fitness test.

If you agree to take part in the study, you will be randomly allocated (like the toss of a coin) to one of two groups:

• **Usual Care Group:** Everyone in this group will receive subsidised (low cost) NRT patches and/or gum or lozenges for eight weeks, to help them with their quit attempt. People in this group will be asked to stop smoking cigarettes and start using the NRT provided.

• **Exercise Group:** As above, everyone in this group will receive subsidised (low cost) NRT patches and/or gum or lozenges for eight weeks, to help them with their quit attempt. However, this group will also receive a comprehensive exercise programme to help them with their quit attempt. The exercise programme will be individually tailored and will include face-to-face and telephone support, goal setting, scheduling and planning of exercise, mood management, and referral to existing community based physical activity programmes, and will be provided over a six month period by trained Green Prescription (GRx) Patient Support Person(s) (PSP’s). The GRx PSP’s will obtain permission from your general practitioner (GP) if you decide to attend a community exercise programme.

If you decide to join this study you will be asked to complete questionnaires over the phone approximately eight weeks after your first assessment session. You will also be asked to attend a second assessment session 6 months after your first session. In this session you will be asked to complete the same measures as your first session: height, weight, a physical activity questionnaire, a questionnaire about your smoking habits, and a
fitness test. If you quit smoking you may also be asked to give a sample of spit (saliva) at six months, so we can measure the level of cotinine (a by-product of nicotine) in your system and/or to confirm that you have managed to quit. The sample will be destroyed at the end of the study unless you indicate that you would like it returned. We anticipate that participation in the study will take approximately 90 minutes at each assessment session and 20 minutes during the phone call in approximately eight weeks.

**Will there be any costs involved?**

Taking part in the study will not cost you any additional money than you would normally pay when enrolling in a quit smoking programme (e.g. $10-15), apart from the cost of travel to the two assessment sessions. However, we will reimburse you for your travel costs with a $20 petrol voucher.

**What are the risks and benefits of this study?**

**Possible benefits**
The different treatments we are looking at in this study may or may not help you with your quit attempt. Your responses will help researchers and health services to better understand the opinions of smokers, and may indirectly benefit people who want to stop smoking in the future.

**Possible risks**
When you give up smoking you may experience nicotine withdrawal symptoms such as agitation, anxiety, depression and disturbed sleep. Taking NRT when you stop smoking may reduce these symptoms. NRT is a safe medication and is associated with few side effects. However some people can experience mild symptoms such as discomfort in the stomach (gastrointestinal discomfort), hiccups, and throat irritation when using products such as the nicotine gum, tablet and inhalator. Jaw ache can also be a side effect of chewing gum. Patches may occasionally cause redness and itching. These side effects will be fully explained by your smoking cessation provider or study researchers at the time you begin the study, and in written or video material provided in the selection box. Like all medication, NRT should be stored safely out of reach of children and animals.

There are no other anticipated physical risks over and above the risks associated with engaging in everyday physical activity.

**Compensation**

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by the Accident Compensation Corporation (ACC) legislation. ACC cover is not automatic and each case is assessed by ACC, according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are a wage earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. If you have any questions about ACC, please contact your nearest ACC office or ask us for more information before you agree to take part.

**Will the information about me be kept confidential?**

The study files and all information that you provide will remain strictly confidential. No material that could personally identify you will be used in any reports on this study. The information will be kept securely at the Clinical Trials Research Unit, The University of Auckland and destroyed after 15 years according to national research guidelines. All computer records will be password protected. All future use of the information collected will be strictly controlled in accordance with the Privacy Act, 1994.

During the study, ethics committee representatives, study personnel, members of the research team and possibly representatives of the study sponsor may check your records. This will only be done to check the accuracy of the information collected for the study and the information will remain confidential.
When will the results be available?

This study will take three years to conduct, so results will not be available until 2012. You will be asked if you would like to be sent a copy of the overall results.

Has the study received ethical approval?

Yes, this study has received ethics approval from the National Multi-region Ethics Committee, which reviews National and Multi-regional studies.

What are my legal rights?

Your participation in this study is entirely voluntary (your choice). You do not have to take part. If you choose not to take part in this study you will not be affected in any way. You may withdraw from the study at any time, without having to give a reason. Your withdrawal from the study will not affect your future health care from the smoking cessation programme or any other health service. You are encouraged to ask questions at any time during the study. If you have any questions please ask a Fit2Quit study researcher or GRx Patient Support Provider at an assessment session or contact:

**Midi Tsai,**  
Study Co-ordinator,  
Clinical Trials Research Unit,  
Faculty of Medical and Health Sciences,  
The University of Auckland,  
Private Bag 92019, Auckland.  
**Ph:** (09) 373-7599 extn 84741  
**Fax:** (09) 373-1710  
**Email:** m.tsai@ctru.auckland.ac.nz

** Vaughan Roberts,**  
Research Fellow,  
Clinical Trials Research Unit,  
Faculty of Medical and Health Sciences,  
The University of Auckland,  
Private Bag 92019, Auckland.  
**Ph:** (09) 373-7599 extn 84718  
**Fax:** (09) 373-1710  
**Email:** v.roberts@ctru.auckland.ac.nz

If you have any questions or concerns regarding your rights as a participant in this study you may wish to contact a Health and Disability Advocate at the Health Advocates Trust:

Northland to Franklin ph 0800 555 050  
Mid and Lower North Island ph 0800 423 638 (4 ADNET)

**Study Investigators**

- Dr Ralph Maddison, Dr Chris Bullen, Dr Yannan Jiang, Clinical Trials Research Unit, Faculty of Medical and Health Sciences, University of Auckland
- Dr Marewa Glover, Auckland Tobacco Control Research Centre, Social & Community Health, University of Auckland
- Marilyn Stephens, The Quit Group, Wellington
- Sue Brewster, Sport Auckland, Auckland
- Matthew Cooper, Sport Waikato, Hamilton
- Dr Hayden McRobbie, Inspiring Ltd., Auckland
- Sue Taylor, T & T consulting, Levin
- Paul Brown, Health Systems, Faculty of Medical and Health Sciences, University of Auckland
- Professor Harry Papavasisis, Exercise and Health Psychology Laboratory, University of Western Ontario, Canada

Please keep this sheet for your information.

Thank you for taking the time to read about this study.
Appendices

APPENDIX 16: FIT2QUIT CONSENT FORM – FACE-TO-FACE ASSESSMENT
Consent Form – Face-to-Face Assessments

Fit2Quit Study: Exercise to Enhance Smoking Cessation Outcomes

Request for an interpreter

<table>
<thead>
<tr>
<th>Language</th>
<th>Request</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>English</td>
<td>I wish to have an interpreter</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Maori</td>
<td>E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero</td>
<td>Ae</td>
<td>Kao</td>
</tr>
<tr>
<td>Samoan</td>
<td>Oute mana’o ia iai se fa’amatala upu</td>
<td>loe</td>
<td>Leai</td>
</tr>
<tr>
<td>Tongan</td>
<td>Oku ou fiema’u ha fakatonulea</td>
<td>Io</td>
<td>Ikai</td>
</tr>
<tr>
<td>Cook Island</td>
<td>Ka inangaro au i tetai tangata uru reo</td>
<td>Ae</td>
<td>Kare</td>
</tr>
<tr>
<td>Niuean</td>
<td>Fia manako au ke fakaaoga e taha tagata fakahokohoko kupo</td>
<td>E</td>
<td>Nakai</td>
</tr>
</tbody>
</table>

- I understand the information sheet for volunteers taking part in this study, which has been read and discussed with study researchers. The study is designed to determine whether using a combination of exercise and NRT, to help you stop smoking, is more likely to have you quit smoking at 6 months compared to smokers using usual methods (with NRT available by patch and/or gum or lozenge).

- I have had the opportunity to discuss this study with study researchers and I am satisfied with the answers I have been given.

- I have had the opportunity to use whanau/family support or a friend to help me ask questions and understand the study.

- I understand that I may be asked to provide a spit (saliva) sample to measure nicotine levels.

- I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my future health care/continuing health care from smoking cessation programmes or other health providers.

- I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.

- I understand that information provided by me to the smoking cessation provider (Quitline) may be shared with the researchers where relevant.

- I understand that the CRx Patient Support Person(s) will need to obtain permission from my general practitioner (GP) if I decide to attend a community exercise programme.

- I understand the compensation provisions for this study.

- I have had time to consider whether to take part.
Consent Form Page 2

- I know whom to contact if I have any questions about the study.

- I understand that there will be no personal details that identify me (such as my name, address) on the questionnaires.

- I understand that any data collected as part of this study will be stored securely for 15 years at the Clinical Trials Research Unit, The University of Auckland, in accordance with the Privacy Act, 1994. After this time the information will be safely destroyed.

- I understand that any information collected, as part of this study will not be used for any other purpose, without my permission and ethical approval, nor given to any other third party outside of the research team.

- I understand that there may be a significant delay between data collection and publication of the results.

Yes  No

〇〇 I wish to receive a copy of the results

〇〇 I wish my saliva sample to be returned to me

I __________________________ (print full name)

of

__________________________ (print address)

hereby consent to take part in this study.

Signature: __________________________

Date: ___________ ___________ ___________

day month year

Project explained by: __________________________

Project role: __________________________

Signature: __________________________

Date: ___________ ___________ ___________

day month year

This study has received ethical approval from the National Multi-region Ethics Committee, which reviews National and Multi regional studies.

FliZZQuilt Study: Exercise to Enhance Smoking Cessation Outcomes
Appendices

APPENDIX 17: FIT2QUIT FORM A
The purpose of this form is to assess the potential participant’s eligibility for and interest in participating in the study.

**Study Researcher:** Complete Form A for all potential participants who have indicated interest in finding out more information about Fit2Quit, and whom you have been able to contact.

**For paper forms only:**
- Answer all questions. **Do not leave blank spaces**
- Tick circles. Write numbers in boxes.
- If the data are unavailable, put an asterisk “*”.
- If the data are not applicable, put a dash “–”.
- Refer to the Manual of Procedures for complete instructions

Please give the participant an explanation about what the study involves, using the Fit2Quit script provided.

Explain to the participant that there are certain criteria for taking part in the study, which you need to check.

### 1. Assessment Details

1.01 [ ] [ ] [ ] Date of assessment

### 2. Participant Details

2.01 [ ] [ ] [ ] Date of birth

2.02 **Sex**

- [ ] Male  or  [ ] Female

Which ethnic group or groups do you belong to? Please indicate Yes/No to every option I will now read to you. **(tick all that apply)**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.03</td>
<td>[ ] [ ] New Zealand Māori</td>
</tr>
<tr>
<td>2.04</td>
<td>[ ] [ ] New Zealand European</td>
</tr>
<tr>
<td>2.05</td>
<td>[ ] [ ] Other European</td>
</tr>
<tr>
<td>2.06</td>
<td>[ ] [ ] Samoan</td>
</tr>
<tr>
<td>2.07</td>
<td>[ ] [ ] Cook Island Maori</td>
</tr>
<tr>
<td>2.08</td>
<td>[ ] [ ] Tongan</td>
</tr>
<tr>
<td>2.09</td>
<td>[ ] [ ] Niuean</td>
</tr>
<tr>
<td>2.10</td>
<td>[ ] [ ] Chinese</td>
</tr>
</tbody>
</table>
2.11  O  O  Indian
2.12  O  O  Other (such as Dutch, Japanese, Tokelauan)
2.13  If Other (specify)  

3. Inclusion Criteria

3.01  O  O  Oral consent to study participation obtained
3.02  O  O  Aged ≥ 18 years
3.03  O  O  Has first cigarette within 30 minutes of waking
3.04  O  O  Is interested in quitting
3.05  O  O  Wants to be physically active
3.06  O  O  Has access to a telephone

If No to any inclusion criteria then they are not eligible. Thank the participant for their interest and time and explain that their circumstances do not meet the criteria for being in the study. Proceed to Section 7.

4. Exclusion criteria

4.01  O  O  Have you had a stroke or heart related condition in the last 2 weeks?
4.02  O  O  Have you had severe angina in the last 2 weeks?
4.03  O  O  Are you enrolled in the Txt2Quit programme?
4.04  O  O  Are you enrolled in NRT online?
4.05  O  O  Do you have a medical condition which may limit your ability to exercise safely?
4.06  O  O  Do you currently exercise for 30 minutes or more on five days per week or more?
4.07  O  O  Do you currently have a Green Prescription?

If Yes to any exclusion criteria then they are not eligible. Thank the participant for their interest and time and explain that their circumstances do not meet the criteria for being in the study. Proceed to Section 7.
5. **Baseline Assessment Appointment**

5.01 Location of baseline assessment (Select one only)
   - ○ Auckland Central
   - ○ Auckland South
   - ○ Auckland Telephone
   - ○ Waikato
   - ○ Waikato Telephone

5.02 [ ] [ ] [ ] Baseline assessment date

5.03 [HH] [:][MM] Time of appointment (24 hour clock)

6. **Consent**

NOTE: If Q5.01 is “Auckland Telephone” or “Waikato Telephone,” leave Q6.01 blank.

6.01 [ ] [ ] Participant attended face-to-face baseline assessment

   If the participant has not attended two scheduled assessments, change assessment to telephone administered.

6.02 [ ] [ ] Consent obtained

   If No, the participant is not eligible. Proceed to section 7.

6.03 [ ] [ ] [ ] Date of consent

6.04 Type of consent
   - ○ Written
   - ○ Oral

7. **Signature of Study Researcher**

7.01 Signature: __________________________ Printed Name: __________________________

   [ ] [ ] [ ] day month year
Appendices

APPENDIX 18: FIT2QUIT FORM B
Participant initials

Participant date of birth

Registration number

FIT2QUIT

Form B:

Baseline and Demographic

- Questionnaire -

Study Manager to complete

Date of assessment

signature

printed name

Study Manager to complete

Date of assessment

signature

printed name

Fit2Quit • Form B: Baseline and Demographics
© Clinical Trials Research Unit, The University of Auckland, 2009
Survey Information Sheet

The purpose of this questionnaire is to collect some background information about you. This survey will take about 5–10 minutes to complete. If you have any questions then you can ask one of the researchers.

Please answer all questions. **Do not leave blank spaces.**

Tick circles and write numbers in boxes.

The answers that you write are private and will not be shared with anyone other than the researchers. You do not need to tell anyone else what you write on this questionnaire.

If you are worried about anything, or have any questions let the researcher know.

**Study Manager’s Contact Details:**
Midi Tsai CTRU, University of Auckland
**Phone:** 09 3737599 ext. 84741
**e mail:** fit2quit@ctru.auckland.ac.nz
Section 1: Quit Date

1.01 Nominated Quit Date

Section 2: Work and Education

2.01 At present are you? (select the one that best applies)
- Self-employed
- Full time salary or wage earner
- Part-time salary or wage earner (less than 30 hrs/week)
- Retired

If you ticked one of the above options, please go to Question 2.02
- Full-time home-maker
- Student
- Unemployed
- Other beneficiary
- Refuse to answer

If you ticked one of the above options, please go to Question 2.04

2.02 What is your current primary occupation?
Or if retired, what was your previous occupation?
(select one only)
- Clerical or sales employee
- Semi-skilled worker
- Technical or skilled worker
- Business manager or executive
- Business owner or self-employed
- Teacher, nurse, police, other trained service worker
- Professional or senior government official
- Labourer, manual, agricultural or domestic worker
- Farmer owner or manager
- Other
- Refuse to answer

2.03 If Other, please specify
2.04 What is your highest educational qualification? (select one only)
   - None
   - 5th form qualification (School Certificate, NCEA)
   - 6th form qualification (6th Form Cert., University Entrance, NCEA)
   - School qualification higher than 6th form (Higher School Certificate, Bursary)
   - Other school qualification (e.g. overseas school, Cambridge examination, A levels)
   - Polytechnic/university course below Bachelors degree
   - Bachelor degree or higher (Bachelors with honours, Masters, PhD)
   - Other
   - Refuse to answer

2.05 If Other, please specify

2.06 Which of these categories best describes you? (select one only)
   - Married/living with partner
   - Separated, divorced, widowed
   - Never married
   - Refuse to answer

2.07 Please indicate which of these categories best matches your household’s income (select one only)
   - Under $20,000
   - $20,001 to $30,000
   - $30,001 to $40,000
   - $40,001 to $50,000
   - $50,001 to $60,000
   - $60,001 to $70,000
   - $70,001 to $80,000
   - $80,001 to $90,000
   - Over $90,000
   - Don’t know
   - Refuse to answer
Section 3: Smoking History

Which types of tobacco do you usually smoke?

3.01 Yes ☐ No ☐ Factory Made

3.02 If Yes, How many on average do you smoke per day?

☐ ☐ Number smoked/day

3.03 Yes ☐ No ☐ Roll your own/loose

If No, go to Q 3.07

3.04 How many on average do you smoke per day?

☐ ☐ Number smoked/day

3.05 What sized package or pouch do you normally buy?

☐ ☐ Enter # of grams, rounding up any decimal places.

3.06 About how many days does it take you to smoke the contents of this size of pouch or package?

☐ ☐ Days

3.07 ☐ ☐ How many cigarettes and/or roll your own do you smoke each day, on average?

3.08 Yes ☐ No ☐ Have you had a single puff of a cigarette/roll your own in the last 7 days?

(If you have had more than a single puff, tick Yes)

3.09 If Yes, what is the total number of cigarettes/roll your own you have smoked in the last 7 days? (Enter 1 if you have smoked ≤1 cigarette/roll your own)

☐ ☐ Total smoked in last 7 days

3.10 At what age did you start smoking cigarettes/roll your own?

☐ ☐ Years

3.11 How many years have you been smoking cigarettes/roll your own continuously?

☐ ☐ Years

3.12 Yes ☐ No ☐ Do you usually smoke tobacco from a pipe?

3.13 If Yes, how many grams do you smoke per week?

☐ ☐ Gms/week

3.14 Yes ☐ No ☐ Do you usually smoke cigars?

3.15 If Yes, how many do you smoke per week?

☐ ☐ Number smoked/week
3.16  

**Yes**  
○  ○ Have you made any previous attempts to stop smoking?  

> If No, go to Section 4.

3.17  

How many other attempts to stop smoking have you made in the **12 months before this attempt**?  
This does not include this attempt to stop. *(Tick one only)*  
○ One other attempt  
○ 2 other attempts  
○ 3 other attempts  
○ 4 or more other attempts  
○ No other attempts  
○ Don’t know  

> If you ticked ‘No other attempts’ or ‘Don’t know’, go to Section 4.

3.18  

How long did you quit smoking for (in the last 12 months)?

[ ] [ ] [ ] [ ] Days

What method(s) did you use to help you stop smoking that time? *(Please answer all questions)*

3.19  

**Yes**  
○ ○ NRT products, such as patches, gum, or lozenge

3.20  

○ ○ Medication, such as zyban, nortriptyline or varenicline

3.21  

○ ○ Nothing

3.22  

○ ○ Other

3.23  

> If Other, please specify


Section 4: Nicotine Dependency

4.01 How many cigarettes do you smoke per day? (select one only)
   ○ 31 or more
   ○ 21–30
   ○ 11–20
   ○ 10 or less

4.02 How soon after you wake up do you smoke your first cigarette? (select one only)
   ○ Within 5 minutes
   ○ 6–30 minutes
   ○ 31–60 minutes
   ○ More than 60 minutes

Yes  No
4.03  ○  ○ Do you find it difficult to stop smoking in smokefree areas, e.g. in cafes, bars, at the movies etc?

4.04 Which cigarette would you most hate to give up? (select one only)
   ○ The first one in the morning
   ○ All others

Yes  No
4.05  ○  ○ Do you smoke more frequently during the first hours after waking than during the rest of the day?

Yes  No
4.06  ○  ○ Do you smoke if you are so ill that you are in bed most of the day?
Appendices

APPENDIX 19: FIT2QUIT FORM S
Form S:

Smoking and Health Economics

Study Manager to complete (tick ONE only)

Date of assessment  [ ] 1 9 2 0

○ Baseline ○ 8 weeks ○ 24 weeks

signature printed name
Survey Information Sheet

The purpose of this questionnaire is to collect some information about you. This survey will take about 10 minutes to complete. If you have any questions then you can ask one of the researchers.

Please answer ALL questions. DO NOT LEAVE BLANK SPACES.

Tick circles and write numbers in boxes.

The answers that you write are private and will not be shared with anyone other than the researchers. You do not need to tell anyone else what you write on this questionnaire.

If you are worried about anything, or have any questions let the researcher know.

Study Manager’s Contact Details:

Midt Tsai CTRU, University of Auckland

Phone: 09 3737599 ext. 84741

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Section 1: Smoking Status (8 and 24 Week Assessment Only)

Complete at 8 week assessment only:

1.01 When was your actual Quit Date?
   - 2:0

Complete at 8 and 24 week assessments:

1.02 Have you had a single puff of a cigarette/roll your own in the last 7 days?
   - Yes
   - No
   (If you have had more than a single puff tick Yes)
   → If Yes, what is the total number of cigarettes/roll your own you have smoked in the last 7 days? (Enter 1 if you have smoked ≤ 1 cigarette/roll your own.)
   - 0

1.03 Total smoked in last 7 days
   - 0

1.04 Have you smoked more than 5 cigarettes/roll your own since your nominated quit date?
   - Yes
   - No
   → If No, go to Section 2.

1.05 Have you gone back to regular (daily) smoking?
   - Yes
   - No

1.06 If No, what is the total number of cigarettes/roll your own you have smoked since your nominated quit date?
   - 0
   → Go to Q 1.09

1.07 Enter date of when you started regular (daily) smoking (approximately if you can not remember)
   - 2:0

1.08 How many cigarettes/roll your own have you smoked each day on average since your nominated quit date?
   - 0
   → 0

1.09 Do you currently smoke roll your own?
   - Yes
   - No
   → If No, go to Q1.12

1.10 What sized pouch or package do you currently buy?
   - Enter # of grams, rounding up any decimal places.
   - 0

1.11 About how many days does it take you to smoke the contents of this size of pouch or package?
   - 0

1.12 Do you currently smoke factory made cigarettes?
   - Yes
   - No
   → If Yes, how many on average do you smoke per day?
   - 0

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Complete at 24 week assessment only:

1.14 How many other quit attempts have you made (of more than 24 hours) since your nominated quite date? If no other quit attempts, enter 0.

Section 2: Nicotine Replacement Therapy Use (All Assessments)

2.01 | Yes | No |
---|---|---|
Are you currently using NRT?

2.02 If No, Why not? (Select most appropriate option).
- I don’t feel I need it
- I didn’t like the NRT I was using
- I haven’t got around to it
- I have started smoking again
- Don’t know
- Other

2.03 If Other, please specify

2.03 Please go to Q 2.14 if you answered Q 2.02

What NRT product(s) are you currently using? Indicate type, dose, and frequency of use

<table>
<thead>
<tr>
<th>NRT Product</th>
<th>Yes</th>
<th>No</th>
<th>If Yes, Quantity per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.04 Patch 21mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.05 Patch 14mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.06 Patch 7mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.07 Fruit gum 4mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.08 Fruit gum 2mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.09 Mint gum 4mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.10 Mint gum 2mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.11 Lozenge 2mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.12 Lozenge 1mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.13 Other:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Complete at 24 week assessment only:

2.14 O O Have you used any other products or methods (eg Zyban, Champix, hypnosis) to help you Quit during the last 6 months?
If No, go to Section 3

What did you use? (Please answer all questions)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.15</td>
<td>O</td>
</tr>
<tr>
<td>2.16</td>
<td>O</td>
</tr>
<tr>
<td>2.17</td>
<td>O</td>
</tr>
<tr>
<td>2.18</td>
<td>O</td>
</tr>
<tr>
<td>2.19</td>
<td>O</td>
</tr>
<tr>
<td>2.20</td>
<td>O</td>
</tr>
<tr>
<td>2.21</td>
<td>O</td>
</tr>
<tr>
<td>2.22</td>
<td>O</td>
</tr>
<tr>
<td>2.23</td>
<td>If Other, please specify</td>
</tr>
</tbody>
</table>
Section 3: Mood and Physical Symptoms (All Assessments)

This section asks you about your mood and any physical symptoms that you have felt over the last week. (Select one only for each question)

3.01 Have you been depressed?
   - 1 = not at all
   - 2 = slightly
   - 3 = moderately
   - 4 = very
   - 5 = extremely

3.02 → If you ticked 2–5 (slightly to extremely), did you seek any treatment for this?
   - Yes
   - No

3.03 → If Yes, how many times? __________

3.04 Have you been irritable?
   - 1 = not at all
   - 2 = slightly
   - 3 = moderately
   - 4 = very
   - 5 = extremely

3.05 → If you ticked 2–5 (slightly to extremely), did you seek any treatment for this?
   - Yes
   - No

3.06 → If Yes, how many times? __________

3.07 Have you had poor concentration?
   - 1 = not at all
   - 2 = slightly
   - 3 = moderately
   - 4 = very
   - 5 = extremely

3.08 → If you ticked 2–5 (slightly to extremely), did you seek any treatment for this?
   - Yes
   - No

3.09 → If Yes, how many times? __________
3.10 Have you had disturbed sleep?
   □ 1 = not at all
   □ 2 = slightly
   □ 3 = moderately
   □ 4 = very
   □ 5 = extremely

3.11 If you ticked 2–5 (slightly to extremely), did you seek any treatment for this?
   Yes No

3.12 If Yes, how many times? □□□

3.13 Have you been anxious?
   □ 1 = not at all
   □ 2 = slightly
   □ 3 = moderately
   □ 4 = very
   □ 5 = extremely

3.14 If you ticked 2–5 (slightly to extremely), did you seek any treatment for this?
   Yes No

3.15 If Yes, how many times? □□□

3.16 How much of the time have you felt the urge to smoke in the past week?
   □ 1 = Not at all
   □ 2 = A little of the time
   □ 3 = Some of the time
   □ 4 = A lot of the time
   □ 5 = Almost all of the time
   □ 6 = All of the time

3.17 If you ticked 2–6 ("A little of the time" to "All of the time"), how strong have the urges been?
   □ 1 = Slight
   □ 2 = Moderate
   □ 3 = Strong
   □ 4 = Very strong
   □ 5 = Extremely strong

Complete at Baseline and 8 week assessment only:

3.18 □ How would you rate your chances of giving up smoking for good this time? On a scale of 1 to 5, with 1 = very low to 5 = very high.
Section 4: Your Household
(Baseline and 24 Week Assessments Only)

4.01 Do you live with other smokers? (Tick one only)
   ○ Yes
   ○ No
   ○ Sometimes

Section 5: Health Service Usage
(Baseline and 24 Week Assessments Only)

This section refers to health services you have used because of an injury or illness to you in the past month. Please do not include visits you have made due to illness to family members or friends.

   Yes   No
5.01 ○   ○ In the past month, have you visited a GP?
5.02    → If Yes, how many times? □□□

   Yes   No
5.03 ○   ○ In the past month, have you visited a specialist?
5.04    → If Yes, how many times? □□□

   Yes   No
5.05 ○   ○ In the past month, have you visited a physiotherapist?
5.06    → If Yes, how many times? □□□

   Yes   No
5.07 ○   ○ In the past month, have you had to go to an emergency room at a public or private hospital?
5.08    → If Yes, how many times? □□□

   Yes   No
5.09 ○   ○ In the past month, have you had to spend the night in a public or private hospital?
5.10    → If Yes, how many times? □□□

   Yes   No
5.11 ○   ○ In the past month, have you had any laboratory tests?
5.12    → If Yes, how many times? □□□
5.13  
  
Yes  
No

In the past month, have you used any other health services?  

If Yes, please list the health services you have used and the number of times you visited each service (Enter one health service per line)

5.14

Other health service

5.15

Number of times

5.16

Other health service

5.17

Number of times

---

Section 6: Health Questions  
(Baseline and 24 Week Assessments Only)

6.01  

[ ] How would you rate your overall health during the past week? On a scale of 1 to 7 with 1 = very poor to 7 = excellent

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

6.02 Mobility
   
   O A  = I have no problems in walking about
   O B  = I have some problems in walking about
   O C  = I am confined to bed

6.03 Self-care
   
   O A  = I have no problems with self-care
   O B  = I have some problems washing or dressing myself
   O C  = I am unable to wash or dress myself

6.04 Usual activities (e.g. work, study, housework, family or leisure activities)
   
   O A  = I have no problems with performing my usual activities
   O B  = I have some problems with performing my usual activities
   O C  = I am unable to perform my usual activities

6.05 Pain/discomfort
   
   O A  = I have no pain or discomfort
   O B  = I have moderate pain or discomfort
   O C  = I have extreme pain or discomfort

6.06 Anxiety/depression
   
   O A  = I am not anxious or depressed
   O B  = I am moderately anxious or depressed
   O C  = I am extremely anxious or depressed

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6.07 To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

---

For study researcher to complete.

---

Your own health state today
Section 7: Value on Smoking Cessation
(Baseline and 24 Week Assessments Only)

We are interested in understanding how much value you place on being able to stop smoking and on the current smoking cessation programme. We are going to ask you two questions. The first designed to see what value you place on stopping smoking and the second on the current smoking cessation programme.

7.01 Suppose there was a pill that you could take that would allow you to stop smoking once and for all with no side effects or withdraw symptoms. Using the above scale as a guide, what would be the maximum amount that you would be willing to pay out of your own money to stop smoking?

7.02 Given what you know about the current smoking cessation programme, and using the above scale as a guide, what would be the maximum amount that you would be willing to pay out of your own money to participate in the programme?
APPENDIX 20: FIT2QUIT FORM E
Form E1:

Physical Activity
- Survey -

Study Manager to complete (tick ONE only)

Date of assessment  2 0 1
    day    month    year

  O Baseline

  O 24 weeks

signature      printed name  2 0 1
    day    month    year
The researcher/s you have met, who will be helping you fill in this survey, are from the Clinical Trials Research Unit. We are doing some research to look at physical activity and smoking cessation.

You have been asked to take part in this study, which will look at the effect of an exercise intervention to increase smoking cessation rates.

In this survey, there are some simple questions that will take about 15–20 minutes to complete. If you have any questions then you can ask one of the researchers.

The answers that you write are private and will not be shared. You do not need to tell anyone else what you write on this questionnaire or compare your answers as everyone will have different responses.

If you are worried about anything, or have any questions let the researcher know.

Study Manager’s Contact Details:

Midi Tsai CTRU, University of Auckland

Phone: 09 3737599 ext. 84741

e mail: fit2quit@ctru.auckland.ac.nz
What is physical activity?

Physical Activity includes taking part in organised sports like – Netball, Rugby, Hockey, Soccer, Athletics, Basketball, Judo, Tennis, etc.

OR

It can also be organised activities like – Gym classes, dancing, aerobics etc

OR

Other activities you do in your spare time like – Cycling, walking the dog, running etc.

What is Regular Activity?

Regular physical activity is doing any of these activities for a total of 30-minutes or more per day (on most days of the week [at least 5]).

Remember: You don’t have to have to do the same activity everyday to be ‘regularly active.’ If it all adds up to more than 30-minutes per day (most days of the week) we call this regular.

What are light/moderate/vigorous activities?

In answering the following questions you will be asked to think about how long you can participate in physical activities that are described as light/moderate/vigorous intensity.

Below is the description of what light, moderate and vigorous intensity activities are:

LIGHT INTENSITY ACTIVITIES: Are when you are moving around, but your heart rate and breathing do not increase very much. You would be able to talk easily through the activity.

MODERATE INTENSITY ACTIVITIES: Are when your breathing and heart rate increase. You may start to sweat and feel out of breath. You may find it hard to talk during the activity.

VIGOROUS INTENSITY ACTIVITIES: Are when your heart beats very fast, your breathing is fast and you start sweating. You may feel exhausted and out of breath. It would be very hard to talk during the activity.
During a typical 7 day period (a week), how many times on the average do you do the following kinds of exercise for more than 15 minutes during your free time?

1.01 Vigorous exercise (heart beats rapidly) (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)
   [ ] [ ] Times per week

1.02 Moderate exercise (not exhausting) (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)
   [ ] [ ] Times per week

1.03 Mild exercise (minimal effort) (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking)
   [ ] [ ] Times per week
Section 2

Rate on the scale below from 0 (not confident at all) to 100% (completely confident) how confident you are that you can perform any physical activity or exercise (including walking) at the different intensities (light, moderate, hard) given below (tick only one circle per row).

How confident are you that you can complete:

<table>
<thead>
<tr>
<th></th>
<th>Not confident at all</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Complete confident</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0%</td>
<td>10%</td>
<td>20%</td>
<td>30%</td>
<td>40%</td>
<td>50%</td>
<td>60%</td>
<td>70%</td>
<td>80%</td>
</tr>
<tr>
<td>2.01</td>
<td><strong>10 minutes</strong> of physical activity at a <strong>light</strong> intensity on most days of next week?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>2.02</td>
<td><strong>30 minutes</strong> of physical activity at a <strong>light</strong> intensity on most days of next week?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>2.03</td>
<td><strong>60 minutes</strong> of physical activity at a <strong>light</strong> intensity on most days of next week?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>2.04</td>
<td><strong>10 minutes</strong> of physical activity at a <strong>moderate</strong> intensity on most days of next week?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>2.05</td>
<td><strong>30 minutes</strong> of physical activity at a <strong>moderate</strong> intensity on most days of next week?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>2.06</td>
<td><strong>60 minutes</strong> of physical activity at a <strong>moderate</strong> intensity on most days of next week?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>2.07</td>
<td><strong>10 minutes</strong> of physical activity at a <strong>vigorous</strong> intensity on most days of next week?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>2.08</td>
<td><strong>30 minutes</strong> of physical activity at a <strong>vigorous</strong> intensity on most days of next week?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>2.09</td>
<td><strong>60 minutes</strong> of physical activity at a <strong>vigorous</strong> intensity on most days of next week?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>
### Section 3

Rate on the scale below from 0 (not confident at all) to 100% (completely confident) how confident you are that you could still do regular (most days of the week) physical activities (exercise, sport, games, dance, walking etc) even when you are faced with any of the following situations (tick one circle per row):

<table>
<thead>
<tr>
<th>Situation</th>
<th>Not confident at all</th>
<th>0%</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.01 If the weather is bad</td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>3.02 If I have a lot of work to do</td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>3.03 If there are good TV programmes on</td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>3.04 If I have a lot of other activities to do with my friends and/or family</td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>3.05 If I am tired</td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>3.06 If I am sore</td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

### Section 4

Rate on the scale below from 1 (strongly disagree) to 7 (strongly agree) how motivated you are to perform physical activity or exercise (tick only one circle per row).

<table>
<thead>
<tr>
<th>Motivation</th>
<th>Strongly disagree</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.01 I exercise because I like to rather than because I feel I have to</td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>4.02 Exercising is not something I would necessarily choose to do, rather it is something that I feel I ought to do</td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>4.03 Having to exercise is a bit of a bind but it has to be done</td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>
Section 5: International Physical Activity Questionnaire

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 activates that you did in the last 7 days.

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.

5.01  Yes  No

○ Do you currently have a job or do any unpaid work outside your home? (tick one only)
  → If 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 travelling to or from work.

5.02 During the last 7 days, 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
  → If No, skip to Question 5.04

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

☐ ☐ ☐ ☐ Hours:Minutes per day

Again, think about only those physical activities that you did for at least 10 minutes at a time.

5.04 During the last 7 days, 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
  → If No, skip to Question 5.06
5.05 How much time did you usually spend on one of those days doing moderate physical activities as part of your work?

[ ]: [ ] Hours:Minutes per day

5.06 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

→ If No, skip to Part 2: Transportation

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

[ ]: [ ] Hours:Minutes per day

---

**Part 2: Transportation Physical Activity**

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

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

☐ Days per week

☐ No travelling in a motor vehicle

→ If No, skip to Question 5.10

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

[ ]: [ ] Hours: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.

5.10 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

→ If No, Skip to Question 5.12

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

[ ]: [ ] Hours:Minutes per day
5.12 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
  - If No, Skip to Part 3: Housework, House Maintenance, And Caring For Family

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

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<th>MIN</th>
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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.

5.14 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, shovelling snow, or digging in the garden or yard?
- Days per week
- No vigorous activity in garden or yard
  - If No, Skip to Question 5.16

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

<table>
<thead>
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<th>HR</th>
<th>MIN</th>
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5.16 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
  - If No, Skip to Question 5.18

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

<table>
<thead>
<tr>
<th>HR</th>
<th>MIN</th>
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</table>
5.18 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 your home

⇒ If No, skip to Part 4: Recreation, Sport And Leisure-Time Physical Activity

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

[ ] : [ ] Hours: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 that you have already mentioned.

5.20 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

⇒ If No, Skip to Question 5.22

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

[ ] : [ ] Hours:Minutes per day

5.22 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

⇒ If No, Skip to Question 5.24

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

[ ] : [ ] Hours:Minutes per day
5.24 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

→ If No, Skip to Part 5: Time Spent Sitting

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

[ ] [ ] Hours: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.

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

[ ] [ ] Hours:Minutes per day

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

[ ] [ ] Hours:Minutes per day
Appendices

APPENDIX 21: FIT2QUIT FORM P
The purpose of this form is to collect information from study participants at the baseline, 8 week and 24 week assessments.

**Study Researcher:** Ask the participant the following questions **exactly** as they are worded (where applicable). Do not explain the question any further to them. If they are confused, read the question out again. Where possible do not read out the answers – but tick the most appropriate answer.

**For paper forms only:**
- Answer all questions. **Do not leave blank spaces**
- Tick circles. Write numbers in boxes.
- If the data are unavailable, put an asterisk "**".
- If the data are not applicable, put a dash "—".
- Refer to the Manual of Procedures for complete instructions

### 1. Assessment Details

1.01 **Date of assessment**

1.02 **Assessment** (Select one only)
- Baseline
- 8 week
- 24 week

1.03 **Information available for this scheduled visit?**
- Yes
- No

1.04 **If No, reason for missed visit**
- Unable to contact participant
- Participant did not attend assessment within timeline
- Participant died [Complete Form X]
- Serious adverse event [Complete Form X]
- Refuses further participation
- Other

1.05 If other, please specify

Go to Section 10 and submit form

If Yes, go to Section 2
Physiological Measures (Baseline and 24 Week Assessments Only)

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Astrand-Rhyming Step Test

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<td></td>
<td></td>
<td>min</td>
<td>Predicted VO₂ max</td>
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Accelerometer (Baseline and 24 Week Assessments Only)

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<td>Accelerometer provided to participant?</td>
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<td>If No, go to Section 4</td>
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<td>Accelerometer serial number</td>
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<th>Yes</th>
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<td></td>
<td>Accelerometer returned</td>
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<td>If Yes, date accelerometer returned</td>
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Pedometer (For Intervention Group at Baseline and 24 Week Assessments)

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<td></td>
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<td></td>
<td>Pedometer provided to participant at baseline assessment</td>
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<th>Yes</th>
<th>No</th>
<th>Not Applicable</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Pedometer returned at 24 week assessment</td>
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<td></td>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Not Applicable</td>
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</table>
5. Pregnancy (All Assessments)

5.01  [ ] Yes  [ ] No  Is the participant female?
      [ ] If No, go to Section 6

5.02  [ ] Yes  [ ] No  Is the participant pregnant?
      [ ] If Yes, when is the expected due date?

5.03  [ ] [ ] [ ] Due date

If the answer to 5.02 is Yes, then ask the participant to discuss their on-going NRT use with their GP or lead maternity caregiver, as per usual Quitline Practice.

6. Current Medication (All Assessments)

Baseline assessment

6.01  [ ] Yes  [ ] No  Are you currently taking any non-study medication?
      [ ] If Yes, complete Form M

8 and 24 week assessments

6.02  [ ] Yes  [ ] No  Since our last contact have there been any changes to your non-study medication?
      [ ] If Yes, complete/update Form M

7. Serious Adverse Events (8 and 24 Week Assessments Only)

7.01  [ ] Yes  [ ] No  Since our last contact have there been any serious adverse changes to your health?
      [ ] If Yes, complete Form X
8. Carbon Monoxide and Cotinine Measures (24 Week Assessment Only)

Yes  No
Has the participant reported that they have stopped smoking, i.e. answered No to Q 1.02 or No to Q 1.04 on Form S?
If No, go to Section 9.

If Yes, complete carbon monoxide and cotinine tests:

8.02 201 Date of carbon monoxide test
day month year

8.03 Carbon monoxide monitor number

8.04  ppm Carbon monoxide measurement

8.05 201 Date of Cotinine test
day month year

8.06 Batch Number

8.07 Cotinine Reading

9. Contact Details (All Assessments)

Yes  No
Have your contact details changed?
If Yes, complete Form Z

10. Signature of Study Researcher

signature printed name  201 day month year
APPENDIX 22: EXAMPLE OF LINEAR REGRESSION GRAPH OF PAI AND HRAR VALUES

Note: The y-axis represents heart rate in beats per minute.

The three regression lines represent the rest, exercise, and recovery phases.
APPENDIX 23: FIT2QUIT QUALITATIVE STUDY PARTICIPANT INFORMATION SHEET
The Fit2Quit Study: what do people think of the exercise programme?

Phone Interviews

PARTICIPANT INFORMATION SHEET

You are invited to take part in a study that looks at people's perceptions of the Fit2Quit exercise programme. To help you make a decision about participating in the study, we ask that you read this information sheet.

Who is co-ordinating this study?
The study is co-ordinated by the Clinical Trials Research Unit (The University of Auckland).

What is the aim of this study?
The aim of the study is to gain in-depth information on the effectiveness of the exercise intervention you received during the Fit2Quit trial. It is important to gain feedback from those who participated in the intervention to determine how useful the intervention was for increasing the amount of exercise you do and for helping you to quit smoking.

What types of people can be in the study?
To take part in the study you must:
- Be able to give informed consent to participate in the study
- Be able to communicate in English
- Have been randomised into the Fit2Quit study intervention group

Where will the study take place?
The phone interview will take place over the telephone at a time that is convenient for you.

How long will the study take?
Your involvement in the study will take approximately 10-20 minutes.

How many people will be recruited into the study?
We are looking to recruit approximately 20-30 people.

What is involved if I take part?
We will be contacting you by phone shortly to see if you are interested in participating in this research. If after reading this information sheet and the attached consent form, you decide that you would like to take part in the study, we will need you to give us your consent verbally. To do this I will read out the consent form and if you agree to the conditions, I will sign on your behalf. Once you have done this, the phone interview will commence. During the interview we would like to hear your opinions around your Fit2Quit intervention experiences. Once this interview has finished the study is over. You have the right to end the interview at any time. During the interview we will tape-record the phone conversation to make sure that we do not miss anything that is raised during the interview. On completion of the study a summary of the results will be provided to you, if you request it.

What are the risks and benefits of this study?
We do not anticipate any risks with this study. However, taking part in this study will take some of your time. You will be required to complete the consent form, and take part in the interview. The total time involved for you will probably be about 10-20 minutes in total. Your participation will help us to better understand the
effectiveness of the Fit2Quit intervention and potential ways to improve services that may benefit people that go through similar programmes in the future.

In acknowledgment of the time taken to participate in this study, you will be compensated with a $20 supermarket voucher.

**Will the information about me be kept confidential?**

All comments from the interview will be processed to remove identifying information. You are free to withdraw from the research at any time. If any of the comments you provide are included in a report or published, this will be done in a way that does not identify you as the source.

As part of Fit2Quit we have collected personal details such as your name and address to communicate with you throughout the Fit2Quit study. This information has been stored separately from any personal data such as background information collected like ethnicity and age. No material that could personally identify you will be used in any reports on this study. Information will be stored for no less than 10 years, at the Clinical Trials Research Unit, University of Auckland after which time they will be deleted or destroyed via secure destruction services. All computer records will be password protected. All future use of the information collected will be strictly controlled in accordance with the Privacy Act, 1994.

**When will the results be available?**

This study will take one year to conduct, so results will not be available until 2011. You will be asked if you would like to be sent a copy of the overall results.

**Has the study received ethical approval?**

This study has received ethics approval from the Northern X Regional Ethics Committee, ethics reference number (MEC/11/EXP/102).

**What are my legal rights?**

Your participation in this study is entirely voluntary (your choice). You do not have to take part. If you choose not to take part in this study you will not be affected in any way. You may withdraw from the study at any time, without having to give a reason. Your withdrawal from the study will not affect your future health care or your relationship with the University of Auckland. You are encouraged to ask questions at any time during the study. If you have any questions please contact:

Vaughan Roberts  
Research Fellow & Principal Investigator  
Clinical Trials Research Unit  
University of Auckland  
Private Bag 92 019  
Ph: (09) 373-7599 extn 84718  
v.roberts@ctru.auckland.ac.nz

If you have any questions or concerns regarding your rights as a participant in this study you may wish to contact an independent health and disability advocate:

Free phone: 0800 555 050  
Free fax: 0800 2 SUPPORT (0800 2787 7678)  
Email: advocacy@hdc.org.nz

**Study Investigators**

- Dr Ralph Maddison, Clinical Trials Research Unit, Faculty of Medical and Health Sciences, University of Auckland  
- Associate Professor Chris Bullen, Clinical Trials Research Unit, Faculty of Medical and Health Sciences, University of Auckland  
- Miss Leila Pfafflin, Clinical Trials Research Unit, Faculty of Medical and Health Sciences, University of Auckland

*Thank you for taking time to read about this study. Please keep this sheet for your information.*
Appendices

APPENDIX 24: FIT2QUIT QUALITATIVE STUDY CONSENT FORM
The Fit2Quit study: what do people think of the exercise programme?

Phone Interview

CONSENT FORM

- I have read and I understand the information sheet dated 3 Oct 2011.
- I have had the opportunity to discuss this study with study researchers and I am satisfied with the answers I have been given.
- I have had the opportunity to use whanau/family support or a friend to help me ask questions and understand the study.
- I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my future health care/continuing health care or my future relations with the University of Auckland.
- I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.
- I have had time to consider whether to take part.
- I know whom to contact if I have any questions about the study.
- I consent to my interview being audiotaped.
- I understand my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.
- I understand that any data collected as part of this study will be stored securely for 10 years at the Clinical Trials Research Unit, The University of Auckland, in accordance with the Privacy Act, 1994. After this time the information will be safely destroyed.
- I understand that any information collected, as part of this study will not be used for any other purpose, without my permission and ethical approval, nor given to any other third party outside of the research team.
- I understand that there may be a significant delay between data collection and publication of the results.

Please turn over
- I wish to receive a copy of the results  YES/NO (please circle one)

I ____________________________ (print full name)

of __________________________ (print address)

______________________________

______________________________ hereby consent to take part in this study.

Verbal consent of participant received  Yes/No (circle one)

Date: __/__/____

day/month/year

Project explained by: __________________________

Project role: __________________________

Signature: __________________________

Date: __/__/____

day/month/year
APPENDIX 25: FIT2QUIT QUALITATIVE STUDY SEMI-STRUCTURED INTERVIEW GUIDELINES
Interview guidelines

Research Question: Fit2Quit intervention group participant perspectives of the study intervention

The one-on-one telephone interviews will be semi-structured to allow for a reflexive discussion to take place and unscripted themes to surface. Demographic information including sex, age and ethnicity, intervention compliance, and smoking status will be taken from Fit2Quit study forms, and will be incorporated into the analysis.

Themes that will be explored:

1. Perceptions of the exercise intervention
   a. Why did you decide to participate in the Fit2Quit study?
   b. When the exercise programme was first explained to you what did you think of it?
   Prompts:
      i. Did you think it would be useful for you?
      ii. Did you understand what was involved when you started the study?
      iii. Did you know what being in the exercise group involved?
   a. What did you like/dislike about the exercise intervention?
      Prompts – Did it help you to exercise more? Did it help you to quit smoking?
   b. Was it what you expected it to be?
   c. Was there any information you felt was missing?
   d. How supportive was your participant support person?
   e. Are there any aspects of the intervention you would like to see changed/improved? Is there anything you would like to see the participant support people do differently?
   f. What did you think of the amount of calls you received?
   Prompts:
      i. Did you not like the frequency of calls?
      ii. Were calls made at times that didn’t suit you?
      iii. Did you screen the calls?

2. Lifestyle changes
   a. What (if any) lifestyle changes have you made since you started the study?
      Prompts: exercise, eat healthy, quit smoking?
   b. Do you think the intervention/participant support person helped you make these changes?