Impulsivity and smoking: Development of a smoking cessation treatment

by

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Abstract

Tobacco smoking is one of the leading preventable causes of illness and mortality worldwide. Despite current available treatments such as pharmacotherapy and psychological/behavioural treatments, relapse rates amongst smokers remain high. Research suggests that response inhibition, or difficulties with impulse control, is a predictor of relapse and may be a target for interventions aimed to improve smoking outcomes.

This thesis consists of two components. The first part aimed to develop and pilot a web-based response inhibition training intervention for dependent smokers. The final intervention involved participants completing 14 training sessions over consecutive days for two weeks. Results from two pilot studies in adult smokers ($n = 16$ and $n = 13$) indicated that the intervention was feasible and acceptable. Preliminary findings yielded generally favourable results of training effects on smoking outcome, indicating a decrease of the number of daily cigarettes smoked at two-week follow-up. As such, the training program will subsequently be investigated in a full-scale randomised controlled trial and should significant results be found, it would assist people in reducing or quitting smoking and generate significant economic and health benefits.

The second part of this thesis reports on a systematic review to investigate 1) whether psychosocial treatments targeting smoking resulted in significant decreases in levels of impulsivity as measured by self-report or behavioural measures and 2) whether decreases in impulsivity were associated with improved smoking outcomes. Out of 1098 unique studies initially identified, 10 studies comprising of nine independent studies fulfilled the inclusion criteria and were reviewed. Results were mixed regarding whether interventions for smoking
reduced impulsivity following treatment, although there was evidence to suggest that contingency management was effective in reducing impulsivity as assessed by delay discounting measures. In regards to the second question of the review, decreases in impulsivity may be associated with smoking outcomes following a long period of abstinence and when measured at a distal follow-up time-point following the end of the intervention period. Given the small number of studies, further research is required to gain a better understanding of the impact of smoking cessation treatment on impulsivity.
Synopsis

Tobacco smoking has been linked to numerous adverse health outcomes such as cancer, cardiovascular diseases, and chronic obstructive pulmonary disease (Australian Institute of Health and Welfare [AIHW], 2014; AIHW, 2017; World Health Organization [WHO], 2012; Yanbaeva, Dentener, Creutzberg, Wesseling, & Wouters, 2007). Relapse rates remain high despite most smokers reporting a desire to quit (Babb, Malarcher, Schauer, Asman, & Jamal, 2017), with those who smoked more than 20 cigarettes a day reportedly more likely to attempt but also more likely to relapse (AIHW, 2017).

At present, pharmacological and psychological/behavioural therapies are the most commonly used interventions to assist with smoking cessation (Cahill, Stevens, Perera, & Lancaster, 2013). Literature suggests that nicotine replacement therapy (NRT), antidepressants, and nicotine partial receptor agonists are effective in aiding adherence and preventing relapse (Cahill, Lindson-Hawley, Thomas, Fanshawe, & Lancaster, 2016; Cahill, Stead, & Lancaster, 2012; Hughes, Stead, Hartmann-Boyce, Cahill, & Lancaster, 2014). Psychological and behavioural treatments such as counselling and contingency management are also found to be efficacious (Cahill, Harmann-Boyce, & Perera, 2015; Stead & Lancaster, 2009), though a combination of pharmacological and psychological/behavioural treatments is deemed to be more successful at increasing abstinence rates (Stead, Koilpillai, Fanshawe, & Lancaster, 2016; Stead, Koilpillai, & Lancaster, 2015). However, despite the positive impact of these treatments on smoking outcomes, there are limitations that may hinder usage and adherence. Pharmacological treatments can entail adverse side effects (Balmford, Borland, Hammond, & Cummings, 2011; Vogt, Hall, & Marteau, 2008), while both types of treatments
may not be financially accessible to all smokers. As such, the search for new and innovative treatments for smoking cessation must continue.

This thesis consists of two components. The first and primary aim of this thesis was to develop and pilot a smoking-cued response inhibition training task. Feasibility, acceptability, and preliminary effects on smoking outcome were also investigated to determine whether a full trial would be warranted. The second component of the thesis was to conduct a systematic review. It has been argued that in order for smoking cessation treatments to be successful, they need to specifically address impulsivity and, by their nature, reduce levels of impulsivity (e.g., Hershberger, Um, & Cyders, 2017). A first step in evaluating this hypothesis is to examine whether smoking cessation treatments result in a reduction in impulsivity following treatment completion and whether this reduction is related to outcome. The two components of this thesis were conducted in parallel and hence will be presented as two separate parts rather than as a sequential process of investigation.

Part 1: Development and Piloting of a Smoking Specific-Response Inhibition Intervention

An effective approach in other health behaviours is to target factors that play a significant role in maintaining behaviour and increase the risk of regressing back to former problematic habits (e.g., Jones et al., 2016; Sloan et al., 2017). In the case of smoking, one such important risk factor is impulsivity. Impulsivity is a multifaceted construct generally defined as rash action with limited forethought or deliberation (Dawe & Loxton, 2004). Impulsivity consists of both a trait level construct, measured by self-report questionnaires, and a state form, measured with behavioural tasks. Examples of such tasks are the Go/No-Go (GNG) task and Stop
Signal Task (SST) which focus on an individual’s difficulties with response inhibition, capturing reaction time and errors in response to a person’s ability to inhibit a prepotent response. This is considered an important aspect of understanding the underlying processes of addiction. Indeed, the dual process Reflective-Impulsive model posits that behaviour is driven by two parallel processes; an impulsive system that is rapid-acting and influenced by automatic appraisals and a reflective system that is slow-acting and requires cognitive control to make decisions (Strack & Deutsch, 2004). From the perspective of this model, it has been argued that targeting cognitive deficits such as inhibitory control could decrease substance use.

There is a substantial body of evidence to suggest smokers experience deficits in response inhibition, or difficulties in inhibiting, delaying or modifying a previously reinforced response (Gullo & Dawe, 2008). Results from a meta-analysis found that smokers exhibit significant deficits in response inhibition compared with non-smokers (Smith, Mattick, Jamadar, & Iredale, 2014). Furthermore, these deficits in response inhibition have been linked to higher rates of relapse (Doran, Spring, McChargue, Pergadia, & Richmond, 2004; Krishnan-Sarin et al., 2007; Luijten, Kleinjan, & Franken, 2016; Powell et al., 2010). Given this vulnerability, it is argued that targeting this deficit will assist smokers in quitting smoking.

Recent studies in the area of cognitive neuroscience indicate that response inhibition can be improved with cued training interventions. These training tasks have been modified from the GNG task and SST, which target divergent aspects of response inhibition and have differing theoretical underpinnings (Verbruggen & Logan, 2008). Studies have supported their efficacy in facilitating changes in
health behaviours such as alcohol consumption (e.g. Houben, Havermans, Nederkoorn, & Jansen, 2012; Jones & Field, 2013) and unhealthy eating behaviours (e.g. Adams, Lawrence, Verbruggen, & Chambers, 2017; Lawrence, O'Sullivan, et al., 2015; van Koningsbruggen, Veling, Stroebe, & Aarts, 2014). Three meta-analyses have suggested that response inhibition interventions yield small-medium effects, with the GNG task producing larger effect sizes than the SST (Allom et al., 2015; Jones et al., 2016; Turton et al., 2016). Interestingly, there is also evidence to suggest that the intervention is most beneficial for individuals who display poorer response inhibition at baseline (Houben, 2011). While most encompassed a single session of training in a controlled laboratory setting, four studies investigated multiple sessions of food-related training in an online format (Allom & Mullan, 2015; Forman et al., 2016; Lawrence, O'Sullivan, et al., 2015; Veling et al., 2014). Two of these studies reported significant impact on snacking frequency and weight loss, with one reporting that this remained significant at six-month follow-up (Lawrence, O'Sullivan, et al., 2015).

Given that these significant results were found in non-clinical samples, it is possible that these interventions would be even more effective in smokers who are dependent on tobacco and receive frequent reinforcement of their behaviour in the form of multiple smoking “sessions” each day. Furthermore, the training may be particularly effective for more severely dependent smokers who have the most difficulty remaining abstinence given that the training has previously been found to be most beneficial for individuals who display high levels of the targeted behaviour (Veling, Aarts, & Stroebe, 2013b). While a recent study (Adams, Mokrysz, Attwood, & Munafò, 2017) published following the completion of this
thesis reported nonsignificant effects of response inhibition training on smoking behaviours, the intervention was a single session administered in a laboratory setting to non-treatment seeking participants. As such, this thesis contributes unique evidence in the form of examining multiple sessions of web-based response inhibition training that translates this treatment approach to a real-world setting where it would be an accessible and cost-effective treatment option.

**Part 2: Systematic Review:**

The second component of this thesis investigated the association between the broader multi-faceted construct of impulsivity and smoking cessation treatments. Given that impulsivity has been strongly linked with smoking (e.g. Bloom, Matsko, & Cimino, 2014; Chase & Hogarth, 2011; Doran et al., 2013; López-Torrecillas, Perales, Nieto-Ruiz, & Verdejo-García, A., 2014), it is argued that levels of impulsivity would decrease following treatments aimed to reduce smoking. It would also be logical to posit that decreased impulsivity would further be significantly associated with smoking outcomes following treatment. However, these questions have yet to be systematically investigated.

**Aims of the Thesis**

As such, this thesis has two primary aims:

1) Develop and pilot a response inhibition training intervention targeting smoking cessation

2) Investigate whether levels of impulsivity decrease following psychosocial interventions targeting smoking and whether such changes are associated with smoking cessation outcomes.
Structure of the Thesis

The first aim is addressed in Chapters One-Seven. Chapter One first provides an overview of the prevalence of smoking, in addition to current available treatments for smoking cessation. Chapter Two examines the relationship between impulsivity and smoking, with a focus on deficits in response inhibition. In Chapter Three, an overview of the interventions targeting response inhibition is provided, followed by a review of the evidence base of these interventions across health behaviours. Chapter Four presents the overarching rationale and aims of the thesis. Chapter Five details the development of the response inhibition training program, outlining considerations in the development of the intervention task and protocol. Chapter Six presents an empirical study examining the validation of pictorial cues included in the training task and another response inhibition measure. Chapter Seven outlines the two pilot studies conducted to examine the feasibility and acceptability of the smoking-cued response inhibition training. Following this, the second aim of the thesis is addressed in Chapter Eight, which presents a systematic review investigating the relationship between the multi-faceted construct of impulsivity and smoking cessation treatments.

Finally, Chapter Nine integrates the findings of this thesis in a general discussion section. It summarises the results of the studies, and discusses the future directions of the research and clinical implications of the findings. Limitations are also addressed before presenting the concluding remarks.
Chapter One: Smoking: Prevalence and Current Treatments

1.1 Prevalence of Tobacco Smoking

Tobacco smoking is a well-established risk factor for numerous diseases and premature death. It has been linked to diseases such as cancer, cardiovascular diseases, chronic obstructive pulmonary disease, tuberculosis, stroke, and pneumonia (Australian Institute of Health and Welfare [AIHW], 2017; World Health Organization [WHO], 2012; Yanbaeva, Dentener, Creutzberg, Wesseling, & Wouters, 2007). One in 10 deaths in the world is attributable to tobacco use (WHO, 2017). The effects of second hand smoke are also a concern, particularly for foetuses, newborns, and children who may be exposed to tobacco smoke (WHO, 2017) as passive smoking is associated with an increased risk of asthma, chest infections, and sudden infant death syndrome (Dunn et al., 2008). Taken together, the substantial health risks of using tobacco are a great burden on the medical system.

Furthermore, tobacco use is estimated to cost the global economy over US$1 trillion each year due to health expenditures and lost productivity (U.S. National Cancer Institute and WHO, 2016). Based on the Australian population in 2008, Magnus et al. (2011) estimated that a reduction in smoking prevalence of 8% would result in 2.2 million fewer lost working days, 158,000 fewer cases of disease, 5,000 fewer deaths, and 3,000 fewer early retirements. Considerable economic and health benefits can thus be yielded by continuing to develop strategies and programs for prevention, reduction, and cessation of smoking.

In recognition of this, strategies and regulations have been introduced by the government and health organisations to reduce smoking prevalence, leading to a decline in tobacco use in recent decades (WHO, 2017). The global rate of
smoking prevalence in individuals over 15 years old has declined from 2007 to 2015, decreasing from 23.5% to 20.7%. However, this decline has not been uniform across countries, with the decline slower in low and middle-income countries. Furthermore, reports indicate that despite most current smokers wanting to quit, they find it difficult to reduce or cease smoking (Centers for Disease Control and Prevention, 2017). In 2016, a majority of Australian smokers attempted to modify their smoking behaviour, primarily due to reasons of costs and health concerns (AIHW, 2017). Compared with 2013, smokers were significantly less successful at quitting smoking for at least a month, with only 1 in 5 being successful. Heavy smokers who smoked more than 20 cigarettes a day were more likely to make attempted changes to their smoking behaviour, but were also more likely to be unsuccessful. As such, there are a proportion of heavily dependent smokers who possess the motivation to change but have difficulty in effectively actioning this change and maintaining abstinence.

1.2 Current Treatments for Smoking Cessation

To address this problematic substance use, a range of smoking cessation interventions have been investigated in a number of Cochrane reviews (Cahill, Stevens, Perera, & Lancaster, 2013). Pharmacological treatments are frequently used to aid in abstinence due to their efficacy and ease of use (Cahill, Lindson-Hawley, Thomas, Fanshawe, & Lancaster, 2016; Cahill, Stead, & Lancaster, 2012; Hughes, Stead, Hartmann-Boyce, Cahill, & Lancaster, 2014), although psychological and behavioural treatments have also yielded effective results (Cahill, Harmann-Boyce, & Perera, 2015; Stead & Lancaster, 2009). These treatments aim to assist smokers in coping better with difficulties faced during smoking cessation in order to encourage maintenance of abstinence. Studies have
also found favourable outcomes when investigating the efficacy of combining pharmacological and psychological/behavioural treatments (Stead, Koilpillai, Fanshawe, & Lancaster, 2016; Stead, Koilpillai, & Lancaster, 2015).

1.2.1 Pharmacological treatments. Pharmacological treatments are often used in self-quit attempts to assist with smoking cessation by targeting withdrawal symptoms. Nicotine replacement therapy (NRT; e.g. nicotine patches, nicotine gum), antidepressants (e.g. bupropion, nortriptyline), and nicotine receptor partial agonists (e.g. varenicline, cytisine) are considered efficacious, first-line medications that can aid in abstinence and relapse prevention in Australia, USA, and the European Union (Cahill et al., 2013; Ellerman, Ford, & Stillman, 2012; Taylor, Leonardi-Bee, Agboola, McNeill, & Coleman, 2011). This is supported by a Cochrane review of 12 systematic reviews investigating a total of 267 studies on pharmacological interventions for smoking cessation (Cahill et al., 2013).

Results indicated that NRT, bupropion, and varenicline improved the chances of smokers successfully quitting compared to placebo, with risk ratios ranging from 1.82-2.88. These treatments are discussed briefly in the sections below.

Nicotine Replacement Therapy. NRT is commonly used to target psychological and physiological withdrawal symptoms that typically occur during a quit attempt by partially replacing nicotine in the blood (Polosa & Benowitz, 2011). These are available in different forms in varying dosages: transdermal patches, chewing gum, lozenges, inhalers, and mouth sprays (Mendelsohn, 2013).

Overall, a Cochrane review of 117 trials deemed NRT to increase rates of successful quit attempts compared with placebo or other control conditions by 50-70%, yielding a risk ratio 1.60 (Stead et al., 2012). Examining the pooled risk ratios for each type of NRT, nicotine gum yielded a risk ratio of 1.49 (n = 55),
oral tablets/lozenges 1.95 \( (n = 6) \), nicotine nasal spray 2.02 \( (n = 4) \), nicotine
inhaler 1.90 \( (n = 4) \), oral spray 2.48 \( (n = 1) \), and nicotine patch 1.64 \( (n = 43) \).
Effects were independent of treatment duration, treatment setting, and intensity of
any additional support provided.

Additionally, there was evidence to suggest that a combination of nicotine
patches and a more rapid form of NRT is more effective than a single form of
NRT (risk ratio 1.34). While the mechanisms are not clearly understood, the effect
is thought to be due to a greater overall dosage of nicotine, and the combination of
a slow delivery system (patches) and faster nicotine consumption for sudden and
intense cravings (lozenges; Henningfield, Fant, Buchhalter, & Stitzer, 2005).

**Antidepressants.** Antidepressants have been used as an alternative to
nicotine-based medications. Bupropion is the most commonly used antidepressant
for smoking cessation and is thought to act as an antagonist by blocking nicotinic
acetylcholinergic receptors in the brain. Nortriptyline, a tricyclic antidepressant, is
another medication used in smoking cessation that targets withdrawal symptoms.
A Cochrane review (Hughes, Stead, et al., 2014) demonstrated that there was high
quality evidence from 44 trials to support the efficacy of bupropion in
significantly increasing the likelihood of a successful quit attempt (risk ratio
1.62); contrarily, there was only moderate quality evidence from six trials for
nortriptyline suggesting that it significantly increased long-term cessation (risk
ratio 2.03). Selective serotonin reuptake inhibitors have also been investigated,
however the review yielded nonsignificant findings for effects on smoking
cessation as a sole treatment or in conjunction with NRT.

**Nicotine receptor partial agonists.** Nicotine receptor partial agonists such
as varenicline and cytisine can aid in smoking cessation by reducing withdrawal
symptoms and the rewarding effects of smoking (Brandon et al., 2011; Radchenko, Dravolina, & Bespalov, 2015). A Cochrane review indicated that in comparison to placebo, varenicline was efficacious in aiding sustained or continuous abstinence for six months or longer \(n = 27\), yielding a risk ratio of 2.24 (Cahill, Lindson-Hawley, Thomas, Fanshawe, & Lancaster, 2016). Furthermore, eight studies suggested that it was more effective than NRT at 24 weeks or longer (risk ratio 1.25), and five suggested that it was more effective than bupropion at six months (risk ratio 1.39). The review also found cytisine to be a more effective treatment than placebo in two trials (risk ratio 3.98) but absolute quit rates were modest and the studies were of low quality.

**1.2.2 Psychological and behavioural treatments.** Smoking cessation can also be aided by treatments that use psychological or behavioural approaches. A Cochrane review examining individual, face-to-face behavioural counselling in smoking cessation reported that it was more effective than control conditions comprised of minimal contact, such as waitlist or self-help (Lancaster & Stead, 2017). Pooling 33 studies, individual counselling was found to increase rates of cessation by 40%-80% after a minimum of six months treatment. That is, out of 100 smokers, between 10-12 individuals who receive counselling would be expected to stay abstinent for at least six months if 7 in 100 smokers were abstinent following brief support obtained from control groups. For studies where all participants also received a pharmacological treatment, 11-16 in 100 smokers who received counselling would be abstinent compared with 11 in 100 who received brief support. There was also evidence to suggest that more intensive counselling was more beneficial than brief counselling, yielding a risk ratio of 1.29.
Another commonly examined intervention for smoking cessation is the behavioural intervention contingency management, which uses non-drug rewards to reinforce abstinence (Krishnan-Sarin et al., 2013; Morean et al., 2015). Twenty-one randomised controlled trials in a Cochrane review suggested that it increased rates of abstinence across a variation of populations. Results suggested that contingency management was effective during the intervention period, though there were only three studies demonstrating that contingency management groups had a significantly higher rate of quitting compared with control groups at six-month follow-up or longer (Cahill, Harmann-Boyce, & Perera, 2015). The review also identified an additional nine studies examining contingency management in pregnant smokers, with eight showing that those receiving contingency management were more likely to quit than control groups at up to 24-month post-partum (odds ratio 3.60). Despite favourable evidence supporting this type of intervention, there have been concerns raised relating to its cost-efficiency and long-term effectiveness.

Group therapy targeting behavioural or psychological aspects of smoking cessation has also been investigated in a Cochrane review of 53 studies (Stead & Lancaster, 2009). It was found to increase cessation rates compared with self-help and less intensive interventions, yielding a risk ratio of 1.98. However, there was limited evidence to suggest that it was significantly more effective than individual counselling or yielded additional benefits when adjunct to treatments such as NRT or advice from a health practitioner.

1.2.3 Combined treatments. A combination of pharmacological and behavioural supports has been proposed to be more effective for smoking cessation than either types of treatment alone. A Cochrane review of 47 trials
suggested that providing face-to-face or telephone behavioural support for smokers using pharmacotherapy increased the chances of abstinence compared with smokers who only received pharmacotherapy, yielding a small but significant effect with a risk ratio of 1.17 (Stead, Koilpillai, & Lancaster, 2015). Another Cochrane review of 53 studies compared a combination of pharmacotherapy and behavioural interventions with usual care or comparatively less behavioural support (Stead et al., 2016). Excluding one study that examined an intensive intervention that resulted in a significant, large effect (risk ratio 3.88), results from the remaining studies suggested that the combined approach significantly increased the chances of successful quitting (risk ratio 1.83). However, there was no evidence to suggest that more intensive behavioural support resulted in larger treatment effects.

1.2.4 Limitations. Despite strong evidence of efficacy, there are limitations to current pharmacological and behavioural treatments that may have implications for their usage. A primary concern of pharmacological treatments is potential adverse side effects, such as hiccoughs, chest pains, dry mouth, insomnia, and nausea (Cahill et al., 2013). Research interviews and surveys with smokers indicate that these worries negatively impact the extent that they use and adhere to the treatment (Balmford, Borland, Hammond, & Cummings, 2011; Morphett, Partridge, Gartner, Carter, & Hall, 2015; Vogt, Hall, & Marteau, 2008).

Furthermore, while pharmacotherapy, psychotherapy, and behavioural therapies yield efficacious results, most smokers do not seek formal treatment to reduce smoking (Centers for Disease Control and Prevention, 2017). The long-term costs of these treatments in a real-world setting may be a deterrent to engagement, particularly given that a majority of smokers cite financial costs as
the main reason for initiating quit attempts or reductions in smoking (AIHW, 2017). Additionally, relapse rates remain high following treatment (Hughes, Solomon, et al., 2014) and many smokers continue to struggle to maintain long-term abstinence (AIHW, 2017), with a majority of smokers relapsing within 5-10 days of a cessation attempt (Hughes, Keely, & Naud, 2004; Japuntich, Piper, Leventhal, Bolt, & Baker, 2011; Piasecki, 2006). In order to address this, there needs to be continued efforts to develop effective treatment options to expand the scope of interventions for smokers who may wish to explore alternative treatments beyond those currently available.

1.3 Chapter Summary

Despite tobacco smoking being identified as one of the leading causes of preventable diseases and death, many smokers have difficulty reducing or quitting smoking. Both pharmacotherapies and psychological/behavioural therapies are often used to assist in abstinence, with a combination of these therapies thought to further increase the likelihood of abstinence. However, these interventions have their limitations, such as cost-efficiency and pharmaceutical side effects. Furthermore, despite decades of research in intervention development, relapse rates following treatment remain high. Hence, the search for additional effective treatment approaches remains a high priority.

In considering novel avenues of interventions, risk factors relating to smoking maintenance and relapse could be incorporated into the formulation of treatments to aid in obtaining abstinence. One such factor identified is response inhibition, a facet of impulsivity that relates to deficits in the ability to inhibit, delay, or modify a previously reinforced response (Gullo & Dawe, 2008). Studies have found it to be consistently linked to smoking (Smith, Mattick, Jamadar, &
Iredale, 2014) in addition to being a predictor of relapse (Powell et al., 2010). As such, response inhibition is a highly relevant treatment target in smoking cessation interventions. This evidence will be further reviewed in the following chapter.
Chapter Two: Impulsivity and Smoking

As argued in the previous chapter, the persistence of smoking as a pressing health and economic issue requires the continued development of effective smoking cessation treatments. One approach is through targeting impulsivity, a broad, multi-faceted construct (Berg, Latzman, Bliwise, & Lilienfeld, 2015; Dalley, Everitt, & Robbins, 2011; Dawe & Loxton, 2004). It encapsulates traits such as action with limited forethought and impaired decision making, particularly in the presence of rewarding stimuli (Dalley et al., 2011; Dawe & Loxton, 2004; de Wit, 2009). A large body of evidence indicates that it is associated with various stages of smoking (Bloom, Matsko, & Cimino, 2014), including smoking initiation (Doran et al., 2013; Kvaavik & Rise, 2012), dependence (Chase & Hogarth, 2011; Ryan, MacKillop, & Carpenter, 2013), maintenance (VanderVeen, Cohen, Cukrowicz, & Trotter, 2008), and relapse (Krishnan-Sarin et al., 2007; López-Torrecillas et al., 2014; López-Torrecillas, Perales, Nieto-Ruiz, & Verdejo-García, 2014; Sheffer et al., 2012; Wegmann, Bühler, Strunk, Lang, & Nowak, 2012). These findings have been reported across different facets of impulsivity using both self-report and behavioural measures (López-Torrecillas, Nieto-Ruiz, et al., 2014; Sheffer et al., 2012; Wegmann et al., 2012). Self-report measures tend to assess more enduring, trait forms of impulsivity, with common measures including the Barratt Impulsiveness Scale (BIS-11; Patton, Stanford, & Barratt, 1995), the Behavioural Inhibition/Activation System (BIS/BAS; Carver & White, 1994), and the Eysenck Impulsiveness Questionnaire (I7; Eysenck, Pearson, Easting, & Allsopp, 1985). In contrast, behavioural measures assess transient, state forms of impulsivity (Meda et al., 2009). These include the Go/No-Go Task (GNG task; Miller, Schäffer, &
Hackley, 1991), Stop Signal Task (SST; Logan, 1994), and Delay Discounting Task (DDT; Rachlin, Raineri, & Cross, 1991).

A facet of impulsivity that has been consistently related to smoking is response inhibition, which, as described previously, refers to difficulties in impulse control where there is an inability to inhibit, delay, or modify a previously reinforced response (Gullo & Dawe, 2008). Evidence suggests that smokers experience significant response inhibition deficits which increase the risk of relapse, indicating that it would be a viable target of smoking cessation treatment. Of note, throughout this thesis, the terms “response inhibition” or “inhibitory control” will be used in relation to difficulties with impulse control while the term “impulsivity” will refer to the broader, heterogeneous construct that includes all facets of impulsivity, not only response inhibition.

This chapter provides a brief overview of the conceptualisation of impulsivity in substance use within a dual-process model. It then reviews the literature examining the significant role response inhibition plays in smoking.

2.1 Impulsivity: The Reflective-Impulsive Model

Impulsivity in addiction has been conceptualised within dual-process models that propose that behaviour is driven by two different but parallel processes (Borland, 2014; Hofmann, Friese, & Wiers, 2008; Stacy & Wiers, 2010; Strack & Deutsch, 2004; Wiers et al., 2007). An example of such is the Reflective-Impulsive model (Strack & Deutsch, 2004). This argues that the “impulsive system” is a fast-acting process that automatically evaluates stimuli and is influenced by affect and motivation. Conversely, the “reflective system” is characterised as a slow-acting process that uses higher-order control to make decisions based on values and facts.
The impulsive and reflective systems can often be in conflict in relation to harmful behaviour such as substance dependence (Hofmann et al., 2008; Wiers & Gladwin, 2017). Poor reflective considerations are exhibited through reduced inhibitory control in response to cues related to their addiction (Deutsch & Strack, 2006). When the reflective system is weak, the behaviour of an individual is more likely to be driven by their impulsive system, especially when there is a strong motivational component (Hofmann, Friese, & Strack, 2009). This competition between the two systems has been proposed to be determined by levels of inhibitory control whereby an inability to inhibit impulses results in the manifestation of a prepotent response (Forman et al., 2016). As such, it has been argued that decreased substance use could be facilitated by improving self-control through training response inhibition (Friese, Hofmann, & Wiers, 2011; Hagger, 2017). Prior to reviewing this treatment approach, the relationship between smoking and response inhibition is first examined to further understand the extent of this deficit in smokers.

2.2 Smoking and Response Inhibition

There is a body of evidence highlighting that smokers experience considerable deficits in response inhibition. This has primarily been assessed using the GNG and SST, but can also include the use of other behavioural measures such as the Stroop test, the antisaccade task, and the Continuous Performance Task (CPT; Dougherty et al., 1999). A meta-analysis by Smith, Mattick, et al. (2014) found that smokers exhibited significantly poorer response inhibition compared with non-smokers. Six studies in the review examining GNG tasks with frequent “go” trials and rare “no-go” trials indicated that there was an overall small but significant effect size (Hedges $g = 0.25$) between the
performance of smokers and controls, specifically in relation to commission errors (i.e. failure to inhibit a response to a “no-go” cue). The lack of difference in omission errors (i.e. failure to respond to a “go” cue) and reaction time on “go” trials provide evidence that the poorer performance was due to deficits in response inhibition as opposed to a speed-accuracy trade-off. Conversely, the effect of the SST as reported by five studies was nonsignificant, possibly due to the different inhibitory control mechanisms being measured by the two tasks whereby GNG measures automatic, bottom-up response inhibition and SST captures top-down inhibitory control. Taken together, results suggest that reduction of smoking and abstinence may be aided by targeting deficits in response inhibition, particularly in relation to automatic bottom-up responding.

Furthermore, studies have found compromised response inhibition in smokers to be linked to a number of smoking-related variables including cessation outcomes. A lower capacity to inhibit responses has been correlated with trait impulsivity, greater nicotine dependence, and a higher number of cigarettes smoked daily (Billieux et al., 2010; Flaudias et al., 2016; Pettiford et al., 2007; Spinella, 2002). This effect was evident after controlling for individual differences in age, craving, and processing speed in one study (Billieux et al., 2010). Deficits in inhibitory control have also been identified as a predictor of relapse following smoking cessation. A study by Powell, Dawkins, West, Powell, and Pickering (2010) found that in an unaided cessation attempt, relapse up to three months following the date of cessation could be predicted by levels of response inhibition. This was measured using the CPT following overnight abstinence prior to the cessation attempt. This positive correlation between poor response inhibition on the CPT and relapse has also been observed in adolescents, yielding a small effect
size of $d = 0.40$ (Krishnan-Sarin et al., 2007). Indeed, this relationship remained significant even after variables of positive affect, negative affect, and craving were eliminated as mediating factors (Doran et al., 2004). Further evidence includes a study demonstrating that poorer inhibitory control on the GNG, as reflected by smaller event-related potentials, is associated with increased risk of relapse at 12 weeks following a quit attempt (Luijten, Kleinjan, & Franken, 2016). Thus, response inhibition deficits are a highly relevant characteristic of smokers and plays a significant role in relapse following smoking cessation.

2.3 Chapter Summary

According to the Reflective-Impulsive model of impulsivity, response inhibition deficits contribute to the maintenance of substance use. This is supported by significant evidence suggesting that smokers experience response inhibition deficits, which in turn predict relapse in those who attempt to quit. As such, it is argued that targeting response inhibition in smoking cessation interventions will assist in achieving abstinence. Such interventions have predominantly been evaluated in other health behaviours such as overeating and alcohol consumption (Jones et al., 2016), although one recent study also examined the effect of training in smokers. This collective evidence will be reviewed in the following chapter.
Chapter Three: Response Inhibition Training Interventions

In determining the most optimal approach of targeting response inhibition in smokers, it is important to first review the breadth of literature examining such interventions. Response inhibition interventions take the form of training paradigms that have primarily been investigated in the unhealthy behaviours of excessive eating and alcohol consumption. The most predominantly used tasks are the Go/No-Go (GNG) task and the Stop Signal Task (SST) (Allom, Mullan, & Hagger, 2015). These tasks are modified to incorporate images related to the targeted problem behaviour as evidence suggests that stimulus-specific training is necessary to induce changes in behaviour given that general inhibition training is ineffective (Lawrence, Verbruggen, Morrison, Adams, & Chambers, 2015).

Results of meta-analyses have indicated that response inhibition training is efficacious in inducing significant changes in eating and alcohol consumption (Allom et al., 2015; Jones et al., 2016; Turton, Bruidegom, Cardi, Hirsch, & Treasure, 2016). These behaviours, when at problematic levels, have also been associated with poor inhibitory control (Guerrieri et al., 2007; Jasinska et al., 2012; Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016; Smith, Mattick, et al., 2014). In the past year, there have also been studies published examining response inhibition training in other types of substances, including one targeting smoking (Adams, Mokrysz, Attwood, & Munafò, 2017). This chapter provides an overview of these tasks and reviews the research evidence of training across health behaviours.
3.1 General Overview of Response Inhibition Interventions

3.1.1 Go/No-Go Task

The GNG task uses images of the target stimuli (i.e. cigarettes) and images of neutral or alternative stimuli, with one type of picture being displayed and paired with either a “go” cue or a “no-go” cue during each trial (Houben, Havermans, et al., 2012). While the representation of these cues can vary between different versions of the task, Figure 3.1 depicts one version of the task used by Lawrence, O’Sullivan, et al. (2015) where stimuli were displayed within a rectangle with a black border. This was a “go” cue and participants were required to use designated letters on the keyboard to indicate whether the stimulus was left or right of the centre of the rectangle. However, when the border of the rectangle was bolded, this was a “no-go” cue and they were not to respond. “No-go” cues were consistently paired with images of the target stimuli to encourage response inhibition. The stimuli appeared on the screen for 1250ms followed by a 1250ms inter-stimulus interval.

*Figure 3.1. Go/No-Go task used to modify eating behaviours in Lawrence, O’Sullivan, et al. (2015).*
The variables of interest in the GNG task are commission errors, omission errors, and reaction times. Deficits in response inhibition are most apparent when there is a high rate of commission errors, the same rate of omission errors, and a slow reaction time (Smith, Mattick, et al., 2014). Conversely, high rates of omission errors suggest difficulties with sustained attention; although in conjunction with long reaction times, this may also suggest a slowing of responses to compensate for perceived response inhibition deficits (Wright, Lipszyc, Dupuis, Thayapararajah, & Schachar, 2014).

**Theoretical basis.** There have been a number of theories proposed to explain the underlying mechanisms of the GNG task (Chen, Veling, Dijksterhuis, & Holland, 2016; Veling, Lawrence, Chen, van Koningsbruggen, & Holland, 2017). The automatic inhibition hypothesis (Verbruggen, Best, Bowditch, Stevens, & McLaren, 2014) proposes that consistent association of stimuli with “no-go” cues will result in automatic response inhibition due to the learned stimulus-stop associations (Bowditch, Verbruggen, & McLaren, 2016). This theory of bottom-up learning is supported by evidence from studies that demonstrated slowed reaction times on “go” trials that present previously trained “no-go” stimuli (Veling, Aarts, & Papes, 2011; Verbruggen et al., 2014).

Conversely, it has been proposed that the training may result in increased top-down inhibitory control. Veling et al (2017) argues that this hypothesis is unlikely given 1) the simplicity of the GNG task would prevent training of response inhibition and 2) the SST, which is a task considered to train top-down control, is less effective than the GNG (Allom et al., 2015; Jones et al., 2016).
Therefore, improvement in top-down inhibition seems unlikely to be the underlying mechanism of effective inhibition training.

Another theory that has been presented is the explanation of devaluation which posits that training response inhibition can affect future behaviour through modifying the evaluation of stimuli (Chen et al., 2016). More specifically, the Behaviour Stimulus Interaction theory has been proposed by Veling, Holland and van Knippenberg (2008) to explain the underlying mechanisms of devaluation. This is based on the tendency of automatic approach behaviour to be evoked by the reward value of positive stimuli. For example, the perceived benefits of smoking, such as increased alertness and decreased withdrawal symptoms, may lead smokers to reflexively smoke a cigarette with minimal forethought. However, the response is ultimately dependent on situational constraints to determine whether engaging in the behaviour would be appropriate. Through pairing stimuli with cues such as “no-go” cues to signal that approach is unwanted, the individual experiences a conflict regarding the behavioural response they should engage in. Consequently, they experience a devaluation of the stimuli to resolve this conflict, specifically through associating negative affect to the stimuli to deem it less desirable. This subsequently minimises the likelihood of approach behaviours towards these stimuli in the future. Of note, this theory has been found to only apply to positively regarded stimuli, as the evaluation of neutral and negative stimuli are unaffected by training (Chen, Veling, Dijksterhuis, & Holland, 2016; Veling et al., 2008). This is thought to be explained by neutral stimuli not requiring inhibition as it does not initially elicit approach behaviour and negative stimuli not responding to devaluation as it may already initiate inhibition.
The general theory of devaluation is supported by a series of experiments conducted in food-cued GNG training to examine the task components of the “no-go” cue and not responding (Chen et al., 2016). The study demonstrated consistent devaluation of “no-go” stimuli compared with “go” stimuli and untrained stimuli (i.e. stimuli not included in the task). Additionally, results suggested that the devaluation of “no-go” stimuli resulted from the act of not responding as opposed to a learned association with the “no-go” cue or due to the evaluative negative connotation of not responding.

Furthermore, a review of theories in relation to the mechanisms of food-cued GNG training suggested that current evidence best supports the theory of devaluation (Veling et al., 2017). However, it was also acknowledged that this was likely due to devaluation being the most commonly investigated mechanism across studies. Interestingly, a meta-analysis by Jones et al. (2016) examining GNG training found no effect of response inhibition training on stimulus devaluation. However, as a majority of studies analysed used measures of implicit evaluations (Houben, Havermans, et al., 2012; Houben, Nederkoorn, Wiers, & Jansen, 2011), measures of explicit evaluation may yield different findings given the weak relationship between implicit and explicit evaluation measures (Friese, Hofmann, & Wänke, 2008).

Of note, the mechanisms described by these above theories are not mutually exclusive (Veling et al., 2017). They may operate at different stages of the training period or interact to yield the observed treatment effects. Further research is required to advance the current knowledge base of these mechanisms to delineate their mediating effects on training outcomes.
3.1.2 Stop Signal Task

The SST also uses images of target stimuli and neutral/alternative stimuli, and consists of “go” and “stop” trials. The modifications and specific instructions vary across studies, but a stimulus will typically appear on the screen during “go” trials, and participants are required to categorise an aspect of the image as quickly as possible. Conversely, participants must withhold their response during “stop” trials where an auditory or visual stop signal occurs after the presentation of a stimulus. Unlike the GNG task, the SST requires rapid responding to both target and neutral stimuli, with stop signals presented only on a proportion of all trials (Jones & Field, 2013). A common proportion of total “stop” trials is 25% of trials (e.g. Adams, Lawrence, et al., 2017), although a proportion of 50% has also been used (e.g. Jones & Field, 2013). The mapping of stop signals to target stimuli may vary in the proportion of target stimuli trials on which it appears (e.g. 50% in Forman et al., 2016, 87.5% in Lawrence, Verbruggen, et al., 2015).

An example use of SST training is illustrated in a study by Jones and Field (2013) targeting alcohol consumption. This required participants to indicate whether images were alcohol-related or neutral by pressing corresponding letters on the keyboard (see Figure 3.2). Of all trials, 50% were “stop” trials where an auditory stop signal would sound after the presentation of a stimulus and participants were required to inhibit their response. These “stop” trials would occur for both alcohol-related and neutral stimuli, and not all alcohol-related stimuli were allocated as “stop” trials. Stop signal tones occurred at four latencies following the presentation of the picture – 50ms, 150ms, 250ms, and 350ms. If participants responded within 2000ms of the auditory stop signal being presented,
this was regarded was an inhibition error. These time specifications can vary across different versions of the task.

Figure 3.2. Stop Signal Task used to train alcohol consumption in a study by Jones and Field (2013).

The primary outcome variable, the stop signal reaction time (SSRT), is calculated based on different delays to the stop signal in the task (Logan, 1994). Longer SSRT reflect deficits in response inhibition (Lijffijt, Kenemans, Verbaten, & Engeland, 2005).

**Theoretical basis.** General performance on the task is most commonly conceptualised using Logan and Cowan’s (1984) “horse-race model”. This describes a “race” between two independent processes; the go process, initiated by the go stimulus (i.e. images of the target behaviour), and the stop process, initiated by the stop signal. Response inhibition is successful when the stop process finishes before the go process, while unsuccessful inhibition results from the go
process finishing before the stop process. Further research has proposed that the
go and stop processes are interactive whereby the presentation of the stop signal
inhibits the go process (Boucher, Palmeri, Logan, & Schall, 2007). While there
has yet to be research on this model in relation to response inhibition training, it
has been suggested that the action cancellation component of the SST, or the
process by which the speed of the stop process is increased (Liddle et al., 2009),
may serve as an extra burden that interferes with the effectiveness of training

In comparison to the GNG task, there has been less empirical research
regarding how the SST evokes behavioural change as an intervention. Response
inhibition towards target stimuli is not consistently required in the SST and as
such, it is unlikely that automatic inhibition would develop as with the GNG task,
where consistent inhibition towards target stimuli results in automatic behavioural
responses. In contrast, controlled executive function is required during the SST to
correctly inhibit responses given the infrequency of stop signals and the need to
cancel an initiated response following a stop signal.

There have been two possible mechanisms proposed to account for the
training effects of the SST (Houben, 2011). Firstly, top-down learning of response
inhibition may occur as repeatedly inhibiting responses to the target stimuli may
result in a learned association between the stimuli and response inhibition. This
learned goal of ceasing behaviour towards the stimuli may then be subsequently
evaluated the effect of food-cued SST training on inhibition control. The Stroop
task (Friedman & Miyake, 2004) was administered to determine whether the
effects of training induced generalizable changes in inhibitory control. While
performance on the Stroop task improved following SST training, this did not differ from the general inhibition training condition nor were the effects maintained at one-week follow-up. Importantly, the SST training itself did not result in significant changes in eating behaviours.

A second hypothesis is that the Behaviour Stimulus Interaction theory could also be applied to the SST, where creating a conflict through requiring response inhibition leads to devaluation of the target stimuli. However, only one study (Adams, Lawrence, et al., 2017) has investigated this using a measure of implicit association and yielded nonsignificant results. Further research is thus required to better understand the mechanisms of the SST as a training task.

3.1.3 Comparison of tasks

The GNG task and SST target different aspects of response inhibition despite being generally regarded as equivalent measures that yield similar findings when assessing inhibitory control abilities (Jones & Field, 2013; Smith, Mattick, et al., 2014). This is supported by findings that the tasks activate common inhibitory regions in brain, but also engage distinct regions across neurocognitive networks (Rubia, Smith, Taylor, & Brammer, 2007; Swick, Ashley, & Turken, 2011; Zheng, Oka, Bokura, & Yamaguchi, 2008).

The GNG task is thought to utilise the automatic, bottom-up processes of inhibition that are initiated by stimuli, given that the task pairs the “no-go” cue with the target stimuli (Jones et al., 2014; Wright et al., 2014). In contrast, the SST is regarded as targeting top-down processes, with the signal for inhibition occurring after an initiated response (Verbruggen & Logan, 2008). It is purported to initiate “action cancellation” as opposed to the “action restraint” required by the GNG task (Eagle, Bari, & Robbins, 2008; Schachar et al., 2007). Given this
difference, SST is thought to demand greater response inhibition and is also regarded as more theoretically developed (Nigg, 2000). However, the GNG task has been suggested to be particularly beneficial for highly automatized behaviour such as snacking or substance use, yielding larger effect sizes when used as a training paradigm compared with SST (Allom et al., 2015; Jones et al., 2016; Marteau, Hollands, & Fletcher, 2012; Spierer, Chavan, & Manuel, 2013; Turton et al., 2016).

3.1.4 Summary

Modification of the GNG task and the SST has enabled their use as interventions to target behaviours regarded as problematic. While both are purported to target response inhibition, their differing underlying mechanisms may have implications for the effectiveness of the training.

3.2 Efficacy of Response Inhibition Interventions in Health Behaviours

The efficacy of response inhibition training has primarily been examined in eating behaviours and alcohol consumption. However, there has also been growing interest in the investigation of training interventions in other substance use populations, with one recent paper published in smokers (Adams, Mokrysz, et al., 2017). This section provides an overview of the evidence base for the training across health behaviours.

For GNG tasks, studies generally allocated participants to two groups; “no-go” where they were required to consistently inhibit their responses to the target stimuli, or “go” where they were required to consistently respond to the target stimuli. Some investigations used a control group where participants were required to inhibit their responses to the target stimuli 50% of the time (e.g.
Houben & Jansen, 2011). Alternatively, other control groups completed training where only neutral stimuli are used (e.g. Lawrence, O’Sullivan, et al., 2015).

In relation to SST training, intervention conditions where stop signals were primarily mapped onto target stimuli were compared to a range of comparison conditions that varied across studies. These included pressing the key twice in response to stop signals (e.g. Adams, Lawrence, et al., 2017), primarily mapping stop signals onto neutral/alternative stimuli (e.g. Jones & Field, 2013), and presenting stop signals across target and neutral/alternative stimuli equally (e.g. Allom & Mullan, 2015).

**3.2.1 Meta-analyses**

Two meta-analyses have investigated the efficacy of training response inhibition in reducing alcohol consumption and eating behaviours (Allom et al., 2015; Jones et al., 2016) and a third in food response inhibition training alone (Turton et al., 2016). The two former studies reported an overall small effect size, while the meta-analysis examining only food response inhibition training found a moderate effect size. Allom et al. (2015) and Jones et al. (2016) reported no difference in training effects when comparing alcohol consumption and eating behaviours, suggesting that there is a relatively homogenous effect of training response inhibition in promoting avoidance of unhealthy stimuli. All three meta-analyses reported that larger effect sizes were observed with GNG training than SST training, congruent with studies by Adams, Lawrence, et al. (2017) and Smith, Dash, Johnstone, Houben, and Field (2017) that directly compared the effects of the two tasks. Jones et al. (2016) further suggested that effects of response inhibition training were predicted by the proportion of successful inhibitions to target stimuli as opposed to the absolute number of inhibition trials.
This may thus account for the comparatively weaker effects of the SST given that the standard programming of the task aims to have participants correctly inhibited their responses only 25% of the time.

In interpreting results, it should be considered that most of the studies included were conducted in a controlled laboratory environment and did not have long term follow-ups. Furthermore, the outcomes of many studies examined how training conditions differed in behaviour following training, as opposed to comparing changes in behaviour pre and post intervention. This would have been a more useful outcome in evaluating the efficacy of the interventions in modifying the targeted behaviour from baseline presentations.

Participants in the studies examined were typically non-clinical samples of undergraduate students who may not have encompassed the characteristics that may facilitate significant change following training. For instance, they may not have sufficiently low baseline inhibitory control to be able to exhibit a significantly large change following the training due to a floor effect. This is supported by evidence suggesting that changes following response inhibition training are particularly evident for individuals who have comparatively poorer baseline inhibitory control (Houben, 2011). Additionally, given that non-clinical samples would not have experienced sufficiently strong reinforcement of their behaviour, they may lack the high appetitive response or motivation to change that appears to facilitate the learning of associations (Jones et al., 2016). This is suggested by high appetite and regular consumption of foods being associated with significant treatment effects in food studies (Veling, Aarts, & Stroebe, 2013b). Therefore, training would likely yield larger effect sizes in populations
that display such characteristics, for instance in clinical populations of substance users.

**3.2.2 Response inhibition training in other substance uses**

In addition to the evidence base of targeting alcohol consumption, two recent studies have been published examining response inhibition training in other substances. Most relevant, Adams, Mokrysz, et al. (2017) examined a single, 30-minute session of GNG training in 55 non-treatment seeking, nicotine-dependent smokers following overnight abstinence of 12 hours. Participants were randomly allocated to one of two smoking-cued training tasks incorporating smoking-related and neutral stimuli: 1) the intervention training where the “no-go” cue was consistently paired with smoking-related stimuli, or 2) the control training where smoking-related stimuli were paired with the “no-go” cue 50% of the time. Findings indicated that there was no significant difference between groups in the number of cigarettes smoked in the week following the intervention.

There are several considerations and methodological limitations that may explain this result. Firstly, being non-treatment seeking, changes in smoking behaviour may have been impeded by participants’ lack of motivation to quit, given that such motivation has been identified by literature as an important factor in treatment outcome (Ali, Green, Daughters, & Lejuez, 2017; Collins, Malone, & Larimer, 2012; Serafini, Shipley, & Stewart, 2016). Secondly, the intervention may have been too brief to sufficiently induce change. The training duration of the session exceeded that of other single session training paradigms where training typically lasted for 5-10 minutes (e.g. Bowley et al., 2013; Folkvord, Veling, & Hoeken, 2016; Houben, Havermans, Nederkoorn, & Jansen, 2012; Houben & Jansen, 2011; Veling, Aarts, & Stroebe, 2013b; Veling et al., 2013a).
Nevertheless, it may be that smoking requires more intensive training over a longer period of time as smokers experience multiple reinforcing “episodes” of smoking each day. Lastly, the conservative design of using a control group to inhibit responses to smoking-related stimuli 50% of time may have prevented a significant effect from being found.

The second study that examined response inhibition training in another substance is by Alcorn, Pike, Stoops, Lile, and Rush (2017). Twenty non-treatment seeking participants with cocaine use disorder completed five sessions of GNG training in a single day; the intervention group completed a cocaine-cued task and the control group completed a task with rectangles as cues. There was also a monetary element where participants commenced each training session with $1.65 with 5c deducted for each commission or omission error. However, cocaine use was not assessed post-intervention as it was a pilot study that did not examine treatment efficacy. Thus, while clinical substance use has been recognised as a promising behavioural target for response inhibition training, there remains much research to be conducted.

### 3.2.3 Web-based training programs

The majority of studies examining response inhibition training were single sessions conducted in a laboratory context. There were four studies that examined the effectiveness of multiple sessions of training delivered online, all using food-cued tasks to target eating behaviours. One of these is a four-week program by Veling, van Koningsbruggen, Aarts, and Stroebe (2014) that required 113 dieters to complete one GNG training session per week on a specified day. Results indicated that it facilitated weight loss in participants and was particularly
effective for those with a high body mass index (BMI), yielding a small effect size \((\eta^2_p = .04)\). Participants were sent reminders to assist in program compliance.

A shorter, four-session online training program using the GNG task was tested by (Lawrence, O’Sullivan, et al., 2015) in a sample of 83 normal and overweight/obese adults. This was completed over a week, with a request for participants to complete the training over consecutive days. Of the 82% of participants who completed all four training sessions, half complied with this request. Unlike Veling et al. (2014), participants were not given reminders to complete the training as the authors wanted to examine the feasibility of the program in the context of participants’ own self-motivation and natural compliance. In the week following the intervention, participants in the intervention condition (i.e. where the “no-go” cue was consistently paired with unhealthy food) displayed reduced daily energy intake and significant weight loss compared with participants in the control condition. Furthermore, they reported a reduced liking of the unhealthy foods paired with the “no-go” cue. Follow-up at one and six months post-intervention showed that the intervention group was associated with reduced snacking frequency \((\eta^2_p = .12-.16)\). At six months, participants in the intervention group also exhibited significantly higher mean weight loss of 2.21kg compared with the control group who reported a mean weight loss of 0.36kg \((d = 0.47)\). However, it should be noted that at the follow-up time-points, participants were no longer blinded to their group allocation and their self-reports of weight may have been influenced by training expectancies.

In contrast, a study by Allom and Mullan (2015) reported no significant effects of a SST training paradigm. Across two studies, 72 and 70 participants completed 10 online training sessions of one of three food-cued training
paradigms: 1) a food-cued condition where stop signals were only presented following unhealthy food cues, 2) a general inhibition condition where unhealthy foods were not consistently paired with stop signals, and 3) a control condition where no stop signals were presented. While the first study reported a significant effect on BMI ($\eta^2_p = .13$), this was nonsignificant in the second study when participants BMI was calculated by researchers. There were no impacts on eating behaviours in either study.

Similar results were reported in a study by Forman et al. (2016) investigating the SST in 119 university students who habitually consumed salty snack foods. Participants were instructed to complete four sessions across consecutive days; one at a laboratory and three booster sessions on their own computers. Findings indicated that there were no significant effects of training on snack consumption in the seven days post-intervention compared with a control condition of psychoeducation. Of note, participants only completed half of the booster sessions on average and exploratory analyses identified that there was a significant reduction of consumption from pre to post training in the intervention group.

A likely explanation for these mixed findings is that the studies by Allom and Mullan (2015) and Forman et al. (2016) did not find significant training effects due to their use of the SST. In both studies, stop signals were presented for only 50% of all unhealthy/salty snack food trials. The low proportion of stop signals in the training may have been insufficient to facilitate significant behavioural change, in line with Jones et al.’s (2016) argument that the effects of training are predicted by the proportion of successful inhibition towards target stimuli.
3.3 Critical Analysis of the Interventions

While evidence supports the efficacy of response inhibition training to facilitate behavioural change, there are a number of concerns that should be considered in interpretation. One such critique of these interventions is that participants may not be learning to better inhibit their responses, but are rather learning methods to complete the specific training that are not generalisable. This concern is particularly relevant to the GNG task given that it modifies automatic processes as opposed to top-down inhibitory control. While there has only been one study to use the GNG as a response inhibition measure following smoking-cued GNG training (Adams, Mokrysz, et al., 2017), the methodology may have obscured any training effects. They used two variations of a GNG task to measure response inhibition; a standard non-cued GNG task comprised of 30% “no-go” trials and a smoking-cued GNG task comprised of 25% “no-go” trials with half of the trials paired with smoking images. Results indicated that participants displayed increased commission errors from baseline to post-intervention on both the non-cued ($\eta^2 =0.08$) and smoking-cued ($\eta^2 =0.17$) GNG measures. Given that it was a 30-minute training intervention, the long duration of the training may have resulted in fatigue, as suggested by the increase in self-reported anxiety, cigarette craving, and drowsiness post-intervention. Additionally, training effects may have been obscured given the low “no-go” contingency rate in both tasks which could have increased prepotent responding and masked any changes in response inhibition, particularly given the similarity between training task and test measures.

Rather, studies investigating response inhibition interventions have more often adopted the approach of incorporating tasks not used in training. This is to
evaluate the true effect of the training on inhibitory control and avoid capturing confounding learning effects. Allom and Mullan (2015), who examined the effects of SST training on eating behaviours, reported performance on the Stroop task improved following SST training; however, critically, the training itself did not result in significant changes in eating behaviours. Houben, Havermans, et al. (2012)’s study in heavy drinkers aimed to measure changes in inhibitory control on the SST as induced by GNG training. They found no changes in performance on the SST, despite significant behavioural effects induced by the GNG training. In contrast, Alcorn et al.’s (2017) study of GNG training in cocaine users found that participants in both the intervention and control training groups displayed reduced inhibitory failures ($\eta^2_p = 0.20$) and lower stop signal reaction times ($\eta^2_p = 0.22$) on a non-cued SST at post-intervention. This suggests training resulted in an improvement in executive control, an unexpected finding given that the GNG task and the SST target different aspects of response inhibition, as previously reviewed (Jones et al., 2014; Verbruggen & Logan, 2008). Given the mixed nature of these collective findings, additional research is required to identify the most appropriate tasks to use as independent measures of response inhibition.

Furthermore, there is the crucial question of whether response inhibition training generalises to untrained stimuli in the real world. In Chen et al.’s (2016) study examining food-cued training, devaluation was observed for trained stimuli but not untrained stimuli. If devaluation is indeed the mechanism responsible for the effectiveness of the training, this suggests that there are limitations to the generalisability of the training to different forms of the targeted behaviour not depicted in the training. However, it should be noted that the results of the study may have been affected by the similarity of the food items used across “go” and
“no-go” trials. For example, two other studies that investigated food-cued training using non-food items (Folkvord et al., 2016) or healthy food items (Adams, Lawrence, et al., 2017) as “go” stimuli reported decreased intake of both trained and untrained unhealthy food. While these studies did not examine devaluation directly, the overall findings suggest that associations learned on a category (i.e. food) or subcategory level (i.e. unhealthy food) may be more conducive to generalised behaviour change. In contrast, using similar items for the two types of trials as in Chen et al.’s study may result in low generalisability due to inhibitory behaviour learned on an item level (Veling et al., 2017). Further research is required to better understand this mechanism and the extent of its generalisability.

It should also be considered that the study results of response inhibition training may be confounded by the design of comparison conditions. Some studies use conditions that incorporate target stimuli to train disinhibition by consistently pairing them with “go” cues (Houben, Havermans, et al., 2012; Houben & Jansen, 2015). However, this is not considered to be a true control condition as exposure to target stimuli may interfere with levels of approach and inhibition. That is, trained disinhibition does not provide an accurate baseline comparison for trained inhibition as it encourages increased approach and consumption (Houben & Jansen, 2011). This is illustrated in a study by Lawrence, Verbruggen, et al. (2015) where there were significant differences in food intake when comparing the intervention group (i.e. target stimuli mostly paired with “no-go” cues to which participants were to not respond) to a “double-response” group that encouraged approach (i.e. pressing a key twice in response to “no-go” cues that were mostly paired with target stimuli). However, there were no differences when comparing the intervention group to a control group that responded to all
trials regardless of whether a “no-go” cue was presented. This suggests that
conditions that encourage approach to target stimuli can inflate the effects of the
training. Similarly, comparison groups that pair target stimuli with “go” and “no-
go” cues inconsistently (e.g. Houben, 2011; Houben & Jansen, 2011) are poor
comparisons as research has indicated that increased motivational salience of cues
can result from inconsistent reinforcement (Anselme, Robinson, & Berridge,
2013). Thus, these limitations should be considered in the interpretation of
efficacy trials and future studies need to carefully design comparison conditions
that can not only control for changes over time, but also measure the true effects
of the training.

3.4 Chapter Summary

Results across studies investigating alcohol consumption and eating
behaviours indicate that response inhibition training with the GNG task and the
SST can elicit behavioural change. Three meta-analyses of response inhibition
training on these behaviours (Allom et al., 2015; Jones et al., 2016; Turton et al.,
2016) revealed that it yielded small-medium effect sizes, with most studies using
non-clinical samples. Furthermore, the GNG task yielded larger effect sizes
compared with the SST. Evidence that behavioural change occurs through
devaluation of targeted stimuli is inconsistent and requires further investigation.

Although a majority of studies examined a single session of training in a
laboratory setting, four studies in eating behaviours used multiple online training
sessions spanning three days (Forman et al., 2016), one week (Lawrence,
O’Sullivan, et al., 2015), 10 days (Allom & Mullan, 2015), and one month
(Veling et al., 2014). While results were mixed, the two studies that used the
GNG task (Lawrence, O’Sullivan, et al., 2015; Veling et al., 2014) reported
decreased snacking frequency and facilitation of weight loss, with one study reporting these changes to remain statistically significant at six-month follow-up (Lawrence, O’Sullivan, et al., 2015).

More recently, a study administering GNG training to smokers yielded nonsignificant effects (Adams, Mokrysz, et al., 2017). However, this was a single training session administered to non-treatment seeking participants in a laboratory whereby the protocol also entailed several methodological limitations. As such, further research is required in relation to the application of response inhibition training in smokers in investigating whether it can aid in smoking cessation. The following chapter will present the rationale and aims of the two parts of the thesis; the development of a smoking-cued response inhibition training and a systematic review examining the association between impulsivity and smoking outcome.
Chapter Four: Rationale and Aims

4.1 Rationale

Significant deficits in response inhibition are experienced by smokers and are a strong predictor of relapse following a quit attempt. As such, this is an important target in smoking interventions to facilitate cessation and prevent relapse. Studies have supported their effectiveness in reducing problematic health-related behaviours such as excessive alcohol consumption and eating of unhealthy foods, in addition to facilitating weight loss in dieters and overweight adults. Three meta-analyses (Allom et al., 2015; Jones et al., 2016; Turton et al., 2016) found that training in these studies resulted in small-medium effect sizes, with Go/No-Go (GNG) training yielding larger effect sizes than Stop Signal Task (SST) training. In the past year, response inhibition training has also been examined in other substances, with one study (Adams, Mokrysz, et al., 2017) applying the training to smokers. While results indicated that it yielded no significant effects on smoking behaviours, further investigation remains necessary given that it was a single training session in non-treatment seeking smokers.

The first part of this thesis examines the development and piloting of a smoking-cued response inhibition training intervention. This was completed prior to the publication of Adam et al.’s study and as such, their methodology and findings did not influence the present thesis. Given that significant effects of the training were found in other response inhibition studies despite the use of non-clinical samples, the training was expected to be particularly effective with smokers as smoking receives the most frequent reinforcement compared with other dependent populations, with multiple smoking sessions each day. Furthermore, it could be particularly beneficial for heavy smokers who report the
greatest difficulty in maintaining abstinence (AIHW, 2017). This is suggested by evidence indicating that greater benefits from response inhibition training are predicted by higher levels of the targeted behaviour (Veling et al., 2013b) and poorer inhibitory control (Houben, 2011), which have been associated with stronger nicotine dependence (Billieux et al., 2010).

The GNG task was used as the response inhibition task given its superior effects in inducing behavioural change as indicated by results from all meta-analyses. This is a particularly appropriate intervention choice for smokers given that research suggests this population exhibits significant deficits in automatised bottom-up inhibition but no apparent deficits in top-down control deficits (Smith, Mattick, et al., 2014). As previous studies have found the training to be effective even when administered over the internet, this study also delivered the training paradigm online. The results of the study aim to not only provide evidence for a cost-effective and accessible smoking cessation treatment, but also further extend literature on response inhibition training in regards to its utility and underlying mechanisms.

The second part of this thesis is a systematic review that examined the broader construct of impulsivity and smoking cessation interventions. Given that impulsivity has been identified as a strong predictor of nicotine dependence and relapse in smokers (e.g. Bloom et al., 2014), it is argued that levels of impulsivity should decrease following effective treatment and this should be associated with a reduction in cigarettes and also a reduced risk of relapse. As yet no review has assessed this hypothesis.

4.2 Aims

The main aims of this thesis are to:
1. Develop and pilot a smoking-cued response inhibition training task targeted at smokers who wish to quit

2. Investigate whether levels of impulsivity change following intervention

In relation to the first aim, Chapters Five-Seven will present the development and pilot studies of the smoking-cued response inhibition intervention whereby the results will inform the design of a potential large-scale randomised controlled trial. The main objectives of this part are as follows:

a) Develop a smoking-cued GNG training task

b) Design the intervention protocol

c) Pilot the training task and protocol

In relation to the second aim, Chapter Eight will present a systematic review of the literature relating to changes in levels of impulsivity following non-pharmaceutical smoking cessation treatments that target psychological, behavioural, cognitive, or social aspects of smoking. It also investigated whether such changes were related to smoking outcomes.

Chapter Nine will then provide a general discussion of the previous chapters’ study findings, and directions for future research. Clinical implications and limitations will be discussed, before the presentation of final conclusions.
Chapter Five: Development of a Smoking-Cued Response Inhibition Intervention

The overall design of the present smoking response inhibition intervention was based on the food-cued training task developed by Lawrence, O’Sullivan, and colleagues (2015) which had yielded efficacious results. Aided by regular consultations with Dr Lawrence, the protocol was developed and given the name, “INhibitory Smoking Training” (INST). Of note, the smoking-cued training by Adams, Mokrysz, et al. (2017) had not yet been published at the time of study conceptualisation and thus was not factored into considerations below.

The process of empirically developing the program involved considerations broadly constituting two categories: 1) intervention development (task design and design of the training program) and 2) protocol development (inclusion criteria, medium of delivery, design of procedure, smoking outcome, measurement of smoking outcome, and task designs of other protocol measures). The chapter outlines each of these considerations as informed by reviews of the literature, followed by decisions made in relation to INST.

5.1 Intervention Development

5.1.1 Training task

Considerations. While both the Go/No-Go (GNG) and Stop Signal Task (SST) have been used as response inhibition training tasks, the GNG task was selected for the present intervention given evidence to suggest that training with this task yields larger effect sizes (Allom et al., 2015; Jones et al., 2016; Turton et al., 2016). Additionally, a meta-analysis found smokers to exhibit significant deficits in response inhibition compared with non-smokers as measured by the GNG, but not the SST (Smith, Mattick, et al., 2014). This would suggest that
smokers would benefit more from training of automatized behaviour as opposed to top-down inhibitory control.

As reviewed in Chapter Three, studies examining the efficacy of GNG training typically use two versions of the training task; an intervention task and a control task. The intervention training task typically consists of 1) images of the targeted problematic behaviour, known as “target stimuli” (e.g. unhealthy food) and 2) images of an alternative behaviour to the targeted behaviour (e.g. healthy food) or neutral stimuli (e.g. empty plates). There is more variation in the design of the control task among studies, where some incorporate both target stimuli and neutral/alternative stimuli and others only use neutral stimuli. As previously discussed, while the comparison condition in some studies incorporate target stimuli to train disinhibition by consistently pairing them with “go” cues (Houben, Havermans, et al., 2012; Houben & Jansen, 2015), such exposure to target stimuli may interfere with levels of approach/inhibition. Thus, trained disinhibition is not considered to be a true baseline comparison for trained inhibition (Houben & Jansen, 2011).

**Present study.** The intervention and control versions of the GNG training task were modelled from the tasks used by Lawrence and colleagues (2015). This has the advantage of using the template of an established task that has yielded significant results in food-cued training. Furthermore, the identical design allows for a direct comparison with Lawrence et al.’s results to yield data across domains of health behaviours. This is an important point given that comparison of study results across the response inhibition training literature is impeded by variations in intervention design. Given that there was no smoking-cued GNG training task available, selection and validation of the stimuli for the intervention task was also
a necessary step in task development. This ensured that the cues are ecologically relevant and elicit craving and appetitive approach behaviour during the training. The process of validation required an empirical study which is reported on in Chapter Six. The other aspects of the training task are detailed below.

In both the intervention and control training, images are presented on the left or right hand side within a rectangular frame for 1250ms followed by a 1250ms inter-stimulus interval. Participants are instructed to respond as quickly as they can to the location of the image within the frame, using the keys “C” and “M” to indicate left and right respectively. On half of the trials, the rectangular frame appears bolded and participants are instructed to withhold their response during these trials. These are termed “no-go” trials while trials where the frame is unbolded are termed “go” trials (see Figure 5.1). There are six blocks of 36 trials with a five second countdown before the start of each block. At the end of each block, participants receive feedback detailing average reaction time and percentage of correct responses for the purposes of maintaining engagement and motivation. It also reiterates the instruction for participants to respond to images as quickly as they can.

The intervention task contains nine smoking images, nine relaxing images, and 18 filler images of clothing. The smoking stimuli are consistently paired with “no-go” signals while the relaxing stimuli are consistently paired with “go” signals. “No-go” signals appear on 50% of the filler trials. The purpose of these filler images is to increase the challenge of the task and make the rules of the training less obvious in order to engage the automatic system of learning in forming associations (Lawrence, O’Sullivan, et al., 2015).
The control task used in this study is identical to the sham training task in Lawrence, O’Sullivan, et al. (2015). It consists of 18 images of clothing and 18 images of household items, with both categories of stimuli paired with “no-go” signals 50% of the time.

<table>
<thead>
<tr>
<th>Intervention task</th>
<th>“Go” trial</th>
<th>“No-go” trial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100% go</td>
<td>100% no-go</td>
</tr>
<tr>
<td>Control task</td>
<td>50% go</td>
<td>50% no-go</td>
</tr>
</tbody>
</table>

*Figure 5.1. Schematic of examples of “go” and “no-go” trials for the intervention and control tasks.*

### 5.1.2 Design of the training program

**Considerations.** A number of factors were considered in determining the number of training sessions that participants would need to complete. While previous studies targeting eating behaviours and alcohol consumption only administered 1-4 sessions, it was hypothesised that targeting response inhibition in smokers would require more training sessions to result in a significant change given the comparatively repetitive nature of smoking where engagement in multiple instances of smoking each day likely results in stronger reinforcement.
However, there needs to be careful consideration of the balance between effectiveness and acceptability. This is illustrated by a study examining web-based cognitive behavioural therapy for depression which found that a brief version of the intervention was not as effective as an extended version but had lower dropout rates (Christensen, Griffiths, MacKinnon, & Brittcliffe, 2006).

Investigation of studies using other forms of web-based cognitive training varied in frequency and duration of sessions. Five sessions a week was a common frequency (e.g. Damholdt et al., 2016; Lebowitz, Dams-O’Connor, & Cantor, 2012; Smith, Housen, et al., 2014), possibly as it enables participants to train for a majority of the week while still allowing leeway for completion should it not be feasible for participants to complete daily sessions. Studies have also included “booster sessions” which are additional sessions external to the main intervention period that aim to maintain or increase any improvements yielded from training (Willis et al., 2006). These can differ greatly in parameters such as dose, frequency, and timing (Kolko & Lindhiem, 2014). For instance, Belleville et al. (2017) examined eight weekly cognitive training sessions for individuals with mild cognitive impairment followed by one booster session three months post-intervention, while Sisco, Marsiske, Gross, and Rebok (2013) examined 10 sessions of cognitive training over 5-6 weeks for older adults, who then received four sessions of booster sessions at one and three years post-intervention.

The timing of when to administer the intervention is also important as previous food-cued response inhibition training studies administered the training during times of increased food craving given evidence to suggest that the training is less effective when individuals are satiated (Veling et al., 2013b, 2014). Applied to smoking, the training may be maximally effective during states of
craving for cigarettes; this is also when smokers are most likely to smoke (Shiffman et al., 2002) and may be particularly sensitive to smoking cues. Of relevance, experiences of cravings and withdrawal symptoms have been found to typically commence two hours after the last cigarette smoked (Mendelsohn, 2015).

**Present study.** The intervention program occurred over a total duration of four weeks. Participants completed five sessions a week for the first two weeks, followed by two sessions a week for the subsequent two weeks. The first two weeks were regarded as the main period of intervention, with the sessions in the last two weeks considered “booster” sessions. To ensure consistency, access to training was restricted to once per day and participants were not be able to exceed the outlined number of sessions per week. Participants were requested to complete the training in a quiet environment when they experienced cravings or after abstaining from smoking for two hours.

5.2 Protocol Development

5.2.1 Inclusion criteria

**Considerations.** The inclusion criteria used was based on considerations of not only characteristics that would be representative of the smoking population, but also the subgroups of smokers that would likely benefit from the training. Previous evidence suggests that training may be particularly effective for those with more severe forms of the targeted behaviour (Veling et al., 2013b), whereby its effects may not be significant in smokers with low dependence. The establishment of the smoking dependence criteria itself was determined based on examination of criteria used in other smoking cessation studies. A common criterion is to require participants to have smoked at least 10 cigarettes daily for
the past 12 months (e.g. Ng et al., 2014; Stead, Koilpillai, Fanshawe, & Lancaster, 2016). Other inclusion criteria can include meeting criteria for Nicotine Dependence or Tobacco Use Disorder (TUD) as defined by the DSM-IV or DSM-5 respectively, or meeting a minimum cut-off score on the Fagerström Test of Nicotine Dependence (FTND), a commonly administered tool to measure nicotine dependence.

However, further specification of inclusion criteria was desirable given the likely range of different smoking behaviour histories and to also avoid any unnecessary exclusion of potential participants. For instance, if the general criteria of a minimum of 10 cigarettes a day for the past 12 months was strictly adhered to, this may result in the exclusion of a large proportion of smokers given that it is likely for smokers to report varying levels of smoking during this extended time frame. Indeed, a majority of Australian smokers have reported making attempts to quit or change their smoking behaviour within the past 12 months AIHW, 2014, 2017), and may therefore not have smoked every day during this period of time. It would seem unnecessary to exclude smokers who, for example, may have ceased smoking for one week four months ago but reported smoking 15 cigarettes a day in the last four months. To determine an acceptable period of time when participants may have been abstinent or smoked minimally, consultation of the DSM-5 criteria for TUD yielded the definition of early remission as not meeting criteria for more than three months but less than 12 months. This period of time was selected by the Substance-Related Disorders Work Group given evidence to suggest that those who adhered to treatment for at least three months yielded better outcomes (Hasin et al., 2013). Additionally, evidence suggests that heavy tobacco smokers who are abstinent for two weeks exhibit levels of nicotine and
cotinine similar to that of non-smokers (Moyer et al., 2002). Taken together, this highlights that the recency and overall duration of an abstinent period should be accounted for during the screening phase.

Furthermore, smokers interested in the study may report current use of NRT given that it is a common, self-administered treatment in Australia (Mendelsohn, 2013). Other pharmacotherapies such as anti-craving medication (e.g. bupropion, varenicline) may also be used. These medications may have an impact on training effects given that the training appears to be less beneficial for those who are in a state of satiation (Veling et al., 2013b, 2014). This would have implications for excluding potential participants given that it would be unethical to advise the prolonged abstinence or cessation of pharmacotherapies, particularly for anti-craving medications which typically have a 12-week course (Hughes, Stead, et al., 2014).

**Present study.** As a general criterion, participants were required to have smoked at least 10 cigarettes daily for the past 12 months. They also needed to fulfil criteria for moderate or severe dependence of TUD as defined by the DSM-5. Participants who reported an abstinence period of longer than two weeks in the preceding three months were excluded.

Participants were requested to abstain from using NRT or anti-craving medications during the training period only. Any subsequent use of pharmacotherapy during the follow-up period was recorded and controlled for in analyses. Potential participants who had already commenced anti-craving medication were excluded from the study.
5.2.2 Medium of delivery

Considerations. While the first stage of intervention studies is typically conducted in laboratories to determine efficacy, there are already promising results for response inhibition training in other health behaviours in both laboratory (e.g. Houben & Jansen, 2011; Jones & Field, 2013) and real-world settings (e.g. Lawrence, O'Sullivan, et al., 2015; Veling, van Koningsbruggen, Aarts, & Stroebe, 2014). A laboratory setting would have limited ecological validity and requiring participants to attend multiple training sessions would likely be deemed too inconvenient. Furthermore, given the aim of the training is to induce behavioural change, it may be more effective in real-world settings where the target behaviour of smoking occurs (e.g. home), as opposed to a laboratory where there is no association with their smoking.

The use of a web-based platform for the present study is supported by literature in GNG training that have reported significant results even when participants have completed web-based training independently (Lawrence, O’Sullivan, et al., 2015; Veling et al., 2014). In general, web-based interventions for smoking are regarded as promising treatments, with tobacco control simulation models suggesting that effective web-based treatments could reduce smoking prevalence in the population if implemented sufficiently (Levy, Graham, Mabry, Abrams, & Orleans, 2010). A Cochrane review of 67 randomised controlled trials (RCT) suggested that web-based smoking cessation interventions that were interactive and tailored to individuals were moderately more effective at six months or longer than non-active control conditions (Taylor et al., 2017). While further research is required given the high risk of bias and methodological issues across some studies, this medium enables the training to be accessible,
cost-efficient, and convenient, with the absence of financial or logistical barriers that are present with pharmacological or face-to-face psychological/behavioural interventions (Richardson et al., 2013).

A mobile phone app could be another medium of delivery due to the popularity and usage of mobile devices (Huang, Wang, Peng, & Huang, 2015). Mobile and tablet usage exceeded computer usage worldwide in 2016 (StatCounter, 2016), with 88% of Australians owning a smartphone in 2017 (Deloitte, 2017). However, there is still limited evidence for mobile-based interventions. While a Cochrane review (Whittaker, McRobbie, Bullen, Rodgers, & Gu, 2016) found that mobile-based smoking cessation treatments were significantly related to six-month cessation outcomes (abstinence risk ratio of 1.67), a majority of these treatments were text message-based as no smartphone apps met the criteria to be included in the review. Additionally, the portability of devices such as mobiles phones and tablets would be more likely to entail external distractions that may interfere with performance and concentration.

Present study. INST was delivered in a web-based format and was investigated directly in a real-world setting where participants could complete the intervention independently. It was only accessible on computers and laptops in the present iteration of the intervention.

5.2.3 Design of procedure

Considerations. Participants will be administered measures at baseline and post-intervention to determine whether the training has resulted in any changes in variables of interest. A follow-up time-point would also be important to examine the stability of any results observed at post-treatment, particularly as some studies have yielded significant reductions of unhealthy behaviours at post-treatment but
reported non-significant results at follow-up (Bowley et al., 2013; Jones & Field, 2013). Previous response inhibition training studies have used follow-up time-points ranging from one day to six months. However, it also needs to be considered that these primary assessment time-points of baseline, post-intervention and follow-up may not adequately capture the immediate effects of the training, such as impacts on cigarette cravings that may subsequently influence smoking behaviour. Should cigarette cravings only be measured at the main time-points, important data regarding any immediate effects of training on craving levels would be omitted.

Given the desirability for participants to remain engaged for the whole course of the study, an important issue to consider in the methodological design is the common occurrence of low adherence or early dropout in web-based interventions (Wangberg, Bergmo, & Johnsen, 2008). This can involve participants not following the specified intervention program and having low exposure to its contents (Donkin et al., 2011), or individuals expressing interest in participating but either do not engage or dropout early in the intervention process (Wangberg et al., 2008). The initial engagement of participants has been found to be critical to the success of web-based smoking cessation treatments (Richardson et al., 2013). General research into the design of interventions suggest that there are a number of factors that can assist in improving adherence to web-based interventions (Kelders, Kok, Ossebaard, & Van Gemert-Pijnen, 2012). These include praise, reminders of their target behaviours, and likeability of the intervention (Oinas-Kukkonen & Harjumaa, 2009). Furthermore, personalising aspects of the training such as using names in message reminders or tailoring feedback can impact adherence through increasing personal relevance (Ludden,
van Rompay, Kelders, & van Gemert-Pijnen, 2015; Wangberg et al., 2008; Wangberg, Nilsen, Antypas, & Gram, 2011).

**Present study.** Researchers had contact with participants at baseline, post-intervention, and follow-up time-points. Baseline assessments and induction into the intervention program were completed face-to-face to not only ensure that they were able to complete the training correctly and independently, but also to increase initial engagement. Subsequent contact at post-intervention and follow-up was conducted over the phone for convenience, following which participants were also required to complete questionnaires via a link sent to them by a researcher. Participants reported their levels of craving, motivation, and confidence in quitting before and after each training session as this yielded information regarding momentary states. Efforts were made to personalise aspects of the intervention where possible. Specifically, SMS reminders for participants to complete the training were addressed with the participant’s first name and a personalised approach was used when attempting to re-engage non-adherent participants via email.

### 5.2.4 Smoking outcome

**Considerations.** Interventions targeting smoking typically have the goal of assisting smokers in quitting and maintaining abstinence. Participants are often requested to select a quit date given that committing to a date has been associated with increased rates of quitting (Balmford, Borland, & Burney, 2010). Most interventions investigated in literature appeared to allow participants to select their own quit dates, although some also provided a time limit according to the intervention protocol. For example, Cobb, Niaura, Donaldson, and Graham (2014) investigating a six-month web-based cessation intervention encouraged
participants to select their own quit date based on their readiness levels, while Muñoz et al. (2009) compared four web-based interventions where participants were requested to select their own quit date within the first 30 days of an eight-week program. However, it has also been noted that having an absolute quit date may be less helpful given the perception of time pressure to quit and remain abstinent (Cobb et al., 2014).

An important consideration is that not all smokers may wish to quit “cold turkey” due to reasons relating to their level of nicotine dependence, self-competency, or readiness (Begh, Lindson-Hawley, & Aveyard, 2015). Smoking reduction, or gradually reducing cigarettes smoked, can be viewed as a more acceptable option or an intermediate step before abstinence. It may be that meeting reduction goals will increase confidence over time such that they will eventually achieve abstinence (Chan et al., 2011). Often these interventions include some form of guidance by researchers, such as using one of two common reduction methods: 1) systematically reducing the number of cigarettes smoked each day, or 2) eliminating cigarettes smoked throughout the day based on which ones are the easiest to give up (Hughes et al., 2011; Klemperer, Hughes, Solomon, Callas, & Fingar, 2017; Riggs, Hughes, & Pillitteri, 2001). Studies have shown that smokers have been able to quit through participating in smoking reduction interventions despite no initial intention to be abstinent in the near future (Asfar, Ebbert, Klesges, & Relyea, 2011; Lindson-Hawley et al., 2016; Wu, Sun, He, & Zeng, 2015). Additionally, while abstinence is preferable for health outcomes, research has shown that a reduction of number of cigarettes smoked may nevertheless decrease the likelihood of experiencing negative health consequences (P. N. Lee, 2013; Lotan, Goldbourt, & Gerber, 2017).
Present study. In consideration of this research, it was decided that either quitting or smoking reduction was acceptable given the likely range of smoking goals among participants. This also allowed for a wider range of participants to be accepted into the study regardless of their present plans for quitting. To provide some form of uniform guidance, participants were asked to select a personalised quit date that was before, during, or after the training period. For those who were reluctant to attempt “cold turkey”, this date marked when they would commence reducing the number of cigarettes smoked. No further guidance was provided on how participants would achieve either type of goal to maintain consistency in procedure. It was emphasised to participants that this date would serve as only a guideline and they could modify their plans based on situational circumstances leading up to the selected date. This strategy was approved by Dr Ron Borland who was consulted regarding the issue of quit dates for participants given his extensive research in the field of smoking.

5.2.5 Measurement of smoking outcome

Considerations. Smoking cessation outcomes are commonly assessed using self-report measures, such as prolonged abstinence (i.e. a continuous period of abstinence since the quit date) or point-prevalence abstinence (i.e. not smoking for a specified period of time leading up to the follow-up time-point). A Delphi study on smoking cessation researchers (Cheung et al., 2017) reported that experts reached an agreement that the four most important self-report outcomes are: 1) prolonged abstinence (six and/or 12 months), 2) seven day point-prevalence, 3) six months of continuous abstinence (i.e. not smoking since the commencement of an intervention), and 4) number of cigarettes smoked in the preceding seven days. A systematic review by Hughes, Carpenter, and Naud (2010) comparing
prolonged abstinence and point-prevalence suggested that they are highly correlated but that both should be reported for ease of comparison with other studies. Biochemical outcome measures can also be obtained through carbon monoxide in the breath or cotinine in saliva or urine. These are regarded as more rigorous objective outcome measures as they do not rely on self-reported outcomes that may be influenced by recall bias or inaccurate reporting. However, they also entail logistical considerations for both researchers and participants, and may subsequently impact adherence. Experts in the Delphi study indicated that biochemical measures are not always necessary for RCTs, although no further information regarding their reasoning is provided beyond authors speculating this may relate to reasons of desirability or feasibility (Cheung et al., 2017).

**Present study.** The primary outcome of the training was assessed as self-reported smoking, specifically using the Timeline Followback. This yielded results that could be presented as continuous, prolonged, or point-prevalence abstinence.

5.2.6 **Task designs of other protocol measures**

**Considerations.** In addition to measuring smoking cessation outcomes following the training task, an additional aim is to explore the underlying mechanisms of the task. At the time of intervention development, the theory of devaluation had received the most attention within the response inhibition training literature as outlined in Chapter Three (Bowley et al., 2013; Houben, Havermans, et al., 2012; Houben et al., 2011). However, results were mixed regarding whether devaluation occurred as assessed by the Implicit Association Task (IAT) which measures implicit attitudes (Houben, Havermans, et al., 2012; Houben & Jansen, 2015; Houben et al., 2011). Explicit measures of stimulus evaluation have
remained largely unexplored by studies despite possibly being more sensitive in assessing changes in stimulus evaluation (Friese et al., 2008). In food-cued training studies, these have been in the form of rating sets of training task images and novel images based on level of attractiveness and/or liking of taste using Likert scales (Veling et al., 2008) or visual analogue scales (Lawrence, O’Sullivan, et al., 2015). Interestingly, Lawrence et al. reported that while there were significant differences detected between the intervention and control groups on ratings of liking of “no-go” foods, there were no differences between groups on ratings of image attractiveness. This suggests that the wording of items is important when measuring explicit evaluations towards stimuli.

Additionally, improvement in inhibitory control is theorised as a possible mechanism of change in training tasks. To avoid learning effects as a confounding factor, an independent measure of response inhibition is typically administered at baseline and post-intervention. The only study examining GNG training to do so was Houben, Havermans, et al. (2012) who used the SST as an independent measure following their alcohol-cued training. They reported no significant changes on the SST despite significant behavioural effects induced by the training. This result was thought to be due to the two tasks measuring different forms of response inhibition, where GNG measures bottom-up, automatic associations while SST measures top-down inhibitory control.

**Present study.** To investigate different hypotheses relating to the theoretical underpinnings of the training task, the SST, the IAT, and stimulus evaluation task was administered to participants. These tasks were tailored to be smoking-cued and programmed in Inquisit. The designs are outlined in the following sections.
5.2.6.1 Stop Signal Task. The SST was used as an independent measure of response inhibition. It is acknowledged that there are limitations to using the SST as an independent measure given that it targets a slightly different inhibitory process to the GNG task. As such, the effects yielded from the training may not be fully captured by the SST. However, there has yet to be an alternative measure proposed that would be a better independent assessment of response inhibition following GNG training.

The SST was programmed using a template on Inquisit which is based on the versions used by Houben, Nederkoorn, and Jansen (2014), Jones et al. (2014), and Logan, Schachar, and Tannock (1997). It was decided that a stimulus-specific SST was necessary for the study as a non-cued SST would assume a generalisation of inhibition training beyond smoking-cued GNG training. The 16 images used in the SST are comprised of eight pairs of images, where one image of the pair is a cigarette pointing to the left, and the second image is its mirror image pointing to the right (see Chapter Six for validation of these stimuli). As such, the presentation of cigarettes pointing left or right is equally balanced. Each of the 16 images is presented a total of 12 times.

At the start of each SST trial, a fixation cross appears on the screen for 500ms, before a 280 x 280 pixel image (the “go” stimulus) appears for 1000ms, followed by a blank white screen for 1000ms (the inter-stimulus interval). Participants must indicate whether the lit end of the cigarette is pointing to the left or right by pressing the keys “C” or “M” on the keyboard respectively. Images are randomised across trials and between participants. On 25% of the trials, a stop signal will appear across the image in the form of two horizontal red lines to signal that the participant should not respond to the image. It will appear after a
short delay (the stop signal delay or SSD) following the appearance of the image and will remain onscreen until the inter-stimulus interval. The stop signal will initially occur at 250ms after the appearance of the image. If the participant successfully inhibits their response, the stop signal duration will increase by 50ms at the next “stop” trial when the stop signal is programmed to appear, thereby increasing the difficulty of inhibition. If the participant is unsuccessful in inhibiting their response, the duration will decrease by 50ms, such that inhibition at the next stop trial will be easier. The task aims for the participant to correctly inhibit their responses on 50% of the “stop” trials. Examples of “go” and “stop” trials are depicted in Figure 5.2.

The task consists of a practice block and a test block. The practice block consists of ten trials where the stop signal will appear on 50% of trials such that participants can practice inhibiting their responses on “stop” trials. The test block consists of 200 trials where the stop signal will appear on 25% of trials.

Figure 5.2. Examples of “go” and “stop” trials in the Stop Signal Task
5.2.6.2 The Implicit Association Test. The IAT (Greenwald, McGhee, & Schwartz, 1998) will be used as a measure of implicit attitudes towards smoking. It was programmed based on the Inquisit template script from Wiers and colleagues (2002) with modifications made as necessary. The task involves categorising stimuli and words into two target categories (“smoking” and “non-smoking”) and two attribute categories (“pleasant” and “unpleasant”). The premise of the task is that respondents will be able to sort categories quicker if there is a strong association between the categories compared with if there is a weaker association.

Decisions regarding items within each category were informed by previous studies that examined implicit attitudes of smokers and non-smokers towards smoking (De Houwer, Custers, & De Clercq, 2006; Swanson, Swanson, & Greenwald, 2001). Sixteen images from the Shutterstock website of stock photography were used for the target categories: eight images of people smoking and eight corresponding images of the same people not smoking (see Figure 5.3). For the pleasant and unpleasant attribute categories, the words used are the same as those in the study by Swanson and colleagues (2001). The eight pleasant words are “cuddle”, “happy”, “smile”, “joy”, “warmth”, “peace”, “paradise”, and “love”. The eight unpleasant words are “pain”, “awful”, “disaster”, “grief”, “agony”, “brutal”, “tragedy”, and “bad”.
Figure 5.3. Pairs of smoking and non-smoking images used in the Implicit Association Task.

The IAT used in the study contains five blocks, similar to the version used in De Houwer et al. (2006). While the seven-block version of the task is more common, this shorter version has been found to be psychometrically valid and will reduce the duration of the task (see Table 5.1 for a summary of the blocks). The first block is a practice block which requires the categorisation of smoking and non-smoking images where each image is presented twice. The second block involves the categorisation of pleasant and unpleasant words that are presented once. The third block is a test block where all images and words are presented twice. One target category and one attribute category is categorised using one key, and the other target category and attribute category is categorised with an
alternative key. Blocks 4 and 5 are the same as blocks 1 and 3 but with the response keys for smoking and non-smoking images reversed.

Table 5.1

*Summary of Implicit Association Test Blocks*

<table>
<thead>
<tr>
<th>Block</th>
<th>No. of trials</th>
<th>Function</th>
<th>Left-key response (“C”)</th>
<th>Right-key response (“M”)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>Practice</td>
<td>Non-smoking images</td>
<td>Smoking images</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>Practice</td>
<td>Pleasant words</td>
<td>Unpleasant words</td>
</tr>
<tr>
<td>3</td>
<td>64</td>
<td>Test</td>
<td>Non-smoking + pleasant</td>
<td>Smoking + unpleasant</td>
</tr>
<tr>
<td>4</td>
<td>32</td>
<td>Practice</td>
<td>Smoking images</td>
<td>Non-smoking images</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>Test</td>
<td>Smoking + pleasant</td>
<td>Non-smoking + unpleasant</td>
</tr>
</tbody>
</table>

Initial assignment of response keys to smoking and non-smoking target categories will be counterbalanced for half of the participants. Presentation of all images and words is randomised and alternate in sequence in test blocks 3 and 5. The combination of categories presented in the test blocks will also be counterbalanced such that “smoking + unpleasant” will be the first combination for half of the participants, and the other half will receive “smoking + pleasant”.

Participants are instructed to complete the task as fast as they can while being as accurate as possible. The category words are presented at the top left and right corners of the screen and participants use corresponding “C” and “M” keys to categorise the stimuli that appear in the middle of a white background. When participants are required to categorise combinations of categories in the test
blocks, both types of category labels are presented in the top corners with one above the other (see Figure 5.4). A red “X” appears if the response is incorrect and the stimulus remains on screen until participants indicate the correct response. The inter-stimulus interval is 250ms.

*Figure 5.4.* Example trials of a combined categorisation test block on the Implicit Association Task.

The IAT scores will be calculated according to the scoring procedure by Greenwald, Nosek, and Banaji (2003). The analysis will involve subtracting the mean latency of responses to “smoking + unpleasant” from the mean latency of
responses to “smoking + pleasant” for each participant. Positive scores suggest that there is a stronger association of smoking with “pleasant” than “unpleasant”.

5.2.6.3 Stimulus evaluation test. In addition to assessing implicit attitudes towards target behaviours, explicit evaluation of smoking will also be measured using a stimulus evaluation test. Participants will rate the likeability of the smoking and relaxing images used in the GNG training task. For each image, participants are presented with the question, “how much would you like to do this activity right now”. The scale is in the form of a horizontal line of 100 units with the left end of the scale labelled “not at all” and the right end labelled “extremely” (see Figure 5.5). The slider bar is initially presented in the middle of the line and participants click and drag the slider bar along the scale to indicate their response. To differentiate responses of those who do not answer the question and those whose ratings are genuinely in the middle of the bar, participants are required to click the slider bar to activate the scale and then drag the bar as necessary. Responses will be calculated to the nearest integer between 1 and 100. The data output will also yield latency of responses.
Figure 5.5. Example of a trial in the stimulus evaluation test.

5.3 Chapter Summary

This chapter described the development of the intervention and protocol as informed by evidence-based literature. Each of the considerations was examined in detail followed by a description of the decision made. The next two chapters will outline the bulk of the empirical work presented in this thesis. First, Chapter Six will describe the empirical process of validating the stimuli used as cues in both the GNG training task and the SST. This will be followed by Chapter Seven that details the pilot studies conducted to examine the feasibility and acceptability of the protocol which further informs whether a larger scale trial is warranted.
Chapter Six: Validation of Stimuli

6.1 Introduction

As previously reviewed, response inhibition training tasks aimed at modifying behaviour are typically cue-specific tasks that are tailored to the targeted behaviour to maximise effectiveness (Allom et al., 2015). The task incorporates two different types of stimuli: 1) images related to the target behaviour and 2) images of neutral stimuli or a desired alternative to the target behaviour. For instance, Go/No-Go (GNG) training by (Lawrence, O’Sullivan, et al., 2015) targeting food consumption in overweight adults used images of high-energy dense foods (e.g. chocolate, chips) to pair with “no-go” cues, and images of healthy foods (e.g. fruits, vegetables) to pair with “go” cues. Similarly, in a study targeting alcohol consumption, Houben, Nederkoorn, Wiers, and Jansen (2011) paired images of beer with “no-go” cues and images of water with “go” cues.

Given that this was the first study examining response inhibition training in smokers at the time of intervention development, there was no smoking-cued training task readily available and the two sets of stimuli needed to be compiled to incorporate into the GNG task for smokers. While there are validated pictorial databases from which stimuli for the training task could be sourced, these were deemed to be unsuitable. The International Affective Picture System (Lang, Bradley, & Cuthbert, 2008) is a widely used, validated, and standardised database but unfortunately only contains two smoking-related images. Similarly, the Normative Appetitive Picture System (Stritzke, Breiner, Curtin, & Lang, 2004), a picture set comprising of appetitive stimuli, only has six smoking-related images. The Geneva Smoking Pictures (Khazaal, Zullino, & Billieux, 2012) was
promising as it is a database of 60 smoking-related images validated in a sample of 91 smokers. Pictures were rated according to the Self-Assessment Manikin rating system that was used to validate the International Affective Picture System where participants rated images on dimensions of valence, arousal, and dominance. Unfortunately, there was an insufficient number of images that were appropriate for inclusion in the training task (criteria detailed below). Furthermore, images were not rated on propensity to facilitate craving, an important variable given that a key purpose of the GNG stimuli is to induce this state if participants are not already craving cigarettes when commencing the training. As such, it was decided that the research team would source a unique set of images for the purposes of the INST study.

For stimuli relating to the target behaviour, it was decided that a variety of smoking-related images would be used as a set of solely images of cigarettes was deemed to likely be too repetitive and not engaging for participants. As such, both inactive stimuli (i.e. the cigarette by itself) and active stimuli (i.e. a person interacting with a cigarette) would be included. Selecting images that are considered alternative behaviours to smoking was less clear than with other health behaviours given that there is no consistent alternative to smoking, unlike with alcohol consumption and unhealthy eating. Other intervention tasks that incorporated non-smoking cues such as cognitive bias modification training used neutral images such as pens, lipsticks, and geometric shapes (Elfeddali, de Vries, Bolman, Pronk, & Wiers, 2016; Kong et al., 2015; Macy, Chassin, Presson, & Sherman, 2015). The need to control for variables such as visual complexity and colour is a notable consideration given that research has suggested that these may affect the emotional processing of stimuli (Bradley, Hamby, Lo, & Lang, 2007;
While stimuli visually similar to cigarettes were considered (e.g. pens) to control for these potential confounds, it was decided that using engaging images would be more beneficial and would serve the purpose of training participants to “approach” an alternative behaviour. In considering motivators for continued smoking, numerous studies have found that the most common motives are reported to be stress relief, enjoyment of smoking, and relief from boredom (Fidler & West, 2009; McEwen, West, & McRobbie, 2008). This is congruent with findings of the Australian National Drug Strategy Household Survey that reported the main reasons for smokers not quitting related to feelings of enjoyment and relaxation (AIHW, 2017). Thus, it was decided that images of relaxation or relaxing activities would serve as the alternative behaviour. However, it remained imperative that both types of images be examined in a sample of the target population to ensure validity.

The primary aim of the study was to determine the most appropriate smoking-related and relaxing stimuli to be incorporated as cues into the cognitive tasks used in the INST protocol. Nine smoking-related images and nine relaxing images were required for the GNG training task, the same number utilised by Lawrence, O’Sullivan, et al. (2015). As outlined in Chapter Five, a smoking-cued Stop Signal Task (SST) would be administered to participants as an independent measure of inhibitory control and as such, an additional eight smoking images were required for this task as using the same images as the training task may confound results.
6.2 Method

6.2.1 Stimuli

Images were downloaded from Google images and *Shutterstock*, an online portfolio of stock photos. Thirty images were selected from an initial pool of 150 images which consisted of different types of smoking-related imagery e.g. ashtrays, people smoking, lighters, cigarette boxes. Images depicting full faces of people were excluded as they were deemed too complex and may confound learning of the smoking cues such that participants may learn to inhibit responses to other people smoking in specific contexts and the effects would not generalise to the participants’ own smoking behaviours and contexts. Unidentifiable hands and mouths were acceptable given that isolated noses, mouths, and hands are processed differently in the brain compared with faces and isolated eyes (Bentin, Allison, Puce, Perez, & McCarthy, 1996), and would thus be sufficiently simple.

The set of 30 relaxing activities were selected from an initial pool of 44. These included images of relaxing activities such as sitting on beaches, exercising, resting, meditating, and watching TV. In order to emphasise that the alternative set of images were intended to be relaxing activities and not mere landscapes or objects, all images included a visual feature of a person who was engaged in the activity (e.g. back of a person’s head). This element further served to control for the human features present in a number of the smoking images.

In deciding the final pools of stimuli to be presented to participants, all images were reviewed by the research team to ensure that there was an adequate range. Where possible, diversity in gender, age, and ethnicity was considered. Images were cropped to 280 x 280 pixels and were excluded if the resolution was unclear.
6.2.2 Participants

Twenty smokers (nine females and eleven males) aged 19-51 years ($M = 29.05$, $SD = 9.00$) participated in this validation study. Potential participants were recruited from social media advertisements and via word of mouth from researchers.

Participants were required to be “regular smokers” who had smoked at least 100 cigarettes in their lifetime and who at present smoked at least one cigarette each day (Centers for Disease Control and Prevention, 2017). Exclusionary criteria included primarily using tobacco in the form of an e-cigarette, not being able to read English, or having a known history of psychosis or brain injury. Seventeen participants identified Australia as their country of birth, two South Africa, and one Brazil.

6.2.3 Measures

*Fagerström Test of Nicotine Dependence (FTND).* The FTND consists of six items that assess dependency on nicotine cigarettes (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). They primarily assess the two factors of smoking in the morning and smoking pattern (Payne, Smith, McCracken, McSherry, & Antony, 1994). It has good test-retest reliability and a Cronbach’s alpha of .64 (Pomerleau, Carton, Lutzke, Flessland, & Pomerleau, 1994). It has an internal consistency of .68 (Etter, 2005).

*Radio button scales.* Images were rated on radio button scales – discrete, Likert-type rating scales that are commonly used in web surveys (see Figure 6.1). The radio button scales used in this study were presented as buttons from 0 to 10 with anchored ends. Two different sets of scales were presented to smoking and relaxing images. Smoking images were rated based on valence of likeability
(“Overall, how much do you like this image?”), craving for cigarettes (“How much does this image make you want to smoke a cigarette?”), and saliency of the cigarette (“How much does the actual cigarette in this image grab your attention?”). Images of relaxing activities were rated based on valence of likeability (“Overall, how much do you like the image?”) and enjoyment (“How enjoyable would you find doing this activity?”).

The basic user interface of radio button scales is considered to be user-friendly and loads easily on web browsers as it does not require JavaScript (Funke, Reips, & Thomas, 2011; Funke, 2016). It has been found to be a reliable scale, yielding high alpha coefficients (Cook, Heath, Thompson, & Thompson, 2001).

![Image of a radio button scale](image)

*Figure 6.1. Example of a radio button scale used in survey.*

### 6.2.4 Procedure

Participants received a website link to *LimeSurvey* where they completed the online plain language statement and survey which took approximately 10 minutes to complete. They were not deprived of smoking for the study.

Participants initially completed demographic information indicating their gender, age, and nationality. They were then required to rate 30 images of
relaxing or enjoyable activities. Participants then completed the FTND, before being asked to rate 30 smoking-related images on the radio button scales. All images were randomised for each participant. Participants were then asked to indicate the types of smoking images that are most effective in inducing cravings, with an optional field to provide qualitative responses. The study was approved by Deakin University Health Ethics Committee (HEAG-H 65_2016).

6.3 Results

The results of the scales were collected from the online database. The mean ratings of each image were calculated and used to rank the images. These are presented in the sections below.

6.3.1 Smoking stimuli

The smoking-related stimuli were primarily chosen based on their ratings by participants who reported moderate or high level of nicotine dependence as measured by the FTND. These were seven participants (four males and three females) aged 22-51 years old ($M = 31.14, SD = 11.36$) with an average FTND score of 6.57 ($SD = 0.79$). The decision to focus on this subset of participants was due to neutral responses yielded by participants who were only mildly dependent as indicated by their FTND score. Additionally, previous studies have found the training task to be particularly effective for people exhibiting poorer inhibitory control (Houben, 2011) which has been associated with high levels of dependence on nicotine (Billieux et al., 2010). As such, the responses of those who indicate greater severity in nicotine dependence would be most relevant in selecting images that are maximally effective for facilitating behavioural change.

Table 6.1 presents the descriptive statistics of the scale ratings. When identifying types of stimuli that tended to induce craving, participants were
permitted to select more than one response. Seven responses indicated “person smoking”, four “two or more people smoking”, four “someone offering another person a cigarette”, two “a cigarette which has been lit”, and two “a cigarette which has not been lit”. Other suggestions included clouds of smoke, personalised environments associated with smoking, and a picture of a cigarette packet.

The images were primarily selected based on their ranking according to the craving scale (see Table 6.2). Results from the other scale rankings and the craving induction question were also considered when finalising the image sets, as was the overall diversity of images.

Table 6.1

*Descriptive Statistics of the Rating Scales for Smoking Images (n = 7)*

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likeability rating</td>
<td>2.43-5.86</td>
<td>3.45</td>
<td>0.73</td>
</tr>
<tr>
<td>Craving rating</td>
<td>1.71-5.86</td>
<td>3.71</td>
<td>0.85</td>
</tr>
<tr>
<td>Attention-grabbing rating</td>
<td>3.57-6.57</td>
<td>4.78</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Images ranked #1-8 according to craving ratings were selected to be incorporated into the GNG task. Image no.18 which was ranked #13 was chosen as the ninth image as there were no images included of male smokers with facial hair. Following this, images for the SST were selected from the pool of remaining images based on their rankings and whether the cigarette in the image clearly
pointed to the left or the right. See Figures 6.2 and 6.3 for the final sets of stimuli for the GNG task and SST respectively.

Table 6.2

*Ranking of Smoking Images According to Induced Craving Levels (n = 7)*

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Image number</th>
<th>Image</th>
<th>Mean rating</th>
<th>Craving*</th>
<th>Likeability</th>
<th>Attention-grabbing</th>
<th>Task allocation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td><img src="image1.png" alt="Image 1" /></td>
<td>5.86</td>
<td>4.00</td>
<td>6.57</td>
<td></td>
<td>GNG</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td><img src="image2.png" alt="Image 2" /></td>
<td>5.00</td>
<td>3.29</td>
<td>4.43</td>
<td></td>
<td>GNG</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td><img src="image3.png" alt="Image 3" /></td>
<td>4.86</td>
<td>3.86</td>
<td>4.71</td>
<td></td>
<td>GNG</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td><img src="image4.png" alt="Image 4" /></td>
<td>4.86</td>
<td>4.86</td>
<td>4.71</td>
<td></td>
<td>GNG</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td><img src="image5.png" alt="Image 5" /></td>
<td>4.86</td>
<td>5.86</td>
<td>4.29</td>
<td></td>
<td>GNG</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>4.57</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
*images ranked from highest to lowest based on this scale

Figure 6.2. Final set of smoking-related stimuli for the Go/No-Go task.
Figure 6.3. Final set of smoking-related stimuli for the Stop Signal Task.

6.3.2 Relaxing stimuli

The relaxing images were ranked based on likeability and enjoyment of activity by all 20 participants. See Table 6.3 for descriptive statistics of the scales.

Table 6.3

Descriptive Statistics of the Rating Scales for Relaxing Images (n = 20)

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likeability rating</td>
<td>4.03-8.03</td>
<td>6.22</td>
<td>1.16</td>
</tr>
<tr>
<td>Enjoyment rating</td>
<td>3.85-8.47</td>
<td>6.60</td>
<td>1.27</td>
</tr>
</tbody>
</table>

Given that the ranking order of the images across both dimensions of likeability and enjoyment were similar (see Table 6.4), the top nine images based on the ranking of likeability were selected as this dimension would be more important for engaging smokers. The overall diversity of images was also
considered when determining the final image set. Figure 6.4 depicts the nine images of relaxing activities selected to be incorporated into the GNG task.
Table 6.4

*Ranking of Relaxing Images According to Likeability (n = 20)*

<table>
<thead>
<tr>
<th>Ranking number</th>
<th>Image number</th>
<th>Image</th>
<th>Mean rating</th>
<th>Task Allocation</th>
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<tr>
<td></td>
<td></td>
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<td>Likeability*</td>
<td>Enjoyment</td>
</tr>
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<td>1</td>
<td>15</td>
<td><img src="image1.png" alt="Image" /></td>
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<td>8.38</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
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<td><img src="image3.png" alt="Image" /></td>
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</tr>
<tr>
<td>4</td>
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<td>8.25</td>
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<td>5</td>
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<td>4</td>
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</table>

*images ranked from highest to lowest based on this scale*
6.4 Discussion

This study identified sets of smoking-related and relaxing stimuli to be incorporated into the response inhibition tasks administered according to the INST protocol. The set of nine smoking stimuli to be incorporated into the GNG training task was selected primarily according to ratings of inducing craving, while the eight images for the SST were selected based on craving ratings and the cigarette placement in the image. The smoking stimuli generally consisted of a white cigarette on the background of darker tones, as these visually contrasted with the smoke from the cigarette.

Three of the smoking images were inactive stimuli where the cigarette appeared by itself, while the remaining six were active stimuli involving human interaction with a cigarette. The comparatively higher rankings of active stimuli were congruent with participant feedback indicating that images of people
smoking were the most craving-inducing type of image. Thus, while the current set of images differs from previous response inhibition training studies in food and alcohol that only included inactive stimuli, it appears that active stimuli are particularly relevant for smoking behaviour. Unfortunately, current literature on smoking cues is limited, with no studies comparing active and inactive smoking cues in relation to cue reactivity or elicitation of appetitive response.

The nine relaxing images for the GNG task depicted people in natural landscapes. These had been rated more favourably than images of other activities such as watching TV or reading. This is consistent with literature finding that viewing images of nature results in diminished stress and physiological arousal (Kjellgren & Buhrkall, 2010; Kweon, Ulrich, Walker, & Tassinary, 2008; Laumann, Gärling, & Stormark, 2003; Ulrich et al., 1991). As such, the set of relaxing images was deemed to be appropriate for the intended purposes.

6.4.1 Limitations

The limitations in this validation process should be noted. The sample size was small, particularly the subset of participants used to determine the sets of smoking stimuli. This may limit the external validity of the images. Given that both active and inactive images are used as smoking cues, it is unknown which type of image would be most effective in improving inhibitory control when incorporated into the task. Literature has differentiated between these two types of images, where the brain processes active stimuli more as they contain people (Bentin et al., 1996), although there is a lack of research regarding the implications of such on emotional reactivity or approach behaviour towards the stimuli. Future studies could compare the effectiveness of GNG training tasks comprising of each type of image.
Furthermore, while efforts were made to maximise the range of images of relaxing activities, seven out of the nine images selected depicted bodies of water, which may elicit neutral or negative feelings in some smokers. This may decrease the effectiveness of the intervention for these participants in redirecting smoking cravings to a favourable alternative behaviour. As previously noted, the relaxing images are more visually complex and colourful than the smoking images, which may interfere with visual processing and response. Additionally, the smoking images were rated low on likeability, congruent with research in the addiction field indicating that the “wanting” motivation of a substance can occur in the absence of hedonistic “liking” (Berridge & Robinson, 2016). However, these ratings were lower than that of the relaxing images and as such, it is possible that the disparity may affect participant response.

6.5 Chapter Summary

The study outlined in this chapter validated the stimuli to be used as cues in the GNG training task and SST. Despite the limitations noted, the stimuli are a vital component of the training task and a strength of the study was using a sample of smokers in the validation process. This ensures that the cues are salient to the target population, thereby increasing the likelihood that the training will be effective in inducing behavioural change. With the completion of the development of all training task and protocol components, the following chapter will present empirical studies piloting the INST program.
Chapter Seven: Piloting of the INST Program

7.1 Introduction

Previous chapters have outlined and reported on the design and procedural considerations pertaining to the INST intervention and protocol development. Piloting these aspects is an essential step in the development process to trial the proposed components. Pilot studies are regarded as a necessary prerequisite to larger trials when examining novel interventions or applications of interventions (Lancaster, 2015; Leon, Davis, & Kraemer, 2011). They are purported to be vital in preventing wastage of funds and mitigating the risk of investments in more expensive, full-scale trials (Morgan, Hejdenberg, Hinrichs-Krapels, & Armstrong, 2018). Pilot studies can explore questions relating to the sample characteristics, recruitment, management of the intervention, treatment adherence, and data collection methods (Lancaster, Dodd, & Williamson, 2004; Tickle-Degnen, 2013). Examining such parameters of study design and examining whether components of the study design can work together successfully are typically the main objectives of pilot studies as opposed to measuring the study outcome or testing hypotheses (Lancaster, Dodd, & Williamson, 2004; Leon et al., 2011). By using a pilot study as a trial version of a randomised controlled trial (RCT), it can yield information regarding not only the feasibility of the project, but also whether the larger full-scale study is warranted (Lancaster et al., 2004; Leon et al., 2011). As these results can lead to changes in study design, it increases the chance of successful implementation of RCTs (Lancaster, 2015; Leon et al., 2011).

Additionally, exploring acceptability of an intervention to participants is an important component of pilot studies. Particularly relevant is that likeability of an intervention has been found to increase adherence in web-based interventions
(Oinas-Kukkonen & Harjumaa, 2009). This can be assessed through qualitative measures such as interviews with participants regarding their experience of the intervention, including facilitators and barriers to engaging with the treatment (Cooper et al., 2014). Indeed, the involvement of participants who are the intended users of an intervention has been identified as an important aspect of health research and regarded as beneficial in contributing to future iterations of an intervention (Boote, Telford, & Cooper, 2002; Sanders & Kirby, 2012; Wolpin & Stewart, 2011). Such consideration of participation feedback in the development process of an intervention has been found to increase usability (Bridgelal Ram, Grocott, & Weir, 2008) and effectiveness (Fennell et al., 2017), and assist in its implementation (Wolpin & Stewart, 2011). Importantly, it also enhances external validity by ensuring the intervention is feasible and acceptable in a real-world context (Wallerstein & Duran, 2010), a vital aspect in relation to INST given its intended purpose of being easily accessed by smokers independently.

Two single-arm pilot studies were conducted to examine the feasibility and acceptability of the INST protocol. A mixed methods approach was adopted for both pilot studies. That is, quantitative data was collected relating to aspects such as sample characteristics and adherence, and qualitative methods enabled the research team to acquire a detailed understanding of participants’ experiences of the intervention and collate feedback and suggestions relating to future iterations of INST. The feasibility of the intervention and the proposed study protocol were examined, including task design, number of training sessions, measurement tools, and specifications relating to the process of smoking cessation. The studies enabled an assessment of both the intervention and the trial methods followed by subsequent amendments to improve the robustness of the methodology. Results
were also used to determine whether a clinical trial of the effectiveness of the intervention is warranted.

The first pilot study was conducted based on the study design outlined in Chapter Five which will be detailed in the methods section 7.2.1 below. Amendments to the research protocol and intervention design were made before a second pilot study was conducted to examine the feasibility and acceptability of the new iteration of the intervention and study protocol. The second pilot study also examined preliminary smoking cessation outcomes of the intervention. This was not possible in the first pilot study due to a technical error that was not discovered until after the completion of data collection. Each pilot study and amendments made are reported on below, followed by an integrated discussion of the findings.

7.2 Pilot study 1

7.2.1 Method

7.2.1.1 Participants. Potential participants were recruited by word of mouth, social media, and flyers around the community (e.g. shopping centres, universities, libraries). Interested individuals were requested to email the research team, following which a phone call was arranged to screen for eligibility. Inclusion criteria required participants to be aged 18-60 years old and to have completed Year 9 at a mainstream school or equivalent. They would smoke at least 10 cigarettes daily on average and would have been regular smokers for the previous 12 months. They must not have been abstinent from nicotine for longer than two weeks in the past three months. They would also meet DSM-5 criteria for Tobacco Use Disorder (TUD) of moderate or severe severity, and would not be dependent on other substances. Participants were excluded if they primarily used
e-cigarettes, were on psychotropic medications, or had a history of traumatic brain injury or loss of consciousness.

Fifty-eight individuals expressed interest in participating in the study and 47 were assessed for eligibility over the phone. Twenty-nine individuals met the inclusion criteria, of which 16 agreed to participate. As presented in Figure 7.1, there were participants who completed the phone call component of the post-intervention or follow-up time-points but did not complete the questionnaires online.
Figure 7.1. Flow chart of participant recruitment and data collection in pilot study.
7.2.1.2 Measures. The schedule and order of the administration of measures is outlined in Table 7.1. Questionnaires were administered first, followed by cognitive tasks. Smoking-related measures were administered last in sequence given their priming effects.

Table 7.1

Schedule of Measurement Administration
<table>
<thead>
<tr>
<th>Study period</th>
<th>Baseline</th>
<th>Training period</th>
<th>Post-intervention</th>
<th>Two-week follow-up</th>
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<tr>
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<tr>
<td>Qualitative feedback questionnaire</td>
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</tbody>
</table>

AUDIT = Alcohol Use Disorders Identification Test; BIS-11 = Barrett Impulsiveness Scale; DASS-21 = Depression Anxiety Stress Scales – 21; FTND-R = Fagerström Test of Nicotine Dependence – Revised; IAT = Implicit Association Test; QSU-Brief = Questionnaire of Smoking Urges – Brief; SPSRQ
= Sensitivity to Punishment and Sensitivity to Reward Questionnaire; SST = Stop Signal Task; TLFB = Timeline Followback.

**Questionnaires**

*Barratt Impulsiveness Scale (BIS-11).* The BIS-11 measures trait impulsivity (Patton et al., 1995). It has 30 items that measure three factors: 1) Motor Impulsiveness, 2) Nonplanning Impulsiveness, and 3) Attentional Impulsiveness. Items are rated from 1 to 4, with high scores indicating higher impulsivity. The BIS-11 has been shown to have good internal consistency, with Cronbach’s alphas ranging from .79 to .83 in populations of university students, substance users, psychiatric patients and prison inmates (Patton et al., 1995).

*The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ).* The SPSRQ measures two dimensions of Gray’s model of personality, anxiety or sensitivity to punishment (SP scale) and impulsivity or sensitivity to reward (SR scale; Torrubia, Ávila, Moltó, & Caseras, 2001). It contains 48 items that are rated using dichotomous responses of “yes” or “no”. The reliability of both subscales are good, with Cronbach’s alphas of .81 for SP and .74 for SR (O’Connor, Colder, & Hawk, 2004).

*Depression Anxiety Stress Scales-21 (DASS-21).* The DASS-21 consists of 21 items that assess dimensions of depression, anxiety, and stress (Henry & Crawford, 2005). Each of the three subscales comprise of seven items that are rated on a 4-point Likert scale. It displays good internal consistency with a Cronbach’s alpha of .93 (Henry & Crawford, 2005) and has been found to be a valid measure in clinical and non-clinical populations (Antony, Bieling, Cox, Enns, & Swinson, 1998).
Alcohol Use Disorders Identification Test (AUDIT). The AUDIT is a screening tool for harmful consumption of alcohol (Saunders, Assland, Babor, de La Fuente, & Grant, 1993). It has 10 items scored from 0 to 4 measuring alcohol intake, alcohol dependency, and issues resulting from alcohol consumption. The AUDIT has high internal consistency (Cronbach’s alpha of .80) and has excellent sensitivity and specificity (de Meneses-Gaya, Zuardi, Loureiro, & Crippa, 2009).

Fagerström Test for Nicotine Dependence – Revised (FTND-R). The FTND-R comprises of six items that assess dependency on nicotine cigarettes (Heatherton et al., 1991; Korte, Capron, Zvolensky, & Schmidt, 2013). It consists of the same items as the FTND (Heatherton et al., 1991), but replaces dichotomous response choices with a 4-point Likert response choice on three items. The FTND-R primarily assesses the two factors of morning smoking and smoking pattern (Payne et al., 1994). Compared with the FTND, it has an improved convergent validity and an improved internal consistency of .69. The total score yielded ranges from 0-16 whereby higher scores indicate a higher level of nicotine dependency.

Timeline Followback (TLFB). The TLFB is a calendar-based assessment that measures recent use of alcohol, cigarette, marijuana, and other drugs by asking participants to retrospectively estimate the frequency of their usage (Robinson, Sobell, Sobell, & Leo, 2014; Sobell & Sobell, 1992). The time period of estimation can vary, ranging from seven days to two years prior to the interview date. It was used in this study to examine use of cigarettes and nicotine replacement therapy (NRT). The TLFB has been found to correlate with daily monitored smoking calendars ($r = 0.67-0.97$; Brown et al., 1998) and self-reported estimates of number of daily cigarettes ($r = 0.81-0.85$; Gariti, Alterman, Ehrman,
& Pettinati, 1998). It has demonstrated good test-retest reliabilities for cigarette smokers who retrospectively reported several aspects of their use up to 360 days prior to the interview ($r = 0.65-0.95$; Robinson, Sobell, et al., 2014).

**Questionnaire of Smoking Urges-Brief (QSU-Brief).** The QSU-Brief measures craving to smoke (Cox, Tiffany, & Christen, 2001). It uses 10 items to assess two factors: 1) the desire and intention to smoke due to the perceived rewarding nature of smoking and 2) the urge to smoke due to anticipated relief from negative affect and withdrawal symptoms. It displays good reliability, with Cronbach’s alphas for each factor of .92-.97 in a lab setting and .78-.89 in an outpatient clinic setting.

*Slider scales.* Slider scales are a popular rating method used in computerised surveys. Using this user interface, participants were asked to rate their craving (“Currently, how much are you craving a cigarette?”), motivation (“Currently, how motivated are you to quit smoking?”), and self-efficacy (“Currently, how confident are you in your ability to quit smoking?”).

The design of the scale used in this study was a plain horizontal line with the left anchor labelled “not at all” and the right anchor labelled “extremely”. The line was comprised of 100 units and responses were converted to a number from 0 to 100, rounded to two decimal places. A slider bar was initially presented at the left end of the scale and participants clicked and dragged the bar along the scale to indicate their response. To differentiate responses of those who did not answer the question and those whose ratings were genuinely at the left end of the bar, participants were required to click the bar to activate the scale and then drag the bar as necessary.
Slider scales are considered to be more engaging and less repetitive than surveys using a radio button user interface (Roster, Lucianetti, & Albaum, 2015; Stanley & Jenkins, 2007) while still yielding similar responses (Arnau, Thompson, & Cook, 2001). They are regarded as a psychometrically acceptable measurement (Cook et al., 2001).

**Cognitive tasks**

The Implicit Association Task (IAT), stimulus evaluation test, and Stop Signal Task (SST) described in Chapter Five are briefly summarised below.

*The Implicit Association Test.* The IAT involved categorising stimuli and words into two target categories (“smoking” and “non-smoking”) and two attribute categories (“pleasant” and “unpleasant”). The premise of the task is that respondents would have been able to sort categories quicker if there was a strong association between the categories compared with if there was a weaker association. Sixteen images were used for the target categories: eight images of people smoking and eight corresponding images of the same people not smoking. The attribute categories used pleasant and unpleasant words (Swanson et al., 2001). The eight pleasant words were “cuddle”, “happy”, “smile”, “joy”, “warmth”, “peace”, “paradise”, and “love”. The eight unpleasant words were “pain”, “awful”, “disaster”, “grief”, “agony”, “brutal”, “tragedy”, and “bad”.

The IAT contained five blocks. Blocks 1 and 2 were practice blocks that required the categorisation of smoking/non-smoking images and pleasant/unpleasant words respectively. Block 3 was a test block that presented all images and words. One target category and one attribute category was categorised using one key and the other target category, and attribute category was
categorised with an alternative key. Blocks 4 and 5 were the same as blocks 1 and 3 but with the response keys for smoking and non-smoking images reversed.

Initial assignment of response keys to smoking and non-smoking target categories was counterbalanced for half the participants. Presentation of all images and words was randomised and alternate in sequence in test blocks 3 and 5. The combination of categories presented in the test blocks was also counterbalanced such that “smoking + unpleasant” was the first combination for half the participants, and the other half received “smoking + pleasant”.

Participants were instructed to complete the task as fast as they could while being as accurate as possible. The category words were presented at the top left and right corners of the screen and participants used corresponding “C” and “M” keys to categorise the stimuli that appeared in the middle of a white background. A red “X” appeared if the response is incorrect and the stimulus remained on screen until participants indicated the correct response. The inter-stimulus interval was 250ms.

*Stimulus evaluation test.* Participants rated the likeability of the smoking and relaxing images used in the Go/No-Go (GNG) task. For each image, participants were presented with the question, “how much would you like to do this activity right now”. The scale was in the form of a horizontal line of 100 units with the left end of the scale labelled “not at all” and the right end labelled “extremely”. Responses were calculated to the nearest integer between 1 and 100.

*Stop Signal Task.* At the start of each SST trial, a fixation cross appeared on the screen for 500ms, before an image of a cigarette (the “go” stimulus) appeared for 1000ms, followed by a blank white screen for 1000ms (the inter-stimulus interval). Participants indicated whether the lit end of the cigarette was
pointing to the left or right by pressing the keys “C” or “M” on the keyboard respectively. The 16 images used in the task was comprised of eight pairs of images, where one image of the pair was a cigarette pointing to the left, and the second image was its mirror image pointing to the right. Each of the 16 images was presented a total of 12 times and was randomised across trials and between participants. On 25% of the trials, a stop signal appeared across the image in the form of two horizontal red lines to signal that the participant was to withhold their response. The stop signal initially occurred at 250ms after the initial appearance of the image. If the participant successfully inhibited their response, the stop signal duration was increased by 50ms at the next “stop” trial when the stop signal was programmed to appear, effectively increasing the difficulty of inhibition. If the participant was unsuccessful in inhibiting their response, the duration was decreased by 50ms, such that inhibition at the next “stop” trial was easier. The task aimed for the participant to correctly inhibit their responses on 50% of the “stop” trials.

The task consisted of a practice block and a test block. The practice block consisted of ten trials where the stop signal appeared on 50% of trials while the test block consisted of 200 trials where the stop signal appeared on 25% of trials.

*Qualitative feedback interview*

Participants were verbally administered a semi-structured interview comprising of questions relating to their experience of the intervention. It addressed feasibility and specific aspects of the program protocol, including length of intervention and barriers to completion of sessions (see Appendix A for full questionnaire). Participants were strongly encouraged to be honest in their
opinions as the feedback would assist in improving future iterations of the intervention.

7.2.1.3 Go/No-Go training task. The GNG training task presented nine smoking images, nine relaxing images, and 18 filler images of clothing individually within a rectangular frame for 1250ms. Participants were instructed to indicate as quickly as they could whether the image was positioned to the left or the right of the frame by using the keys “C” and “M” respectively. The inter-stimulus interval was 1250ms. The rectangular frame appeared bolded on half of the trials and participants were instructed to withhold their response during these trials. These are termed “no-go” trials while trials where the frame is unbolded are termed “go” trials. The smoking images were consistently paired with “no-go” signals while the relaxing images were consistently paired with “go” signals. “No-go” signals appeared on 50% of the filler images trials.

Each training session consisted of six blocks where each of the 36 images were presented once per block. At the end of each block, participants received feedback detailing average reaction time and percentage of correct responses for the purposes of maintaining engagement and motivation. It also reiterated the instruction for participants to respond to images as quickly as they could.

7.2.1.4 Procedure. The intervention required participants to complete training sessions over a period of four weeks. They were requested to complete five training sessions a week during the first two weeks and two training sessions a week during the last two weeks. Overall, participants had a total of 14 training sessions to complete.

Eligible participants met with a researcher for an hour during which they completed a consent form, the battery of questionnaires and cognitive tasks, and
the first training session. The structure of the intervention was explained and participants were instructed to adhere to specific guidelines as outlined in a hard-copy calendar provided to them (see Figure 7.2). The training link and dates of follow-up calls were provided on the back of the calendar. This information was also written on an INST business card that participants could keep in their wallet for easy access. Participants were also encouraged to provide a quit date or a date on which they planned to reduce the number of cigarettes smoked. Following the meeting, participants were also emailed the link to the training task and the date of the first follow-up phone call.

![Participant Timeline Calendar](http://psych.hosted-sites.deakin.edu.au/inst/pilot2/training/)

Figure 7.2. Example of a training calendar provided to participants.

Each time participants accessed the training link by logging in with their email address, they were shown a calendar visually depicting the number of sessions they had already completed. They were then required to manually input
the days or hours since their last cigarette and answered three slider questions regarding craving, motivation, and confidence in quitting. They completed the training session on the next screen before answering the same slider questions again post-training. Participants received automated text messages twice a week reminding them to complete their sessions.

At the end of the intervention period, participants received a phone call from a researcher during which they completed the TLFB and qualitative feedback verbally. Depending on the length of participant responses, the interview lasted between 10-20 minutes. They were then sent an email link to complete the same battery of questionnaires that had been completed at baseline. Participants received another phone call at two-week follow-up to complete the TLFB and provide further observations regarding their smoking. They were also required to complete the same battery of questionnaires online, which took approximately 20-30 minutes. Participants who did not answer the researcher’s phone calls at follow-up time-points received text messages and emails, with later contact attempts offering to obtain brief feedback over email. Participants who did not complete the questionnaires within 24 hours received up to three email reminders.

Following completion of all components of the study, participants were mailed a $20 Coles/Myer gift card as compensation for the completion of questionnaires. Ethical approval for this study was granted by the Deakin University Human Research Ethics Committee (2015-298).

7.2.1.5 Data analysis. Descriptive statistics of the GNG training calculated the accuracy percentage, number of errors, and reaction time. Feasibility and acceptability of the INST program was investigated through participants’ adherence to the training schedule in addition to the qualitative feedback gathered.
from the phone interview at post-intervention. The findings were integrated to yield a general summary of conclusions. All analyses were calculated with SPSS Statistics version 23 and Microsoft Excel.

7.2.2 Results

Participant ages ranged from 19-53 years old. Table 7.2 presents participant demographics and clinical characteristics.
Table 7.2

*Baseline Demographics and Clinical Characteristics of Participants (n = 16)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ($M, SD$)</td>
<td>35.50 (12.24)</td>
</tr>
<tr>
<td>Gender (male/female)</td>
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<td>Location of birth</td>
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<td>Middle East</td>
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<tr>
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<td>Year 12 or equivalent</td>
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<tr>
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<tr>
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<tr>
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<tr>
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<tr>
<td>$25,001- $45,000</td>
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<tr>
<td>$45,001- $65,000</td>
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<tr>
<td>$65,001- $85,000</td>
<td>3</td>
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<td>Income Range</td>
<td>Count</td>
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<td>$105,001- $125,000</td>
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</table>

Relationship status

- Single: 8
- De facto/long term partner: 2
- Married: 4
- Divorced: 1
- Widowed: 1

Cigarettes per day (M, SD) 14.52 (4.88)

FTND-R (M, SD) 6.31 (2.41)

Attempted to quit smoking in past 12 months (at least 24 hours abstinence) 10

Average number of quit attempts in past 12 months (M, SD) 2.7 (1.25)

Motivation to quit as rated out of 100 (M, SD) 76.31 (24.32)

Age when first started smoking daily (M, SD) 17.81 (3.41)

At least one parent who was a regular smoker: 13

Another regular smoker in household: 4

At the completion of the pilot study, it was discovered that there was a technical error where the smoking-related stimuli only appeared for the first two blocks of each training session and the last four blocks were comprised of the
filler imagery of clothing. Albeit unfortunate, this was deemed to not invalidate the results given this pilot study focused on the feasibility of the study in relation to recruitment and adherence to sessions as opposed to effectiveness of the training.

In relation to management of participant recruitment, there was an average of 2.38 days between the date of initial contact from the participant and the date of the eligibility screening phone call. There were 5.94 days on average between the date of a participant’s phone call and their scheduled face-to-face meeting. Thus, participants did not have to wait for a prolonged period of time between their expression of interest and enrolment into the study.

7.2.2.1 Go/No-Go training performance. The data of one participant was not included as their data was invalid. Participants engaged with the training well, yielding a mean accuracy of 98.39% and an overall average reaction time of 579.52ms on “go” trials. Participants made an average of 5.69 errors each session ($SD = 3.89$, range = 0.54-14.5), specifically 1.43 omission errors and 4.06 commission errors. Unfortunately, mean reaction times and number of errors could not be calculated separately for different types of images as the data output did not distinguish between the image types in each trial. As such, stimulus-specific learning effects could not be examined.

Data indicated that when participants completed the training, there was an average of 11.54 hours since their last cigarette ($SD = 29.61$, range = 0.5-216).

7.2.2.2 Feasibility. The number of sessions completed by participants over the intervention period in represented in Figure 7.3 by coloured blocks. The total number of sessions completed ranged from 1-14 ($M = 6.88$, $SD = 5.54$). Of
the participants who completed more than one session, the mean number of sessions completed was 9.55 (SD = 4.57).

All participants who completed only the first training session at the face-to-face meeting were lost at follow-up (n = 6). There was only one participant (#4) who completed an additional training session at home who was also lost at follow-up.

Of note, participant #18 had a two-week break between their first two sessions and their remaining sessions. At their scheduled post-intervention phone call, they requested to continue the intervention if possible as they had only completed two training sessions due to personal circumstances. Following discussion with the primary supervisor, the participant was allowed to complete their remaining sessions over 12 additional days.

No adverse effects were reported relating to the completion of the battery of questionnaires and cognitive tasks at each time-point.
<table>
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<th>Participant no.</th>
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<th>Week 2</th>
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*Participant had a two-week break between the first two sessions and the remaining sessions.

Figure 7.3. Number of training sessions completed by pilot study 1 participants.

Qualitative feedback was obtained from 10 participants. In relation to the duration of the program and number of sessions, seven participants reported that completing all 14 training sessions was feasible. Identified barriers to completing sessions included busy schedules, forgetting to complete the training, and the inconvenience of needing to use a computer instead of a mobile device. Some participants highlighted that motivation to quit was an important component as it influenced whether they made time to complete the training sessions. A number of participants also observed that because the training had occurred during the
Christmas and end of year period, increased commitments and stressors may have interfered with their ability to adhere to the intervention.

Modification suggestions to the intervention program included increased sessions particularly in the first two weeks. This was illustrated in the following feedback:

“I think doing the first two weeks is better. Doing it every day would’ve been good, especially when you’re actively quitting. Or leaving it open for the person to decide.” – Participant #18

“The more you do the more effective it was getting. I would rather more sessions.” – Participants #14

### 7.2.2.3 Experience of the intervention.

Participants generally provided positive feedback regarding their experience of INST, reporting that the GNG training was easy to complete and was not time-consuming. For instance:

“I had a positive experience of the whole program itself...my stressful situation did not change (co-parenting with ex-partner), more things also occurred during this time (car accident, health procedures, etc). I should’ve been smoking more but didn’t feel the urge to smoke...I was surprised every day with how effective it was...I didn’t think I would quit smoking.” – Participant #6

In relation to the training itself, four participants felt that the training was mundane due to its repetitive nature. Several participants reported that the pictures of cigarettes initially made them want to smoke more but that this subsided as the intervention progressed. Three participants experienced technical difficulties that
were resolved by the website developer promptly after reporting the issue to the research team.

**7.2.2.4 Facilitators of adherence.** Aids of adherence were evaluated to better understand aspects of the program protocol that may have assisted in facilitating adherence. While the content of the face-to-face meeting was viewed as clear and straightforward, almost all participants rated the meetings as necessary as it helped engage participants in the study and ensure that they were completing the training correctly. The SMS reminders were also rated as helpful by 8/10 participants in prompting completion of training sessions, with most approving the frequency of two messages per week.

The training calendar and card were deemed as less necessary but some participants still regarded the calendar as helpful in keeping track of intervention weeks.

**7.2.2.5 Perceived effects on smoking.** Participants were asked to rate how effective they considered the training in helping them quit smoking. On a scale of 0 (“not at all effective”) to 10 (“really effective”), one participant rated it 0/10, three rated it 5/10, one rated it 6/10, four rated it 7/10, and one rated it 10/10. Several participants observed that the intervention had helped them reduce the number of cigarettes smoked and felt that they were on the “right track” to quitting, while others felt it had made them think more seriously about quitting in the near future.

Eight of the participants were able to identify the mechanisms of the intervention, observing that it encouraged the formation of a negative association with cigarettes. Seven participants believed that this had a direct impact on their smoking. For example:
“It was to do with associations – triggering the brain so that when you look at the bold black box you see a cigarette and say ‘no’. It’s creating a negative and positive pathway in your brain...you’re responding to positive images and not responding to negative images you get. But even though I figured it out I found it effective.” – Participant #14

Three participants (#15, #18, #21) reported that they had commenced using NRT during the intervention period while they continued to complete training sessions. However, Participant #18 observed that NRT had not previously been effective and believed the training had contributed a unique effect to her ability to quit.

Initial expectations regarding the intervention were varied, with a majority of participants having no expectations while some were expecting to have reduced their smoking or to have quit. This did not appear to be related to participants’ evaluations of intervention effectiveness.

7.2.2.6 Quit/reduction dates. Quit dates selected by participants varied but were typically at the start or end of specific intervention weeks (e.g. start of week 3). Many participants did not adhere to their quit date as they felt unprepared on the day or did not remember the date selected. Several participants purposefully opted to gradually reduce the number of cigarettes smoked over time, commencing on an unspecified day. There were mixed opinions from participants regarding who should set the quit date. Four participants stated that they preferred to set their own date, while only one stated it would be better for researchers to allocate a set quit date. Others did not have an opinion or believed setting a quit date in general would create counterproductive pressure. The following excerpt was provided by a participant who believed they should set their own dates:
“Personally, I think letting participants make their own date would be better because if you were to say to me that I had to quit on a particular day, I would think ‘what if I don’t want to’ and rebel a bit. It’s a big thing for people to quit smoking because, like for me, I’ve been smoking since I was 13.” – Participant #18

7.2.2.7 Other feedback. In relation to general feedback relating to the intervention, some participants suggested the training should be accessible from mobile devices for increased convenience and personalised images would assist in increasing the relevance of the training.

7.2.3 Discussion

This pilot study investigated the feasibility and acceptability of the INST program in 16 treatment-seeking smokers. The intervention was generally well-received by participants, with many reporting a positive experience with both the training and the overall intervention program. The training was deemed easy to complete, with results suggesting that participants completed the training task well, yielding a mean accuracy of approximately 98%.

Participants reported that the training was feasible to complete in a real-world context. However, adherence rates were lower in comparison to previous web-based response inhibition interventions. Despite not using reminders, Lawrence, O’Sullivan, et al. (2015) reported that 82% of participants completed all four training sessions, with half completing them on consecutive days as requested. In contrast, participants in Forman et al. (2016) and Veling et al. (2014) received reminders to complete sessions; Forman et al. reported that on average, participants only completed half of the three online booster sessions requested.
over consecutive days while Veling et al. did not report adherence to the training. Allom and Mullan (2015) did not report on adherence rates or whether they used reminders. The rates of adherence in the studies by Lawrence, O’Sullivan, et al. and Forman et al. may have been higher than the present pilot study due to their comparatively shorter intervention periods.

In examining patterns in recruitment and retention, there were 10 eligible participants who could not be contacted following the eligibility phone call and six participants who were lost at follow-up following the face-to-face meeting. While reasons for disengagement could not be established due to lack of feedback from these groups, it may have been the result of diminished motivation to quit smoking or commit to a four-week intervention. Despite the relatively short periods of time between the initial contact from participants, the screening phone call, and the face-to-face meeting, it may have been inadequate in capitalising on fleeting motivation, a factor that was highlighted by participants in the qualitative feedback as important to adhering to the training. Furthermore, the festive time of year during which the study occurred may have also exacerbated the need to prioritise other commitments in their lives. This is supported by participant reports that common barriers to intervention adherence related to time constraints due to other commitments, forgetting to complete the training, and the inconvenience of not being able to access the training on a mobile device.

Interestingly, four participants rated the training at least 7/10 in terms of effectiveness despite the technical error in the task where they were only exposed to smoking-related images in two of the six blocks each session. While this alludes to a possible placebo effect, it may be possible that given the repeated
number of times they completed the sessions, they nevertheless experienced an intervention effect from the cumulative smoking-cued training blocks.

While there was concern regarding the smoking-related images eliciting desire to smoke or cravings as established in literature (Gamito et al., 2014; Heishman, Lee, Taylor, & Singleton, 2010; Shiffman et al., 2013), some participants reported that any desire to smoke provoked by the intervention subsided over time. This is congruent with literature examining other smoking cessation interventions that also incorporate cues, such as cue exposure therapy (Pericot-Valverde, Secades-Villa, Gutiérrez-Maldonado, & García-Rodríguez, 2014; Unrod et al., 2014) or mindfulness based therapies (Witkiewitz, Bowen, Douglas, & Hsu, 2013), which report attenuated cravings over the duration of the intervention.

7.2.3.1 Modifications made in response to findings

Recruitment and retention. Overall, the conversion rate of expressions of interest to eligible participants who agreed to participate was low at 27.59%. As such, additional methods were considered to improve the recruitment process. In consultation with the university’s media liaison team, a brief segment on the local news was produced to advertise the study to a wider range of potential participants for the second pilot study. The contents of this segment are detailed further in the methods section of the study (7.3.1.).

Aids in adherence. Facilitators in intervention adherence were generally well-received, with the face-to-face meeting and SMS reminders deemed helpful. While the INST card was discarded in the second pilot study due to neutral feedback, the training calendar was retained as it was regarded as useful by some
participants and also detailed the guidelines regarding how to complete the training.

*Go/No-Go training task.* The data output for the GNG training task was modified such that the type of image presented on each trial was identifiable (i.e. smoking, relaxing, or filler). This would enable examination of stimulus-specific learning effects similar to that of Lawrence, O’Sullivan, et al. (2015) and Stice, Yokum, Veling, Kemps, and Lawrence (2017).

Given feedback that the training could be experienced as boring and impact negatively on continued adherence, the training instructions were modified to suggest to participants that they should attempt to beat their own reaction time with each subsequent training block. This aimed to add an element of interest and game-like competitiveness, in line with evidence suggesting that digital game-based interventions are engaging and motivating with their intention to challenge users (Li, Theng, & Foo, 2014; Schuurmans, Nijhof, Vermaes, Engels, & Granic, 2015).

*Intervention duration.* In relation to the duration of the intervention, participants generally requested an increased number of training sessions be made available, specifically in the first two weeks. As such, it was decided that participants would complete a training session every day for 14 consecutive days in the next iteration of the intervention. The total number of training sessions was not increased due to adherence rates suggesting that most participants had difficulty completing all 14 sessions over the four weeks. However, it was thought that by increasing the frequency of sessions within a shorter time period, adherence to the training sessions would be improved and the feedback from participants would be adequately addressed.
**Quit/reduction dates.** Results relating to quit dates were difficult to compare as many did not adhere to their selected date. These were typically chosen to be at the end of an intervention week. Nevertheless, most participants believed that participants should select their own quit dates. To provide an element of uniformity where possible, researchers continued to encourage participants to select a quit/reduction date that best suited them, but also suggested a date at the end of the first intervention week as a possible option. It was thought that this time would allow participants to experience the effects of the first week of training, while then being supported by the second week of training in their quit attempt or reduction in cigarettes. This is congruent with findings of a web-based smoking intervention indicating that participants who set a quit date for earlier in the intervention period had comparatively higher levels of confidence in their ability to quit and also benefited from the support provided by the remainder of the intervention in relation to maintaining abstinence (Cobb et al., 2014).

**Evaluation of stimuli.** Due to the technical error, the results of the IAT and stimulus evaluation test could not be compared. However, following the data collection for this present study, the meta-analysis by Jones et al. (2016) had been published suggesting that although there was no significant supporting evidence for the devaluation hypothesis as measured by implicit measures, explicit measures may be a more sensitive measure. As such, the second pilot study only used the stimulus evaluation test to measure attitudes as this also reduced the burden of participation on participants.

**7.2.3.2 Conclusion.** A second pilot study was conducted following the above modifications to further assess feasibility and acceptability. It also
examined the effectiveness of the training task following the correction of the technical error.
7.3 Pilot Study 2

The primary aim of this study was to investigate the feasibility and acceptability of the INST program following modifications made after the first pilot study. Secondary outcomes related to preliminary results on smoking outcome and underlying mechanisms of the training task.

7.3.1 Method

7.3.1.1 Participants. The same inclusion criteria were applied to participants as in the first pilot study. In addition to the recruitment methods outlined previously, participants were also recruited from a brief news segment on the local television channel. This featured one of the participants from the first study detailing the positive impact that INST had had on their smoking, in addition to an interview with the chief researcher discussing the need for further investigation into the intervention. This was approved and managed by the university’s media liaison team. The first 15 people who showed interest following the media interview were invited to participate in the pilot study and were assessed for eligibility. Of these participants, 13 participants aged 19-58 were eligible and agreed to participate. Figure 7.4 depicts the flow chart of participant recruitment.
Figure 7.4. Flow chart of participant recruitment and data collection in pilot study.

2.

Expressions of interest ($n=15$)

Assessed for eligibility ($n=15$)

Excluded ($n=2$)
- Not meeting inclusion criteria ($n=1$)
- Declined to participate ($n=1$)

Completed face-to-face meeting ($n=13$)

Post-intervention Follow-up

Completed TLFB and qualitative feedback via phone ($n=11$)
Completed questionnaires via online link ($n=11$)
- Lost to follow-up ($n=1$)
- Withdrew ($n=1$)

Two-week Follow-up

Completed TLFB via phone ($n=10$)
Completed questionnaires via online link ($n=7$)
- Lost to follow-up ($n=1$)
7.3.1.2 Measures. The same measures from the first pilot study were used in this study and were administered to participants in the same sequence. The questions on the qualitative feedback questionnaire were modified from the previous version; specifically, questions regarding aids of adherence were removed and questions relating to craving and smoking during stressful situations were added (see Appendix B for questionnaire).

7.3.1.3 Procedure. The screening process and face-to-face meeting remained unchanged from the first study. Modifications as outlined in the previous discussion section were applied. Primarily, participants were requested to complete sessions every day over 14 consecutive days.

7.3.1.4 Data analysis. Methods of data analysis were the same as in the first study to address the first aim of feasibility and acceptability. Additionally, following the modification of the GNG data output, task performance over time and stimulus-specific learning effects were examined using the same approach as Lawrence, O’Sullivan, et al. (2015) and Stice et al. (2017). The reaction time of “go” trials towards filler images (i.e. 50% “go” and “no-go” contingency) was compared with the reaction time of “go” trials towards relaxing images (i.e. 100% “go” contingency). The commission errors towards filler images was also compared to commission errors towards smoking images (i.e. 100% “no-go” contingency). The reaction times and errors of the first and fourth training sessions were computed to allow for comparison with the results of Lawrence, O’Sullivan, et al. (2015) who only had four training sessions. Learning effects are evidenced by faster reaction time towards relaxing images and fewer errors towards smoking images due to the 100% “go” and “no-go” contingencies respectively.
Secondary outcomes related to the number of cigarettes smoked and craving ratings. In addition, the stimulus evaluation test ratings and SST data from each time-point were analysed to investigate the underlying mechanisms of the GNG training. The primary outcome variable of the SST, the stop signal reaction time (SSRT), was calculated by subtracting the mean stop signal delay (SSD) from the mean reaction time on “go” trials. Lower SSRT indicates better response inhibition. At each time-point, participant data was removed if the “stop” trial accuracy was not between 40-60% and the “go” trial accuracy was less than 70%. All data from a participant was excluded if their baseline data was excluded, resulting in the exclusion of two participants. Given that this is a pilot study with a small sample size, results of the outcome measures are presented descriptively.

7.3.2 Results

Table 7.3 shows the demographics and baseline clinical characteristics of participants.
Table 7.3

Baseline Demographics and Clinical Characteristics of Participants (n = 13)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ($M, SD$)</td>
<td>44 (11.99)</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>9/4</td>
</tr>
<tr>
<td>Location of birth</td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>12</td>
</tr>
<tr>
<td>Europe</td>
<td>1</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Left prior to Year 12</td>
<td>3</td>
</tr>
<tr>
<td>Year 12 or equivalent</td>
<td>3</td>
</tr>
<tr>
<td>Certificate level</td>
<td>1</td>
</tr>
<tr>
<td>Diploma/advanced diploma</td>
<td>3</td>
</tr>
<tr>
<td>Bachelor degree</td>
<td>1</td>
</tr>
<tr>
<td>Graduate diploma/graduate certificate</td>
<td>1</td>
</tr>
<tr>
<td>Postgraduate degree</td>
<td>1</td>
</tr>
<tr>
<td>Paid employment</td>
<td>8</td>
</tr>
<tr>
<td>Personal income</td>
<td></td>
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<td>3</td>
</tr>
<tr>
<td>$105,001-$125,000</td>
<td>1</td>
</tr>
<tr>
<td>Income Level</td>
<td>Count</td>
</tr>
<tr>
<td>----------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Over $145,000</td>
<td>2</td>
</tr>
<tr>
<td>Prefer not to say</td>
<td>1</td>
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</table>

Relationship status

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<td>2</td>
</tr>
<tr>
<td>De facto/long term partner</td>
<td>2</td>
</tr>
<tr>
<td>Married</td>
<td>7</td>
</tr>
<tr>
<td>Divorced</td>
<td>1</td>
</tr>
<tr>
<td>Widowed</td>
<td>1</td>
</tr>
</tbody>
</table>

Cigarettes per day ($M, SD$) 21.63 (7.20)

FTND-R ($M, SD$) 7.77 (3.11)

Attempted to quit smoking in past 12 months (at least 24 hours abstinence) 6

Average number of quit attempts in past 12 months ($M, SD$) 3.17 (2.14)

Motivation to quit as rated out of 100 ($M, SD$) 80.87 (23.00)

Age when first started smoking daily ($M, SD$) 15.92 (3.09)

At least one parent who was a regular smoker 9

Another regular smoker in household 3

There was an average time of 5.69 days between initial contact from participants and the eligibility screening phone call, and 7.54 days between the time of the phone call and the face-to-face meeting.
One participant (#34) withdrew following the face-to-face meeting due to scepticism regarding the effectiveness of the training.

7.3.2.1 Go/No-Go training performance. Participants performed this task well, yielding a mean accuracy of 97.77%. Participants made an average of 4.34 errors each session ($SD = 2.09$, range = 1.21-8.50), specifically 0.96 omission errors and 3.12 commission errors.

To investigate task performance over time and learning effects, the data of 10 participants who completed both the first and fourth training sessions were examined. Table 7.4 depicts the mean group commission errors of smoking and filler images, and reaction time on “go” trials of relaxing and filler images for these sessions.

Table 7.4

*Comparison of Session 1 and Session 4 on Mean Number of Commission Errors and “Go” Trial Reaction Time on the GNG Training (n = 10)*

<table>
<thead>
<tr>
<th></th>
<th>Commission errors</th>
<th>Commission errors</th>
<th>Go RT ms – relaxing</th>
<th>Go RT ms – filler</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>smoking</td>
<td>filler</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>0.031 (.040)</td>
<td>0.05 (.018)</td>
<td>576.43 (80.74)</td>
<td>577.44 (79.64)</td>
</tr>
<tr>
<td>Session 4</td>
<td>0.006 (.009)</td>
<td>0.033 (.30)</td>
<td>551.82 (69.13)</td>
<td>555.44 (70.33)</td>
</tr>
</tbody>
</table>

Note: Standard deviations are in parentheses. Go RTs are calculated from mean RTs of correct trials. Errors are expressed as a proportion of “no-go” trials. ms = milliseconds; RT = reaction time.
Data indicated that when participants completed the training, there was an average of 2.68 hours since their last cigarette ($SD = 2.97$, range = 0.33-18).

7.3.2.2 Feasibility. The total number of training sessions completed by participants ranged from 1-14 ($M = 8.92$, $SD = 5.01$). See Figure 7.5 for the breakdown of sessions completed by each participant.

<table>
<thead>
<tr>
<th>Participant no.</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
<td>Day 3</td>
</tr>
<tr>
<td>19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<tr>
<td>98</td>
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<td></td>
</tr>
<tr>
<td>76</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>196</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Figure 7.5. Number of training sessions completed by pilot study 2 participants.*

Qualitative feedback was obtained from 11 participants. They reported an overall positive experience of the intervention and deemed completing training sessions feasible in a real-world context. In rating the feasibility of completing the training sessions every day for two weeks, one participant rated it 4/10, one rated
it 5/10, two rated it 7/10, two rated it 8/10, and five rated it 10/10. The lower ratings were reported to be due to personal circumstances such as unpredictable study or work schedules. Participants generally denied barriers to completing the training with the exception of four participants who identified barriers relating to prioritising other commitments (e.g. work) and the inability to access the training on their mobile phones.

While completion rate of questionnaires was generally good across time-points, there were participants who did not complete the cognitive tasks at post-intervention and follow-up despite completing the questionnaires. No adverse effects were reported from completing the battery of questionnaires and cognitive tasks.

7.3.2.3 Experience of intervention. Participants generally reported positive experiences of the training, stating that it was time-efficient and easy to complete. For example:

“It was really good, I looked forward to doing it each day and took it seriously. I experienced a change from Day 1, I cut down on half that day and then went down from there.” – Participant #76

Six participants suggested that the effectiveness of the intervention may be improved by increasing the duration of the training to 4-6 weeks or by allowing participants the opportunity to complete the training multiple times each day.

7.3.2.4 Impact on smoking. Table 7.5 presents the average FTND-R score and number of cigarettes smoked daily at each stage of the intervention. Each participant’s data relating to cigarettes smoked is also depicted in a graph in Figure 7.6. Of the seven heavy smokers who reported smoking at least 20
cigarettes daily at baseline, only two participants reported a decrease in cigarettes smoked at post-intervention and a further decrease at follow-up.

Table 7.5

*FTND-R and Average Number of Cigarettes Smoked Daily Across Time-points*

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n = 13)</th>
<th>Post-intervention (n = 11)</th>
<th>Two-week follow-up (n = 7; n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FTND-R (M, SD)</td>
<td>7.77 (3.11)</td>
<td>6 (3.63)</td>
<td>5.71 (4.23)</td>
</tr>
<tr>
<td>Number of cigarettes</td>
<td>21.63 (7.20)</td>
<td>17.79 (10.40)</td>
<td>13.50 (11.28)</td>
</tr>
</tbody>
</table>

FTND = Fagerström Test for Nicotine Dependence – Revised.
* lost at follow-up or withdrawn from the study

**Commenced NRT on day 14 of intervention period

Figure 7.6. Graph of average number of daily cigarettes smoked at baseline, during the intervention period, and at two-week follow-up.

When asked to rate from 0 (“not at all effective”) to 10 (“really effective”) how effective they considered the training was in helping them quit smoking, four participants rated it 0/10, one rated it 2/10, two rated it 5/10, two rated it 6/10, and two rated it 10/10. Ratings of 5-6/10 were reportedly given as participants had reduced their smoking but had not quit.

At two-week follow-up, three participants reported a reduction in cigarette smoking and one participant reported abstinence. The following excerpts are from two of these participants:

“I haven’t smoked for three weeks. I still have access to cigarettes – I know in the back of mind that I can have some but the willpower to not have one is strong. I
would attribute the influence of the intervention to quitting as 55-60%. Training would stop the cravings then and there but would wear off. It would be good to have access to it all the time.” – Participant #37

“My smoking is much better off. Good days, I have four cigarettes; bad days/weekend I have six cigarettes. I’m very happy with the intervention. It has brought to my attention some other problem behaviours e.g. drinking, difficulty coping with my kids.” – Participant #76

However, one participant (#196) reported adverse effects:

“At first I was fine, but as I got further into it, I started smoking more. As I was doing it, I felt like I was constantly looking at cigarettes and it made me want to smoke more, especially after quit date...it also increased my cravings.”

Interestingly, this observation contrasted with their ratings of craving where they reported a decrease in craving levels post-training session for five of the six sessions completed, with only the third session resulting in an increase in craving. Furthermore, the number of daily cigarettes remained unchanged in the week they completed the training sessions according to their TLFB. The participant theorised that these adverse effects had occurred because they had understood the mechanisms of the task and this had eradicated any potential subconscious effects. However, this is unlikely to be the cause as other participants also correctly identified the mechanisms and did not report adverse effects. Participant #196 consequently ceased the training sessions after the first week and commenced NRT (i.e. nicotine patches and gum) on the last day of the intervention period, which was reportedly effective in reducing their smoking.
Overall, nine participants correctly observed that the “no-go” cue was consistently paired with smoking-related images, with two detailing that this translated to them explicitly “saying no” to cigarettes in real life. Six participants believed that this mechanism directly impacted on their smoking.

A common observation was that the training increased their awareness of their smoking, such that they were consciously making the choice to not smoke. These are illustrated in the following examples:

“When I was going through [the training], I would say yes and no in my head, and I think of the smoking pictures and say no – there were a few times I would put off smoking for maybe an hour” – Participant #38

“It possibly had an impact on my smoking, I don’t know. I stopped to think about it a little bit more and yeah… I can’t say definitely from that. But I did stop sometimes and think about it which I never usually do, like ‘what are you doing?’” – Participant #37

“I feel like I have the ability to stop smoking – [it’s] not as much an important part of my life any more. I can wait a bit longer before I have a cigarette. Even after the one I did at the meeting, I got back to the car and couldn’t have a cigarette. After I have a cigarette, I feel really grossed out and don’t want another.” – Participant #29

Interestingly, one participant (#98) who reported no change in smoking remarked that they had developed a strategy where they did not look at the stimuli at all and would only look at the border to determine how to respond. Another participant (#33) also stated that they would alternate between concentrating on the stimuli and on the border.
In relation to smoking during stressful situations, most participants reported that they did not tend to smoke when stressed so there were no specific effects of the intervention on smoking in that particular state. One participant stated they smoked regardless and another participant stated that they did not smoke when stressed due to overall decreased cravings.

While a majority of participants reported having no expectations of the intervention, four participants reported expecting to have reduced their smoking or quit. This appeared to align with the smoking outcomes for two of these participants who reported decreased smoking (#37 and #76).

**7.3.2.5 Craving levels.** The average craving rating pre-first training session was 59.19 as rated on a 100-unit scale \((n = 13)\), with the average change following the first session being 8.53. The average rating post-7\(^{th}\) session was 49.20 \((n = 8)\) and post-14\(^{th}\) session was 43.14 \((n = 4)\). Average change from pre to post training across all sessions was 6.09. Figure 7.7 depicts the ratings of cravings pre and post each training session for the four participants who completed all 14 training sessions.
Seven participants qualitatively reported decreased cravings for cigarettes at post-intervention. Duration of these decreased cravings ranged from 1 hour post-training to a general decrease over the intervention period:

“[My craving levels are] definitely different to two weeks ago. I used to be really irritable, couldn’t go without [a cigarette]. I can now go to bed without a cigarette.” – Participant #29

“I used to experience craving in my body, like a stomach ache, but now I don’t anymore. This started the first time I did the intervention so I think it’s because of the intervention.” – Participant #31

“After the session, my cravings would improve slightly. I’d feel differently, like suddenly I [didn’t] need a cigarette. I can’t explain it. I feel more relaxed. I do
[the training] in the afternoon and then I sometimes take a nap... 1.5-2 hours my cravings would increase again.” – Participant #97

7.3.2.6 Quit/reduction date. Participant experiences with their quit/reduction dates varied considerably. None of the participants adhered to their date; two participants reported that they had forgotten about their date, four participants reported not quitting on their chosen date, and one had quit before the date. Two participants stated it was good to have a quit date, while two stated that they found it stressful.

7.3.2.7 Stop Signal Task. Following exclusion of SST data according to the criteria outlined in the data analysis section, there was valid data for 11 participants at baseline, four at post-intervention, and four at follow-up.

Table 7.6 outlines the “go” trial success rate, average reaction time on “go” trials, the “stop” trial error rate, the SSD, and SSRT for the five participants who provided valid data for at least two time-points. Average SSRT across participants was 288.55ms at baseline, 278.57ms at post-intervention, and 270.91ms at follow-up. Specifically, four participants displayed a decrease in SSRT from baseline to post-intervention or follow-up. Of the three participants who yielded valid data for all three time-points, one displayed increases in SSRT across time-points, one displayed a decrease at post-intervention followed by an increase at follow-up, and one displayed an increase at post-intervention and a decrease at follow-up.
Table 7.6

Mean “Go” Trial Success Rate, “Go” Trial Reaction Times, Stop Signal Delay, and Stop Signal Reaction Time

<table>
<thead>
<tr>
<th>“Go” trial success rate</th>
<th>Mean “go” RT</th>
<th>“Stop” trial error rate</th>
<th>Mean SSD</th>
<th>Mean SSRT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Post-intervention</td>
<td>Follow-up</td>
<td>Baseline</td>
</tr>
<tr>
<td>19 98.67%</td>
<td>786.91</td>
<td>-</td>
<td>748.56</td>
<td>44%</td>
</tr>
<tr>
<td>31 95.33% 96%</td>
<td>573.89</td>
<td>750.24</td>
<td>-</td>
<td>50%</td>
</tr>
<tr>
<td>38 96% 93.33% 97.33%</td>
<td>591.15</td>
<td>764.57</td>
<td>751.27</td>
<td>48%</td>
</tr>
<tr>
<td>76 98.67% 96.67% 98%</td>
<td>705.22</td>
<td>548.51</td>
<td>558.54</td>
<td>48%</td>
</tr>
<tr>
<td>97 95.33% 92.67% 76%</td>
<td>700.58</td>
<td>794.95</td>
<td>851.28</td>
<td>46%</td>
</tr>
</tbody>
</table>

RT = reaction time; SSD = stop signal delay; SSRT = stop signal reaction time.
7.3.2.8 Stimulus evaluation. Figure 7.8 depicts the results of the stimulus evaluation test where participants rated GNG smoking stimuli based on how much they would have liked to engage in the activity in the image. Only participants who completed the test for at least two time-points were included. Due to missing data, results from a total of eight participants were included, with six participants yielding data for all three time-points.

Table 7.7 presents the percentage decrease of liking ratings across the three time-points. All participant ratings decreased across time-points, with the exception of participant #97 who reported an increase in rating of the images from post-intervention to follow-up. Three of the six participants with ratings across the three time-points reported steeper decreases between baseline and post-intervention compared with post-intervention to follow-up, while two participants reported steeper decreases at post-intervention to follow-up.

Figure 7.8. Participant ratings on the stimulus evaluation test across time-points.
Table 7.7

Percentage Decrease of Liking Ratings Across Time-points

<table>
<thead>
<tr>
<th>Participant number</th>
<th>Baseline – Post-intervention</th>
<th>Post-intervention – Follow-up</th>
<th>Baseline – Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>36.51%</td>
<td>22.11%</td>
<td>50.55%</td>
</tr>
<tr>
<td>29</td>
<td>94.42%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>31</td>
<td>84.81%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>37</td>
<td>75.98%</td>
<td>42.86%</td>
<td>86.27%</td>
</tr>
<tr>
<td>38</td>
<td>16.51%</td>
<td>18.26%</td>
<td>31.75%</td>
</tr>
<tr>
<td>76</td>
<td>40.41%</td>
<td>74.10%</td>
<td>84.57%</td>
</tr>
<tr>
<td>97</td>
<td>9.07%</td>
<td>+7.61%*</td>
<td>2.15%</td>
</tr>
<tr>
<td>98</td>
<td>16.53%</td>
<td>0.22%</td>
<td>16.71%</td>
</tr>
</tbody>
</table>

*Participant reported an increase in liking rating

7.3.3 Discussion

This second pilot study aimed to investigate the feasibility and acceptability of the INST program following modifications made after the first pilot study. It further examined preliminary results of the intervention including smoking cessation outcomes and underlying mechanisms.

Improved recruitment methods following the first study resulted in a vastly larger proportion of eligible participants from the initial pool of interested individuals (86.67% compared with 27.59% in the first study). This is thought to be due to the wider reach of the television medium to the general population whereby there were more interested individuals who met the inclusion criteria.
Thirteen participants were recruited, with 11 completing the qualitative feedback at two-week follow-up. Participants displayed generally good task performance, consistent with previous studies that reported 95-99% accuracy (Lawrence, O’Sullivan, et al., 2015; Veling et al., 2011, 2013a, 2014).

7.3.3.1 Feasibility. Participants reported positive experiences of the intervention. INST was deemed to be acceptable and was regarded as simple and quick to complete. It was reported to be generally compatible with participants’ daily lives, with the exception of personal circumstances of some participants. Compared with the first study, drop-out rates were significantly improved, with most participants completing more than one training session. This is thought to be due to the shorter duration of the intervention and the higher levels of motivation to quit reported by participants in the present study. Of note, there were differing characteristics between samples whereby participants in this study were of an older age, had a higher personal income, reported an earlier age of smoking onset, and smoked more cigarettes at baseline. Of these factors, only older age has been associated with higher adherence to non-pharmacological smoking cessation treatments (Ben Taleb, Ward, Asfar, Bahelah, & Maziak, 2015; Figueiró et al., 2017), while earlier age of smoking onset and higher number of cigarettes smoked at baseline have been associated with poorer adherence (Ben Taleb et al., 2015; Moreno-Coutiño, Pérez López, & Gallegos, 2016). Therefore, it is unclear the extent to which these baseline differences influenced adherence levels.

Of the 13 participants in this study, four completed all 14 training sessions. As predicted, results indicated that adherence was improved in this study following increased frequency of sessions in a shorter training period. Interestingly, some participants suggested extended the duration of the
intervention to increase effectiveness, deeming the two-week period too short. Nevertheless, the consideration of balancing acceptability and adherence with effectiveness resulted in the decision to leave this aspect of the intervention protocol unchanged. This was informed by the comparison of feasibility data between the two studies which suggested that a longer period of time was less feasible due to the greater time commitment.

7.3.3.2 Impact on smoking outcome. There appeared to be mixed but generally favourable results regarding the intervention’s impact on smoking. Examining the sample collectively, there was a decrease in the average number of daily cigarettes smoked from baseline to post-intervention, followed by a further decrease from post-intervention to follow-up. Qualitative data indicated that perspectives about the effectiveness of the training sat in largely two groups – participants who felt that it was not at all effective, and participants who reported that it had reduced their smoking. Only two participants reported that it had assisted them in quitting smoking. At the follow-up time-point, only one participant reported abstinence from smoking, identifying the training as partially responsible.

Unfortunately, one participant reported adverse effects where the intervention resulted in increased smoking and craving levels such that they ceased completing training sessions after the first week. However, this was incongruent with other data such as post-training session ratings and TLFB results. The increase in craving levels experienced by this participant contrasts with results from the first study where several participants reported that any cravings elicited by the smoking images diminished over time.
Almost all participants were able to identify the mechanisms of the training (i.e. consistent pairing of smoking images with “no-go” cues) and further noted that the intervention resulted in them consciously reducing their smoking due to increased awareness. For some participants, this occurred through delaying smoking a cigarette. Although there may have been a placebo effect experienced by participants who were recruited by the news segment where a previous participant had recounted its effectiveness, most participants denied having expectations regarding the intervention.

While it was suggested that the training would be most effective for heavy smokers, this association was not observed in the sample. Only two out of seven participants who reported smoking more than 20 cigarettes per day at baseline reported decreased levels of smoking at post-intervention and follow-up. This appears to contradict previous research finding that response training interventions yield the greatest benefits for individuals who display poorer response inhibition at baseline (Houben, 2011) which has been associated with stronger nicotine dependence (Flaudias et al., 2016). However, this will need to be investigated further in future studies with a larger sample size.

Adams, Mokrysz, et al. (2017) is the only study to date that has examined response inhibition training in smokers. Their results indicated that there was no significant difference between groups in number of cigarettes smoked in the week following the intervention. As discussed in the Chapter Three, this may be due to several reasons: 1) their intervention of a single 30-minute session of training, while intensive, may have been too brief to induce change in smoking, 2) participants were non-treatment seeking and may thus have been less responsive to the effects of the intervention, and 3) their control training group was exposed
to neutral and smoking-related cues where there was a 50% “no-go” contingency to each type of cue; this conservative research design may have prevented the detection of a significant difference between the two training groups.

7.3.3.3 Craving. Many participants observed an impact on their craving levels, with cravings decreasing after each training session and over the intervention period. This was highlighted by some participants as a key factor in why the intervention was helpful in assisting them to reduce their smoking. No previous studies in response inhibition have examined changes in craving levels for the targeted behaviour. The reduction of craving levels could aid in achieving and maintaining abstinence given that craving has been identified as a key characteristic in tobacco dependence (American Psychiatric Association, 2013; DiFranza, 2016; Ferguson & Shiffman, 2009) and a predictor of relapse (Potvin, Tikàsz, Dinh-Williams, Bourque, & Mendrek, 2015; Tiffany & Wray, 2012; Wray, Gass, & Tiffany, 2013). The training may decrease smokers’ reactivity to the experience of cravings; this is suggested by the findings of a neuroimaging study indicating that smokers who exhibited increased activation in brain areas associated with inhibitory control when completing a GNG task were less likely to smoke in response to cravings (Berkman, Falk, & Lieberman, 2011). Furthermore, given that smokers who have more positive evaluations of smoking have been found to experience greater cravings (Huijding & de Jong, 2006; Palfai, 2002; Waters et al., 2007), devaluation of smoking cues may result in reduced cue-induced craving. Therefore, response inhibition training may impact craving levels via a number of different pathways which subsequently contribute to the change in
smoking behaviour. However, further research is needed to explore these hypotheses.

**7.3.3.4 Mechanisms of the training.** Learning of stimulus-specific “go” and “no-go” associations was demonstrated by lower error rates and marginally faster reaction time towards the 100% contingent stimuli of smoking and relaxing stimuli compared with the 50% contingent filler images. These results are similar to that of Lawrence, O’Sullivan, et al. (2015) and Stice et al. (2016), suggesting that stimulus-stop associations were acquired following the training.

Participants completed the SST as an independent measure of response inhibition. Only five participants provided valid data on this task for at least two time-points. The SSRT at baseline (288.55ms) is comparable to other studies examining a non-cued SST in smokers (Billieux et al., 2010; de Ruiter, Oosterlaan, Veltman, van den Brink, & Goudriaan, 2012), which ranged from 237.15-271ms. While it was higher in some participants in the present study, this may have been due to the use of a smoking-cued version of the SST which may be more likely to detect inhibitory deficits given the appetitive salience of the cues incorporated (Stevens et al., 2014). The average “go” trial reaction time was 701.97ms on average across time-points and was higher than that of other studies which reported approximately 449ms (Billieux et al., 2010; de Ruiter et al., 2012) as was the SSD, which was 421.92ms compared with 178ms (de Ruiter et al., 2012). This may have resulted from increased attention towards the motivationally salient smoking cues. Additionally, compared to the numerical (Billieux et al., 2010) and airplane stimuli (de Ruiter et al., 2012) used in other studies, the smoking stimuli consisted of different images and are more visually complex.
Four out of five participants displayed an improvement in response inhibition from baseline to either post-intervention or follow-up as indicated by decreased SSRT. This is congruent with the results of another smoking cessation study examining the effects of varenicline, a nicotinic acetylcholine receptor partial agonist (Rhodes, Hawk, Ashare, Schlienz, & Mahoney, 2012). They reported a significant SSRT decrease of approximately 18ms on a non-cued SST from baseline to three weeks, yielding a moderate effect size.

However, when examining each participant’s data, the direction of SSRT change from baseline to post-intervention and post-intervention to follow-up only corresponded to the change in number of daily cigarettes smoked 50% of the time. Furthermore, the three participants who yielded data at all three time-points differed in the direction of change in response inhibition across time. Given the small sample size, this will require further investigation in a large trial before any conclusions can be drawn.

Participants also completed the stimulus evaluation test as an explicit measure of liking of smoking to investigate the devaluation hypothesis. All eight participants who completed the test at baseline and post-intervention reported decreased ratings. Six participants who also completed the test at follow-up displayed a decrease in liking from baseline, although the direction of change in ratings was more mixed from the post-intervention to follow-up time-points. In general, the steepest declines in ratings (84.81-94.42%) reflected the steepest decreases in number of cigarettes smoked between baseline and post-intervention (52.38-62.67%). Overall, the trend suggests that training over time results in a reduction in liking of smoking. This is congruent with findings of Lawrence, O’Sullivan, et al. (2015) who reported that participants in the intervention group
who completed a food-cued training task reported a significant decrease in liking of unhealthy “no-go” food images, yielding a medium effect size \((d_z = 0.41)\).

However, three of the 14 ratings between two time-points were not congruent with the changes in number of daily cigarettes smoked between the time-points. That is, there were two instances where participants reported decreased ratings (16.51-16.53%) but an increase in cigarettes smoked (2.20-27.27%), and one instance where a participant reported an increased rating (7.61%) but a decrease in cigarettes smoked (10.71%). It may be possible that the decreased ratings could be influenced by how much participants liked the training task. That is, the decrease in their liking of cues could have been due to the development of boredom, as opposed to intervention effects. Further work could allow for analyses to investigate whether changes in stimuli evaluation mediate the effects of training on smoking outcome. This will further add to the broader literature regarding underlying mechanisms of response inhibition training tasks.

7.3.3.5 Quit/reduction dates. The diversity in participant experiences prevented a clear solution regarding the management of quit/reduction dates. None of the participants adhered to their date and opinions on its necessity were mixed. It was decided that the current approach would be retained as there did not appear to be overwhelming evidence suggesting an alternative method.

7.3.3.6 Protocol modifications. The results also yielded important information regarding how to instruct participants to correctly complete the training. The two participants who stated that they were not consistently engaging with the stimuli in the study reported no or minimal impact of the intervention on their smoking. In future trials, there would need to be explicit emphasis to participants on the importance of looking at the stimuli to prevent them from
developing counterproductive strategies in completing the training. This active engagement in the smoking images is essential for intervention efficacy given that the cue-specific component of response inhibition training is proposed to be the main facilitator of change.

Furthermore, given that the rate of completion of cognitive tasks was lower than that of the questionnaires and TLFB, researchers would need to stress to participants that completion of all measures is an important component of the study as it provides further information regarding the mechanisms of the training.

7.4 Limitations

Limitations of these pilot studies should be considered in interpretation. Sample sizes in both studies were small and the results collected to inform modifications to the protocol may not be representative of the general population of smokers. Furthermore, it was a homogenous sample, with a majority of participants reporting that they and their parents were born in Australia. The studies were single-arm and hence did not pilot the randomisation and blinding aspects of the protocol. However, inclusion of the control arm was deemed unnecessary as the primary aim of feasibility and acceptability of the intervention could be examined with the intervention training task alone. Interpretation of preliminary results was instead facilitated by comparison to existing literature.

The administration of questionnaires prior to cognitive tasks at each assessment time-point may have induced mood states that could have influenced subsequent performance on cognitive tasks. Results were dependent on self-report measures which may have been prone to incorrect recall, particularly in relation to retrospective reporting of daily cigarettes smoked at each time-point. It should also be considered that there may be other confounding factors that influenced
levels of smoking. Namely, both samples of participants remarked that the intervention made them more conscious of their smoking behaviours which thus resulted in them choosing to reduce their smoking. Similarly, motivation was observed to be an important factor that may have influenced results as it impacted upon the degree to which participants engaged and persevered with the intervention, particularly amongst pilot study 1 participants. This importance of motivation is similar to findings in past studies (Richardson et al., 2013), and literature identifying it as a critical variable in predicting quit attempts (Vangeli, Stapleton, Smit, Borland, & West, 2011) and cessation outcomes (Layoun et al., 2017). While a majority of participants denied having positive expectations of the intervention, they may have experienced a placebo effect nonetheless.

7.5 Chapter Summary

Results from the two pilot studies presented in this chapter suggest that INST is a feasible and acceptable program with promising evidence of effectiveness for a proportion of participants. As such, it was concluded that a full trial investigating INST is warranted (see Appendix C for the manuscript of the study protocol submitted to *BMC Public Health*).

This chapter concludes the first part of the thesis focusing on the development and piloting of INST. The next chapter will address the second aim of the thesis and present a systematic review investigating the relationship between smoking outcome and the broader construct of impulsivity.
Chapter Eight: A Systematic Review Examining Changes in Impulsivity Following Treatment for Smoking

8.1 Introduction

Impulsivity is a multi-faceted construct that has been reported to be strongly associated with the initiation and maintenance of smoking (e.g. Doran et al., 2013; Ryan, MacKillop, & Carpenter, 2013; VanderVeen, Cohen, Cukrowicz, & Trotter, 2008) and to play a role in predicting treatment outcomes (Loree, Lundahl, & Ledgerwood, 2015; Stevens et al., 2014). However, there is limited knowledge regarding whether impulsivity itself may be susceptible to change following smoking cessation treatment, with findings generally reporting mixed results (e.g. Loughead et al., 2016; Secades-Villa, Weidberg, García-Rodríguez, Fernández-Hermida, & Yoon, 2014; Yi et al., 2008). Of relevance, studies that have focused on other substances such as alcohol, cannabis, and cocaine have reported decreases in baseline levels of impulsivity following substance use treatment (Amaro et al., 2010; Bankston et al., 2009; Blonigen, Timko, Moos, & Moos, 2009; Hershberger, Um, & Cyders, 2017). These findings across a range of substances suggest that smoking cessation treatment may also have an impact on impulsivity but this remains to be systematically explored. As such, a review examining this question within the smoking literature is relevant and timely.

This chapter provides a brief overview of the construct of impulsivity and reviews its relationship with smoking. This is then followed by the reporting of a systematic review of the current literature. The two questions of the review are: 1) whether there are changes in impulsivity following psychosocial interventions for smoking, and 2) whether these changes are correlated with smoking cessation outcomes.
### 8.1.1 Impulsivity

Impulsivity is a broad, heterogeneous construct that encompasses a range of characteristics such as action with limited forethought and impaired decision making, particularly in the presence of rewarding stimuli (Dalley, Everitt, & Robbins, 2011; Dawe & Loxton, 2004; de Wit, 2009). It is generally considered as a dysfunctional trait that has been associated with problematic behaviours such as delinquent behaviours (Mann et al., 2017) and gambling (MacLaren, Fugelsang, Harrigan, & Dixon, 2011), and is particularly pervasive in psychiatric disorders (Hirschtritt, Potenza, & Mayes, 2011; Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001). Nevertheless, impulsivity can also play a role in adaptive functioning and has been linked with positive psychosocial outcomes (Gullo & Dawe, 2008).

Impulsivity is generally measured using either self-report or behavioural measures (López-Torrecillas, Nieto-Ruiz, et al., 2014; Sheffer et al., 2012; Wegmann et al., 2012). Self-report measures tend to capture more enduring, trait forms of impulsivity (Cyders & Coskunpinar, 2011), with example measures including the Barratt Impulsiveness Scale (BIS-11; Patton, Stanford, & Barratt, 1995), UPPS-R+P (Cyders et al., 2007; Whiteside & Lynam, 2001), Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ; Torrubia, Ávila, Moltó, & Caseras, 2001), and the Behavioural Inhibition/Activation System (BIS/BAS; Carver & White, 1994). Conversely, behavioural measures tend to assess state forms of impulsivity that are more transient (Dalley et al., 2011; Meda et al., 2009), often requiring an immediate response to relevant or rewarding stimuli (Stevens et al., 2014). For instance, the Go/No-Go Task (GNG; Miller, Schäffer, & Hackley, 1991) and Stop Signal Task (SST; Logan, 1994) require
inhibition of responses that have previously been reinforced or learned, and delay
discounting tasks measure preferences for small, immediate rewards compared
with larger, delayed rewards (Kirby, Petry, & Bickel, 1999). While research has
found a small significant correlation between self-report and behavioural
measures, these two types of measures largely index different facets of
impulsivity with minimal overlap, thus accounting for unique variance (Cyders &
Coskunpınar, 2011; Reynolds, Ortengren, Richards, & de Wit, 2006). As such, it
is important to consider both types of measurements when investigating the
construct of impulsivity.

There are several theoretical models that characterise impulsivity as
comprising of separate but related traits (Berg et al., 2015). The two-factor model
of impulsivity consists of “rash impulsivity” or disinhibited behaviour, and
“reward sensitivity” or a drive to pursue rewards despite potential long-term
consequences (Dawe, Gullo, & Loxton, 2004; de Wit & Richards, 2004). Used
primarily in the field of substance use research, this model is yielded from factor
analytic studies and is based on neurobiological data from theoretical frameworks
of personality researchers such as Hans Eysenck, Robert Cloninger, Marvin
Zuckerman, and Jeffrey Gray (Gullo, Loxton, & Dawe, 2014). Both factors have
been positively associated with smoking (Flory & Manuck, 2009; Lyvers,
Bremner, Edwards, & Thorberg, 2017; Potts, Bloom, Evans, & Drobes, 2014),
with rash impulsivity associated with escalation of smoking and tobacco
dependence (Balevich, Wein, & Flory, 2013; Chase & Hogarth, 2011; Doran,
McChargue, & Cohen, 2007), and reward seeking with the initiation of smoking
(Balevich et al., 2013; Spillane et al., 2012).
A second model is the five-factor personality UPPS-P model which purports to measure a wider variation of impulsive traits (Cyders et al., 2007; Whiteside & Lynam, 2001). A factor analysis of self-report inventories of impulsivity yielded the following five constructs: negative urgency, or the tendency to act rashly when in a negative mood; positive urgency, or the tendency to act rashly when in a positive mood; lack of premeditation, or the tendency to act without forethought; lack of perseverance, or difficulty remaining focused on a task; and sensation seeking, or the tendency to seek novel, thrilling experiences. In contrast to the two-factor model, this was derived from the broader literature of personality research and uses the Five Factor Model of personality as a framework (Costa & McCrae, 1992). The UPPS model has been examined extensively in a range of issues such as aggressive behaviours (e.g. Carlson, Pritchard, & Dominelli, 2013; Derefenko, Dewall, Metze, Walsh, & Lynam, 2011; Miller, Zeichner, & Wilson, 2012), borderline personality disorder (e.g. Bøen et al., 2015; Jacob et al., 2010; Tragesser & Robinson, 2009), eating disorders (e.g. Claes, Vandereycken, & Vertommen, 2005; Lavender et al., 2017), nonsuicidal self-injury (e.g. Lynam, Miller, Miller, Bornovalova, & Lejuez, 2011; Mullins-Sweatt, Lengel, & Grant, 2013), and suicidality (e.g. Dvorak, Lamis, & Malone, 2013; Klonsky & May, 2010).

In recent literature, UPPS has been used as a framework to explore the relationship between impulsivity and substance use (e.g. Coskunpınar, Dir, & Cyders, 2013; Cyders, Flory, Rainer, & Smith, 2009; Lee, Peters, Adams, Milich, & Lynam, 2015; Robinson, Ladd, & Anderson, 2014; Shin, Chung, & Jeon, 2013; Stautz & Cooper, 2013; Zapolski, Cyders, & Smith, 2009). For example, a meta-analysis by Kale, Stautz, and Cooper (2018) examined the relationship between
current smokers and UPPS-P traits, in addition to the trait of reward sensitivity which is not encapsulated within the model (Dawe & Loxton, 2004). Analyses of 97 studies suggested that positive urgency ($r = 0.24$) yielded the strongest significant association with smoking status, followed by lack of premeditation, sensation seeking, negative urgency, and lack of perseverance, which yielded $r$ values ranging from 0.18-0.20. Positive urgency was most strongly associated with severity of nicotine dependence ($r = 0.23$), followed by negative urgency, sensation seeking, and lack of premeditation, which yielded $r$ values ranging from 0.15-0.10. Although all small in size, these significant effects provide evidentiary support that various impulsivity traits are relevant to smoking behaviours.

8.1.2 Impulsivity and treatments for smoking cessation

A number of studies have reported a significant relationship between high levels of impulsivity and poorer smoking outcomes following treatment. A systematic review by Loree, Lundahl, and Ledgerwood (2015) found that regardless of whether self-report or behavioural measurements were used, higher levels of baseline impulsivity predicted a greater likelihood of relapse following psychosocial or pharmacological treatments for smoking as reported in 12 papers. Another systematic review of 25 papers by Stevens et al. (2014) investigated the relationship between specific neurocognitive aspects of impulsivity and treatment outcomes in individuals with substance use disorders (SUD), including smokers. They found that the majority of smoking studies used measures of delay discounting ($n = 6$), though others also used interference control ($n = 3$), response inhibition ($n =1$), and risky decision-making ($n = 1$). Results suggested that there was consistent evidence for the significance of delay discounting in influencing clinical outcomes, including abstinence, predictors to first lapse, and relapse.
Significant relationships with abstinence and early relapse were also noted for deficits in response inhibition and disinhibition respectively in response to cognitive tasks that incorporated drug-related words as cues.

In examining the broader literature of substance use, impulsivity is purported to decrease following treatment given the positive relationship between high levels of impulsivity and increased risk of substance use. Indeed, a recent meta-analysis by Hershberger, Um, and Cyders (2017) reporting on 10 studies indicated that impulsive traits of negative urgency and sensation seeking significantly decreased following substance use treatment, including cognitive behavioural therapy (CBT), motivational interviewing, and Alcoholics Anonymous (Aklin, Tull, Kahler, & Lejuez, 2009; Axelrod, Perepletchikova, Holtzman, & Sinha, 2011; Crawley, 2015; Gonçalves et al., 2014; Irwin & Stoner, 1991; Jones et al., 2011; Kazemi, Levine, Dmochowski, Anghing, & Shou, 2014; Littlefield et al., 2015; Maddox, 2011; Piedmont & Ciarrocchi, 1999). This yielded small effect sizes (Hedges g ranging from -0.25 to -0.10). Of note, the paper only included studies that used measures assessing self-reported impulsivity traits and did not include studies examining smokers or studies using behavioural measures of impulsivity. Furthermore, should impulsivity decrease following treatment of smoking, it is plausible that the changes may be related to treatment outcomes given the strong relationship between the two variables as reviewed above. However, this was not examined in Hershberger et al.’s study and other literature has yet to systematically examine this question.

8.1.3 Present study

Given these gaps in the literature, the aims of this systematic review were to determine whether 1) psychosocial interventions for smoking led to a
significant decrease in impulsivity-related constructs as measured by self-report or behavioural measurements, and 2) whether a reduction in impulsivity was related to improved smoking cessation outcomes following treatment.

8.2 Method

This systematic review was designed and reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009; Moher et al., 2015). The PRISMA checklist can be found in Appendix D.

8.2.1 Study eligibility criteria

Inclusion criteria for the review included studies that:

1) used quantitative data methods

2) were published in peer-reviewed journals in any language

3) used adult samples (as defined by a minimum age of 18 years old) who were smokers

4) examined the efficacy of one or more psychosocial interventions addressing smoking and measure impulsivity at pre and post-treatment using validated self-report or behavioural measures. Of note, this review defined “psychosocial intervention” as a treatment comprised of a cognitive, behavioural, affective, and/or social component targeting smoking. Experimental studies examining treatments in non-treatment seeking smokers were also included.

5) if examining changes to attentional bias as measured by Stroop tests, reported changes in terms of numbers of correct responses or errors.

Studies were excluded if they:

1) were single case studies
2) examined interventions aimed to prevent smoking initiation
3) examined the sole effects of physical exercise, pharmacotherapy, or abstinence from smoking
4) examined changes to attentional bias as measured using dot or visual probe tasks.

8.2.2 Information sources and search strategy

Publications meeting the eligibility criteria were identified through databases CINAHL, PsycINFO, MEDLINE Complete, and EMBASE. The search date was from database inception to 20th February 2018. The reference lists of all included studies were searched for additional studies that may potentially be eligible.

The search strategy used keywords in the title and abstract relating to:

1. Impulsivity (e.g. impulsiv* OR disinhibit* or "sensation seek*" OR "novelty seek*" or "reward seek*" or "reward sensitiv*" or "reward dependen*" or "reward drive" or premeditation or "behavi* approach" or “behavi* activation” or BAS or urgency or “positive urgency” or perseverance or “boredom proneness” or “boredom susceptibility” or "response inhibit*" or "motor inhibit*" or "cognitive inhibit*" or "inhibitory control" or "delay discounting" or interference or "exec* #function*" or "exec* #control*" or "attention# bias")

2. Smoking (e.g smoking or smoker* or “nicotine use*” or “nicotine abuse*” or “nicotine addict*” or “nicotine dependen*” or “tobacco use*” or “tobacco abuse*” or “tobacco dependen*” or “tobacco addict*”)
3. Treatment (e.g. treatment, intervention, therapy, inhibitory control training, response inhibition training)

Controlled vocabulary from each database were also included in the search. A full search strategy for one of the databases (i.e. MEDLINE Complete) is provided in Appendix E.

8.2.3 Study selection

Records were screened by the author (KG) using information found in the titles and abstracts of all publications obtained from the search. A random selection of 20% of the records was also screened by another doctoral candidate, yielding a 98.58% inter-rater reliability. If the abstracts did not allow for conclusive exclusion, the full-text articles were retrieved and evaluated in detail by the author and supervisor PS in order to confirm their eligibility for inclusion. Questionable cases were discussed with PS until a consensus was achieved.

8.2.4 Quality assessment

The methodological quality of studies was evaluated by the author using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool (Thomas, Ciliska, Dobbins, & Micucci, 2004). The EPHPP tool assesses the six domains of selection bias, study design, confounders, blinding, data collection method, and withdrawals or dropouts. Studies were given a rating of weak, moderate, or strong for each domain. Studies with no weak ratings for any domain receive an overall rating of strong, studies with one weak rating receive an overall rating of moderate, and studies with two or more weak ratings receive an overall rating of weak.
8.3 Results

8.3.1 Study selection

The initial database search identified a total of 1778 publications. Removal of duplicates yielded 1098 unique publications. Of these, 1035 were excluded as they did not meet the eligibility criteria as outlined above. In reviewing the remaining 63 studies, one additional article was identified from the reference lists that also met the inclusion criteria. At full-text review, 54 studies were excluded. This left a total of 10 publications, comprising of nine independent studies, to be included in this review. The two studies using the same sample will henceforth be counted as one study (Weidberg, Landes, López-Núñez, et al., 2015; Weidberg, Landes, García-Rodríguez, Yoon, & Secades-Villa, 2015). Figure 8.1 summarises the process used in the selection of publications. A meta-analysis could not be conducted given the small number of studies and the heterogeneity of measures used.
8.3.2 Study characteristics

The nine studies contained a total of 598 smokers receiving the intervention condition and 239 smokers as control participants. The sample size, participant characteristics, study design, and methodological quality of each study...
are summarised in Table 8.1. All studies were published within the last 11 years.

All studies were published in English and in USA, Spain, or UK.
Table 8.1

Summary of Study Sample Size and Characteristics, Design, and EPHPP Rating

<table>
<thead>
<tr>
<th>Source</th>
<th>Design</th>
<th>Country</th>
<th>No.</th>
<th>Mean age, years (SD)</th>
<th>Smoking criteria</th>
<th>Mean cigarettes smoked daily</th>
<th>EPHPP global rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoon et al. (2007)</td>
<td>Cohort</td>
<td>USA</td>
<td>48 F</td>
<td>25.9 (5.1)</td>
<td>Pregnant women who had quit smoking</td>
<td>9.6 (6.0)</td>
<td>Weak</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Abstinence verified by urine sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yi et al. (2008)</td>
<td>CCT</td>
<td>USA</td>
<td>56 (20 F)</td>
<td>I: 26.6 (8.1)</td>
<td>≥20 cigarettes/day</td>
<td>I: 23.2 (5.3)</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(28I, 28C)</td>
<td>C: 25.2 (9.8)</td>
<td>FTND score ≥ 6</td>
<td>C: 24.1 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Yoon et al. (2009)</td>
<td>CCT</td>
<td>USA</td>
<td>28 (13I, 15C)</td>
<td>I: 29.1 (11.5)</td>
<td>≥10 cigarettes/day</td>
<td>I: 18.2 (5.5)</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Breath CO sample ≥18 ppm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C: 21.7 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Source</td>
<td>Design</td>
<td>Country</td>
<td>No.</td>
<td>Mean age, years (SD)</td>
<td>Smoking criteria</td>
<td>Mean cigarettes smoked daily</td>
<td>EPHPP global rating</td>
</tr>
<tr>
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</tr>
</tbody>
</table>
| Bradstreet et al. (2014)       | RCT    | USA     | 30  | I: 24.6 (5.3)       | ≥10 cigarettes/day for at least 1 year  
Breath CO sample ≥15 ppm                                                          | I: 15.1 (4.5)                | Strong               |
| Secades-Villa et al. (2014)    | Cohort | Spain   | 80  | 38.90 (13.12)       | ≥10 cigarettes/day for at least 1 year                                             | 19.33 (8.69)                | Weak                |
| Weidberg, Landes, García-Rodríguez, et al. (2015); Weidberg, Landes, López-CCT | CCT    | Spain   | 116 | I: 43.36            | ≥10 cigarettes/day for at least 1 year  
DSM-IV-TR nicotine dependence                                                        | I: 20.52 (8.52)              | Moderate             |
<p>|                                |        |         |     | C: 47.53            |                                                                                | C: 23.66 (9.41)              |                     |</p>
<table>
<thead>
<tr>
<th>Source</th>
<th>Design</th>
<th>Country</th>
<th>No.</th>
<th>Mean age, years (SD)</th>
<th>Smoking criteria</th>
<th>Mean cigarettes smoked daily</th>
<th>EPHPP global rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2015)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C: 43.39 (12.38)</td>
<td>C: 15.73 (5.23)</td>
<td></td>
</tr>
<tr>
<td>Lougheed et al.</td>
<td>RCT</td>
<td>USA</td>
<td>213</td>
<td>(108I, 105C)</td>
<td>- ≥5 cigarettes/day for at least 6 months</td>
<td>I: 16.42 (6.14)</td>
<td>Moderate</td>
</tr>
<tr>
<td>(2016)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Breath CO sample ≥8 ppm</td>
<td>C: 15.73 (5.23)</td>
<td></td>
</tr>
<tr>
<td>Hughes et al.</td>
<td>Cohort</td>
<td>USA</td>
<td>211</td>
<td>(95F)</td>
<td>- ≥10 cigarettes/day for at least 1 year</td>
<td>19 (8)</td>
<td>Moderate</td>
</tr>
<tr>
<td>(2017)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Breath CO sample ≥8 ppm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Source</td>
<td>Design</td>
<td>Country</td>
<td>Participant data</td>
<td>EPHPP global rating</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>No.</td>
<td>Mean age, years (SD)</td>
<td>Smoking criteria</td>
<td>Mean cigarettes smoked daily</td>
<td></td>
</tr>
<tr>
<td>Adams et al. (2017)</td>
<td>RCT</td>
<td>UK</td>
<td>55 (26F)</td>
<td>I: 23 (7)</td>
<td>- ≥10 cigarettes/day or ≥15 roll-ups/day</td>
<td>I: 14 (4)</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(27I, 28C)</td>
<td>C: 25 (8)</td>
<td>- Smoke within 1 hr of waking</td>
<td>C: 14 (4)</td>
<td></td>
</tr>
</tbody>
</table>

C = comparison group; CCT = controlled clinical trial; CO = carbon monoxide; DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision; EPHPP = Effective Public Health Practice Project; F = female; FTND = Fagerström Test of Nicotine Dependence; I = intervention group; ppm = parts per million; RCT = randomised controlled trial.
8.3.3 Study quality

Table 8.2 outlines the domain ratings of methodological quality of studies included in the review. Global quality was generally good across studies. The selection bias domain examines both representativeness of the target population and the percentage of participants who agreed to participate in the study. That is, studies were only rated as strong if they used participants who were very likely representative of the target population and had a participation percentage of at least 80%. Studies rated as strong in study design were randomised controlled trials (RCT) or controlled clinical trials (CCT) while those rated as moderate used a cohort design. Studies were rated as moderate in the domain of blinding if either the outcome assessor or study participants were not aware of the research question, while studies where both parties were aware of the research question were rated as weak. Only one study (Adams, Mokrysz, et al., 2017) was rated as strong for using a double-blinded design. In the withdrawals and dropouts domain, studies were rated as strong only if they reported withdrawals and dropouts, and retained at least 80% of participants. All studies used valid and reliable data collection methods. All studies that used control groups and reported controlling for confounding factors controlled for at least 80% of relevant confounds.
Table 8.2

*Component and Global Ratings of Methodological Quality of Studies*

<table>
<thead>
<tr>
<th>Domain Rating</th>
<th>Weak</th>
<th>Moderate</th>
<th>Strong</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yi et al. (2008)</td>
<td>Yoon et al. (2009)</td>
<td></td>
</tr>
<tr>
<td>Domain Rating</td>
<td>Weak</td>
<td>Moderate</td>
<td>Strong</td>
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</tr>
<tr>
<td>Study design</td>
<td>-</td>
<td>Hughes et al. (2017)</td>
<td>Adams et al. (2017)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Secades-Villa et al., (2014)</td>
<td>Bradstreet et al. (2014)</td>
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<td></td>
<td></td>
<td>Yoon et al. (2007)</td>
<td>Loughead et al. (2016)</td>
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<td></td>
<td>Weidberg, Landes, García-Rodríguez, et al. (2015);</td>
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<td></td>
<td></td>
<td>Yi et al. (2008)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Yoon et al. (2009)</td>
</tr>
<tr>
<td>Domain Rating</td>
<td>Weak</td>
<td>Moderate</td>
<td>Strong</td>
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<td>---------------------------------------------------------</td>
</tr>
<tr>
<td>Controlling for confounding</td>
<td>Adams et al. (2017)</td>
<td>-</td>
<td>Bradstreet et al. (2014)</td>
</tr>
<tr>
<td>factors between groups</td>
<td></td>
<td>Loughead et al. (2016)</td>
<td>Weidberg, Landes, García-Rodríguez, et al. (2015);</td>
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<tr>
<td></td>
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<td></td>
<td>Weidberg, Landes, López-Núñez,</td>
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<td>Yi et al. (2008)</td>
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<td>Yoon et al. (2009)</td>
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<tr>
<td></td>
<td>Loughead et al. (2016)</td>
<td>Weidberg, Landes, García-</td>
<td></td>
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<tr>
<td></td>
<td>Secades-Villa et al. (2014)</td>
<td>Rodríguez, et al. (2015);</td>
<td></td>
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<tr>
<td></td>
<td>Yi et al. (2008)</td>
<td>Weidberg, Landes, López-Núñez,</td>
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<tr>
<td></td>
<td>Yoon et al. (2007)</td>
<td>et al. (2015)</td>
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<tr>
<td>Domain Rating</td>
<td>Weak</td>
<td>Moderate</td>
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<tr>
<td>Yoon et al. (2009)</td>
<td>-</td>
<td>-</td>
<td>Adams et al. (2017)</td>
</tr>
<tr>
<td>Data collection method</td>
<td>-</td>
<td>-</td>
<td>Bradstreet et al. (2014)</td>
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<tr>
<td></td>
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<td></td>
<td>Hughes et al. (2017)</td>
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<td>Loughead et al. (2016)</td>
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<td>Secades-Villa et al. (2014)</td>
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<td>Weidberg, Landes, García-Rodríguez, et al. (2015);</td>
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<td>Yi et al. (2008)</td>
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<td>Yoon et al. (2007)</td>
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<td>Yoon et al. (2009)</td>
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<tr>
<td>Domain Rating</td>
<td>Weak</td>
<td>Moderate</td>
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<td></td>
<td>Yoon et al. (2007)</td>
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<td>Hughes et al. (2017)</td>
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<td></td>
<td>Loughead et al. (2016)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Secades-Villa et al. (2014)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Weidberg, Landes, García-Rodríguez, et al. (2015);</td>
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<td>Yoon et al. (2009)</td>
</tr>
<tr>
<td>Domain Rating</td>
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<td>Moderate</td>
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<td></td>
<td>Yoon et al. (2007)</td>
<td>Hughes et al. (2017)</td>
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<td>Loughead et al. (2016)</td>
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<td></td>
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<td>Weidberg, Landes, García-</td>
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<td></td>
<td></td>
<td>Rodríguez, et al. (2015);</td>
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<td>Weidberg, Landes, López-Núñez,</td>
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<td></td>
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<td>et al. (2015)</td>
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<td></td>
<td></td>
<td>Yi et al. (2008)</td>
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<tr>
<td></td>
<td></td>
<td>Yoon et al. (2009)</td>
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</tr>
</tbody>
</table>
8.3.4 Synthesis of results

Table 8.3 presents a summary of the interventions, impulsivity and substance use measures, and outcomes of each study. Four different types of interventions were identified: behavioural therapy (Bradstreet et al., 2014; Yi et al., 2008; Yoon et al., 2007; Yoon, Higgins, Bradstreet, Badger, & Thomas, 2009), cognitive training (Adams, Mokrysz, et al., 2017; Loughead et al., 2016), psychotherapy (Secades-Villa et al., 2014), and combined behavioural therapy and psychotherapy (Hughes et al., 2017; Weidberg, Landes, López-Núñez, et al., 2015; Weidberg, Landes, García-Rodríguez, et al., 2015). There were five studies examining the efficacy of smoking cessation treatments (Adams, Mokrysz, et al., 2017; Hughes et al., 2017; Loughead et al., 2016; Secades-Villa et al., 2014; Weidberg, Landes, López-Núñez, et al., 2015; Weidberg, Landes, García-Rodríguez, et al., 2015), one relapse prevention study (Yoon et al., 2007), and three experimental studies (Bradstreet et al., 2014; Yi et al., 2008; Yoon et al., 2009). Three studies identified examined whether changes in impulsivity were related to substance use outcome (Secades-Villa et al., 2014; Weidberg, Landes, García-Rodríguez, et al., 2015; Yoon et al., 2007).

Intervention duration ranged from a day to 12 weeks. Four studies assessed participants at the two time-points of pre and post intervention (Adams, Mokrysz, et al., 2017; Bradstreet et al., 2014; Hughes et al., 2017; Yi et al., 2008), while five studies assessed participants at a minimum of three time-points (Loughead et al., 2016; Secades-Villa et al., 2014; Weidberg, Landes, López-Núñez, et al., 2015; Weidberg, Landes, García-Rodríguez, et al., 2015; Yoon et al., 2007; Yoon et al., 2009). All studies utilised behavioural measures of impulsivity with the exception of one study which used a self-report version of the
delay-discounting task (Yi et al., 2008). Five studies used the monetary Delay Discounting Task (DDT; Hughes et al., 2017; Secades-Villa et al., 2014; Weidberg, Landes, López-Núñez, et al., 2015; Weidberg, Landes, García-Rodríguez, et al., 2015; Yoon et al., 2007; Yoon et al., 2009), two used the GNG task (Adams, Mokrysz, et al., 2017; Bradstreet et al., 2014), and one used the GNG task and Continuous Performance Task (CPT; Loughead et al., 2016). The remaining study measured delay discounting with two self-report questionnaires, one comparing monetary amounts and another comparing cigarette amounts (Yi et al., 2008). Given the variability in treatment type, studies are categorised based on type of treatment and discussed accordingly. Of note, a number of studies used small sample sizes which may have been underpowered to detect a treatment effect on smoking cessation outcomes. However, there did not appear to be a consistent pattern between sample size and effect sizes.
### Table 8.3

**Summary of Study Interventions, Impulsivity Measures, Substance Use Measures, and Results**

<table>
<thead>
<tr>
<th>Source</th>
<th>Intervention (vs comparison)</th>
<th>Impulsivity outcome measure</th>
<th>Substance use outcome measure</th>
<th>Impulsivity outcomes</th>
<th>Substance use outcomes</th>
<th>Relationship between impulsivity changes and substance use outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoon et al. (2007)</td>
<td>Voucher based incentives, both contingent and non-contingent on abstinence</td>
<td>DDT (Johnson &amp; Bickel, 2002) – ln k</td>
<td>- Self-report (7 days pp)</td>
<td>No significant changes in discount rates for the sample as a whole</td>
<td>Majority of women sustained abstinence throughout the study, but 46% had relapsed at the 24-week assessment</td>
<td>No significant interaction between eventual smoking classification and time on DDT results</td>
</tr>
<tr>
<td>Yi et al. (2008)</td>
<td>CM (vs no intervention)</td>
<td>Delay-discounting questionnaire (Rachlin et al., 1991) – g</td>
<td>- Breath CO (abstinence defined as ≤12ppm)</td>
<td>There were significant decreases in discounting in the intervention group on both the monetary DDT $(d = 0.85)$ and cigarette CO levels of ≤12ppm at each assessment.</td>
<td>Approximately 90% of participants in the CM group achieved</td>
<td>N/A</td>
</tr>
<tr>
<td>Source</td>
<td>Intervention (vs comparison)</td>
<td>Impulsivity outcome measure</td>
<td>Substance use outcome measure</td>
<td>Impulsivity outcomes</td>
<td>Substance use outcomes</td>
<td>Relationship between impulsivity changes and substance use outcomes</td>
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</tr>
<tr>
<td>Yoon et al. (2009)</td>
<td>CM (vs mostly non-contingent condition)</td>
<td>DDT (Johnson &amp; Bickel, 2002) − ln k</td>
<td>- Breath CO (abstinence defined as ≤4ppm)</td>
<td>No significant differences between groups pre, mid, or post-intervention</td>
<td>Significantly lower mean CO levels and urine cotinine levels in CM group compared with comparison group on days 1-13. Levels of comparison group lowered to that of CM group on day</td>
<td>N/A</td>
</tr>
<tr>
<td>Source</td>
<td>Intervention (vs comparison)</td>
<td>Impulsivity outcome measure</td>
<td>Substance use outcome measure</td>
<td>Impulsivity outcomes</td>
<td>Substance use outcomes</td>
<td>Relationship between impulsivity changes and substance use outcomes</td>
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</tr>
<tr>
<td>Bradstreet et al. (2014)</td>
<td>CM (vs mostly non-contingent condition)</td>
<td>Non-cued GNG – % of correct “no-go” trials</td>
<td>Breath CO (abstinence defined as ≤4ppm)</td>
<td>No significant differences between pre and post-intervention in intervention group</td>
<td>Significantly lower mean CO levels and urine cotinine levels in CM group compared with</td>
<td>N/A</td>
</tr>
</tbody>
</table>

14. Collapsing across conditions, 87% of specimens submitted during the CM periods met the abstinence criterion compared to 0% of the specimens submitted on non-contingent days.
<table>
<thead>
<tr>
<th>Source</th>
<th>Intervention (vs comparison)</th>
<th>Impulsivity outcome measure</th>
<th>Substance use outcome measure</th>
<th>Impulsivity outcomes</th>
<th>Substance use outcomes</th>
<th>Relationship between impulsivity changes and substance use outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Urine cotinine</td>
<td></td>
<td></td>
<td>comparison group (d) = 3.22 and (d = 2.83), respectively) on days 1-13. Levels of comparison group lowered to that of CM group on days 14-15. Collapsing across conditions, 88.8% of specimens submitted during the CM periods met the abstinence criterion compared to 0.5% of the specimens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Source</td>
<td>Intervention (vs comparison)</td>
<td>Impulsivity outcome measure</td>
<td>Substance use outcome measure</td>
<td>Impulsivity outcomes</td>
<td>Substance use outcomes</td>
<td>Relationship between impulsivity changes and substance use outcomes</td>
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</tr>
<tr>
<td>Secades-Villa et al. (2014)</td>
<td>Group CBT</td>
<td>DDT (Garcia-Rodriguez et al., 2013) – ln k</td>
<td>- Self-report (7 days pp)</td>
<td>No significant changes in discounting at post-intervention or follow-up for sample as a whole</td>
<td>61% abstinent for past 24 hrs at post-treatment, 35% abstinent for previous 7 days at follow-up</td>
<td>At 12-months follow-up, delay discounting had decreased in participants who had abstained from smoking, but remained unchanged in participants who were still smoking ($d = 0.54$)</td>
</tr>
<tr>
<td>Weidberg, Landes, García-Rodriguez, et al. (2015)$^1$</td>
<td>CM + CBT (vs CBT)</td>
<td>DDT – AUC</td>
<td>- Self-report (7 days pp)</td>
<td>Women who received CM+CBT showed greater discounting decreases compared</td>
<td>CM+CBT group achieved higher rates of abstinence than CBT group at</td>
<td>No significant effect of treatment, smoking status, or interaction on DDT</td>
</tr>
<tr>
<td>Source</td>
<td>Intervention (vs comparison)</td>
<td>Impulsivity outcome measure</td>
<td>Substance use outcome measure</td>
<td>Impulsivity outcomes</td>
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<td>Relationship between impulsivity changes and substance use outcomes</td>
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</tr>
<tr>
<td>Weidberg, Landes, López-Nuñez, et al. (2015)¹</td>
<td>CM + CBT (vs CBT)</td>
<td>DDT – AUC, ln k</td>
<td>- Self-report (7 days pp)</td>
<td>with women who received only CBT (d = 0.70). Participants with high delay discounting at baseline experienced greater discounting decreases.</td>
<td>Breath CO (abstinence defined as ≥4 ppm)</td>
<td>Averaging over post-treatment and follow-up change from intake discounting did not significantly differ between the two groups. CM+CBT displayed decreased...</td>
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<td>- Breath CO (abstinence defined as ≥4 ppm)</td>
<td>post-treatment (d = 0.84). No significant difference at 6-month follow-up</td>
<td>Urine cotinine (abstinence defined as &lt;80 ng/ml)</td>
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</tr>
<tr>
<td>Source</td>
<td>Intervention (vs comparison)</td>
<td>Impulsivity outcome measure</td>
<td>Substance use outcome measure</td>
<td>Impulsivity outcomes</td>
<td>Substance use outcomes</td>
<td>Relationship between impulsivity changes and substance use outcomes</td>
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<tr>
<td>Loughead et al. (2016)</td>
<td>Cognitive training + NRT (vs relaxation control + NRT)</td>
<td>Non-cued GNG – commission errors, reaction time</td>
<td>- Self-report (7 days pp) - Breath CO (abstinence defined as ≤8 ppm)</td>
<td>No significance in either task between groups across time</td>
<td>No significant effect of treatment condition on quit rates at post-treatment or follow-up</td>
<td>N/A</td>
</tr>
<tr>
<td>Source</td>
<td>Intervention (vs comparison)</td>
<td>Impulsivity outcome measure</td>
<td>Substance use outcome measure</td>
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<tr>
<td>Hughes et al. (2017)</td>
<td>CM + brief supportive counselling</td>
<td>DDT – ln k</td>
<td>- Breath CO (abstinence defined as ≤8ppm)</td>
<td>There was a significant decrease in delay discounting score in participants abstinent at post-intervention ($d = 1.23$)</td>
<td>52% abstinent for at least 1 week but only 29% of participants were abstinent at post-treatment</td>
<td>N/A</td>
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<tr>
<td>Adams et al. (2017)</td>
<td>Response inhibition training (vs control training)</td>
<td>Non-cued and smoking-cued GNG tasks – commission errors</td>
<td>- Self-report on TLFB (7 days post-intervention)</td>
<td>Compared to baseline, all participants made significantly more commission errors on both the non-cued ($d = 0.59$) and smoking-cued ($d = 0.91$) GNG tasks post-intervention</td>
<td>No significant effect of treatment condition on number of cigarettes smoked post-treatment</td>
<td>N/A</td>
</tr>
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</table>
AUC = area under the curve; CBT = cognitive behavioural therapy; CM = contingency management; CPT = continuous performance task; CO = carbon monoxide; $d = \text{Cohen's } d$; DDT = delay discounting task; GNG = go/no-go task; $g = g$ parameter; $\ln k = \text{logarithm } k$ parameter; NRT = nicotine replacement therapy; pp = point prevalence; ppm = parts per million; TLFB = Timeline Followback.

8.3.4.1 Changes in impulsivity following treatment

Behavioural therapies. Four studies examined behavioural therapies and all utilised contingency management (CM) interventions (Bradstreet et al., 2014; Yi et al., 2008; Yoon et al., 2007; Yoon et al., 2009). All studies reported no significant reduction in impulsivity as measured by the DDT with the exception of Yi et al., (2008) who reported a significant effect as measured by a delay discounting questionnaire.

Yoon et al. (2009) and Bradstreet et al. (2014) both compared two groups of participants on different contingency schedules. Yoon et al. conducted a 14-day intervention where 13 participants in the intervention group could earn daily monetary payments contingent on biochemically verified smoking status. $20.50 was earned the first time the abstinence criterion was met, with amounts on subsequent days beginning at $4.50 and reaching a maximum of $40. They were compared with 15 participants in the comparison condition who received $28 per day on days 1-13 independent of smoking status and $40 on day 14 if they met the abstinence criterion. On days 1-13, the CM group reported significantly lower mean breath CO levels and urine cotinine levels compared with comparison group on days 1-13; however, the levels of CO and urine cotinine of the comparison group lowered to that of the CM group on day 14. There were no significant differences on the DDT between groups at pre, mid or post-intervention.

Similarly, Bradstreet et al. (2014) conducted a 15-day intervention where 14 participants in the smoking-contingent intervention group were compared with 16 participants in the comparison condition where incentives were only contingent on smoking on days 14-15. The incentive amounts and schedule were the same as that in Yoon et al. (2009). Results indicated that the CM group had
significantly lower mean breath CO levels and urine cotinine levels compared with comparison group on days 1-13, with effects of a large size. As with Yoon et al.’s study, the levels of the comparison group were lowered to that of the CM group on days 14-15. There were no significant differences in performance on the GNG task for the intervention group from pre to post intervention. Of note, the studies by Bradstreet et al. and Yoon et al. were not treatment efficacy studies and used participants who were non-treatment seeking.

Yoon et al. (2007) examined CM as a method of increasing rates of abstinence in 48 women who had quit smoking upon discovering they were pregnant. The authors combined two conditions of retail voucher incentives that were contingent and non-contingent on biologically verified smoking status. Voucher values began at $6.25 and could reach a maximum of $45. Smoking status was biochemically assessed monthly until delivery, weekly in the first month postpartum, then every second week until 12 weeks postpartum. Vouchers were available throughout this period but not at the final assessment time-point of 24 weeks postpartum. While a majority of women sustained abstinence throughout the study, 46% had relapsed at the 24-week assessment as measured by self-report and urine cotinine. Results suggested that there were no significant decreases in the DDT across time. However, unlike the other studies included in the review, the treatment was for the purposes of preventing relapse, and participants in this study had already quit smoking and had a clear motivation for staying abstinent for a minimum period of time as determined by their pregnancy.

In contrast, Yi et al. (2008) reported significant decreases in delay discounting in non-treatment seeking participants \( (n = 56) \). This was measured by a monetary delay discounting questionnaire and a cigarette delay discounting
questionnaire, with both yielding large effect sizes. The intervention occurred over five days where the smoking status of participants in the CM group were biologically tested three times a day. Participants received $10 each time they met the abstinence criterion as measured by breath CO levels. In order to eliminate limited access to cigarettes as a confounding variable to results, both groups were permitted to go to the laboratory each day to obtain a free pack of their preferred brand of cigarettes. Approximately 90% of participants in the CM group met the abstinence criteria at each assessment. Overall, participants in CM group reduced CO levels by 55% on average. No significant decreases in impulsivity were reported in a control group who received no intervention ($n = 28$). Of note, they used parameter $g$ to index participant’s delay discounting rate given that it is normally distributed, unlike parameter $k$ used by other studies. However, both parameters have the same regression mean and interpretation of the parameters do not differ (Yi et al., 2008).

**Cognitive training.** Two studies examined cognitive training in smokers. One study targeted training in the form of a web-based cognitive training game (Loughead et al., 2016). These games purported to target attention, working memory, and executive functioning. They examined the effects of a combined cognitive training and nicotine replacement therapy (NRT) intervention where the training was completed four times a week over 12 weeks. One hundred and eight participants in the intervention group were compared with an active control group of 105 smokers who received visual relaxation and NRT. There was no significant effect of treatment condition on quit rates at post-treatment or follow-up as measured by self-report and breath CO levels, and no significant decreases in
impulsivity found between groups on the GNG task or CPT at post-intervention or six-month follow-up.

The second study examined response inhibition training using a smoking-cued GNG training task (Adams, Mokrysz, et al., 2017). Twenty-seven participants completed the active training, where smoking-related stimuli were paired consistently with “no-go” cues and neutral stimuli were paired consistently with “go” cues. Twenty-eight participants completed the control version of the training that paired smoking-related and neutral stimuli with “no-go” cues at equal frequency. Both groups completed a single training session that was approximately 30 minutes in duration following overnight abstinence of 12 hours. There was no significant effect of the intervention on smoking outcomes as measured by self-report. All participants displayed significantly greater impulsivity from pre to post-intervention on both non-cued and smoking-cued GNG tasks that were used as measures of response inhibition. These were medium and large effect sizes, respectively. Of note, while this was a treatment efficacy study, participants were non-treatment seeking smokers.

*Psychotherapy.* Only one study used cognitive-behavioural therapy (CBT) and examined six weekly sessions of group therapy in 80 smokers (Secades-Villa et al., 2014). Session content included information regarding tobacco, a behavioural contract, self-monitoring, nicotine fading, stimulus control, strategies for managing nicotine withdrawal symptoms, physiological feedback consumption, training in alternative behaviours, social reinforcement of objection completion and abstinence, and relapse prevention strategies. At post-treatment, 61% of participants had been abstinent for the past 24 hours as assessed by self-report and breath CO levels; in contrast, at 12-month follow-up, 35% had been
abstinent for the previous seven days. No significant changes in impulsivity as measured by the DDT were found at post-intervention or follow-up.

Combined behavioural therapy and psychotherapy. Two studies examined a combination of behavioural therapy and psychotherapy. Weidberg and colleagues (2015) examined a combination of CM and group CBT administered once weekly over six weeks. Participants in the intervention group (n = 69) were compared with a control group (n = 47) who only received CBT. The CBT program was the same as that used in Secades-Villa et al.’s (2014) study. Two conditions of CM were combined for the purposes of this study given that no significant differences in abstinence rates were observed. The “CM for smoking abstinence” condition targeted abstinence according to an escalating schedule of reinforcement. The “CM for shaping abstinence condition” involved individualised percentile schedules that aimed to progressively reduce levels of cotinine. The incentives used by both conditions were vouchers which were exchangeable for goods and services such as activities, food, and retail items. The first biological sample that met the abstinent criteria resulted in participants receiving a voucher valued at €80, with €20 vouchers for subsequent days when they met the criteria.

Compared with the CBT group, the CM+CBT group achieved higher rates of abstinence at post-treatment as measured by self-report, breath CO levels, and urine cotinine, yielding a large effect size. However, no significant difference was observed at six-month follow-up (Weidberg, Landes, García-Rodríguez, et al., 2015). Results from Weidberg, Landes, López-Núñez, et al. (2015) found that CM+CBT displayed significant decreases on the DDT at post-intervention and follow-up while there were no significant decreases in CBT group. However, the
two groups did not significantly differ on the DDT when averaged over post-intervention and follow-up change from baseline. Analyses in Weidberg, Landes, García-Rodríguez, et al. (2015) further revealed that women who received CM+CBT showed significantly greater discounting decreases compared with woman who received CBT. This was a medium effect size. Furthermore, participants with high delay discounting at baseline experienced significantly greater decreases in discounting rate.

The second study examined the combination of CM and brief supportive counselling over four weeks (Hughes et al., 2017). Participants attended the laboratory twice a week and provided biochemical samples of breath CO and urine cotinine whereby abstinent-contingent monetary incentives were available based on an escalating payment schedule across weeks. Payments commenced at $16 and increased for each subsequent sample that met the abstinence criterion. Bonus payments of $50-100 were also rewarded for continuous abstinence. Results indicated that 52% of participants were abstinent for at least one week but only 29% of participants were abstinent at post-treatment. There was a significant decrease in DDT score in participants abstinent at post-intervention, yielding a large effect size. However, this group of participants was found to be older, more educated, and had smoked fewer cigarettes daily. As such, results may not be generalizable.

8.3.4.2 Association between changes in impulsivity and substance use outcome. Three studies examined whether changes in levels of impulsivity were related to smoking cessation outcome following treatment. Results in the study by Yoon et al. (2007) suggested that there was no significant interaction between eventual smoking classification and DDT results following CM in postpartum
women. Similarly, Weidberg, Landes, García-Rodríguez, et al. (2015) did not find a significant effect of CM treatment, smoking status, or interaction on DDT changes at post-intervention or follow-up. Conversely, Secades-Villa et al. (2014) reported that abstainers exhibited significant changes on the DDT at 12-month follow-up while there were no changes on the DDT in participants who were still smoking. This yielded a medium effect size.

8.4 Discussion

The aim of the present systematic review was to investigate whether impulsivity levels decreased following psychosocial treatments for smoking. It also aimed to examine whether decreases in impulsivity were associated with improved smoking outcomes. A review of the literature yielded 10 relevant studies (nine independent studies) that were analysed. There were five studies examining the efficacy of smoking cessation treatments, three experimental studies, and one relapse prevention study. Methodology of studies were diverse and hence a meta-analysis was not feasible. The durations of the interventions varied significantly and there did not appear to be a consistent pattern between the length of intervention and effect size.

Given the heterogeneity in interventions, studies were categorised into the following four types of therapies for ease of comparison and interpretation: behavioural therapy, cognitive training, psychotherapy, and combined therapies. A majority of studies examined CM either as the sole treatment (n = 4) or a component of treatment (n = 2). Only response inhibition training explicitly targeted a facet of impulsivity (Adams, Mokrysz, et al., 2017), although it is acknowledged that CM can address reward sensitivity through the introduction of incentives into the external environment (Staiger, Kambouropoulos, & Dawe,
The overall methodological quality of studies was generally rated as moderate. Studies were RCT, CCT, or cohort in design, with six of the nine identified studies using a comparison group. Interpretations of the findings are discussed in the sections below.

**8.4.1 Contingency management**

CM was utilised in a total of six studies and was the primary intervention in the three studies in this review that reporting a significant reduction in impulsivity post-intervention, yielding effect sizes ranging from small to large. CM is based on principles of operant conditioning whereby smoking, which has been maintained by the reinforcing nature of cigarettes, can be reduced using alternative, non-drug reinforcers (Higgins et al., 2008; Krishnan-Sarin et al., 2013).

While all three studies reporting significant effects also utilised delay discounting as their measure of impulsivity, their methodology and comparisons varied slightly; Yi et al. (2008) used monetary and cigarette delay discounting questionnaires comparing CM with no intervention, Hughes et al. (2017) used the DDT to examine CM and brief supportive counselling, and Weidberg, Landes, López-Núñez, et al. (2015) used the DDT to compare a combination of CM and CBT to CBT alone. Participants across the three studies were heavy smokers, with the number of daily cigarettes smoked at baseline ranging from 19 to 24. The comparatively greater number of studies examining CM may be reflective of the susceptibility of impulsive individuals to rewards (Doran et al., 2007) and evidence suggesting that CM may be an effective treatment for impulsive individuals with SUD (see review by Tomko, Bountress, & Gray, 2016). Indeed, CM was found to be more effective than CBT in adolescent smokers who reported
high levels of impulsivity (Morean et al., 2015). Possible explanations are that impulsive individuals may benefit from external incentives which modify the reinforcing value of drug incentives (Tomko et al., 2016) or that the simple contingency of CM may be more effective for impulsive individuals, especially during the initial phase of abstinence (Morean et al., 2015).

Nonetheless, three of the six studies in this review which examined CM reported nonsignificant results in relation to changes in impulsivity levels post-intervention. Two of these studies used the DDT (Yoon et al., 2007; Yoon et al., 2009) and one used the GNG task (Bradstreet et al., 2014) as the measure of impulsivity. The methodology in the study by Yoon et al. (2007) differed from other studies in the review in two respects: 1) a specific sample of pregnant woman was used and 2) it was a relapse prevention intervention for individuals who had already quit smoking. However, further consideration of research evidence suggests that these points may not explain the results given that CM has been shown to be an effective smoking cessation treatment in pregnant women (K Cahill et al., 2015; Hand, Ellis, Carr, Abatemarco, & Ledgerwood, 2017).

Furthermore, previous cross-sectional research suggests that there are no differences in delay discounting among smokers who quit without assistance, abstinent and non-abstinent smokers in treatment, and non-treatment seeking smokers (Celma-Merola, Abella-Pons, Mata, Pedra-Pagés, & Verdejo-Garcia, 2017). Potentially, the nonsignificant results may be related to the comparatively lower number of cigarettes smoked by Yoon et al.’s sample. Participants in their study reported smoking a mean of 9.6 daily cigarettes compared to other study samples that reported a mean of 15-23 daily cigarettes. CM may be less effective
in inducing decreases in impulsivity for smokers of lower dependence, although there are no studies at present that have investigated this association.

The remaining two CM studies that reported nonsignificant effects were experimental studies that used non-treatment seeking participants (Bradstreet et al., 2014; Yoon et al., 2009), suggesting that motivation to change one’s smoking behaviours may be an important factor. However, this appears to contradict the findings of Yi et al (2008) who implemented a CM regime in a group of non-treatment seekers and reported a decrease in impulsivity. The differing results may be due to their CM regime being comparatively more intensive within a shorter period of time whereby participants were biologically verified for abstinence three times a day compared with other CM studies that only tested participants once a day or less.

While an additional explanation for the contrasting results may relate to Yi et al.’s (2008) use of delay discounting questionnaire instead of the DDT as an impulsivity measure, previous research has not found the two types of measures to be significantly different (MacKillop et al., 2011). Namely, two meta-analyses of 110 studies (MacKillop et al., 2011) and 64 studies (Amlung, Vedelago, Acker, Balodis, & MacKillop, 2017) investigated the difference between a computerised version of the monetary DDT (e.g. Richards, Zhang, Mitchell, & de Wit, 1999) with the Monetary Choice Questionnaire (MCQ; Kirby et al., 1999). Both types of measures present items that require the respondent to make a choice between an immediate reward and a delayed reward, though the MCQ uses a set of 27 items while the DDT comprises of an average of 110 questions which adjusts the immediate monetary amount in questions based on preceding responses. They did not find a significant difference in effect sizes between MCQ and DDT in samples
of substance users and gamblers, suggesting that the two types of delay
discounting measures may be comparable as they are assessing similar processes.
Furthermore, an important distinction is that the questionnaire used by Yi et al.
(Rachlin et al., 1991) was more comprehensive than the MCQ, and assessed every possible combination of delay and reward by systematically decreasing the immediate reward. There are currently no studies comparing this version of delay discounting questionnaire with DDT, though it is unlikely that this difference in assessment accounts for the significant effect found by Yi et al.

8.4.2 Other treatments and measures

There were three studies that did not examine CM; two examined cognitive training (Adams, Mokrysz, et al., 2017; Loughead et al., 2016) and one examined CBT (Secades-Villa et al., 2014). Two studies reported no decreases in impulsivity (Loughead et al., 2016; Secades-Villa et al., 2014), while the third study reported increased impulsivity (Adams, Mokrysz, et al., 2017).

The study examining CBT (Secades-Villa et al., 2014) reported no decreases in impulsivity as measured by the DDT. Weidberg, Landes, López-Núñez, et al. (2015) used the same CBT group therapy program as Secades-Villa et al. (2014) but as a comparison group to a combined CM and CBT treatment, and also reported nonsignificant changes in impulsivity as measured by the DDT in the CBT only group. While interpretation is limited by the small pool of studies examining non-CM treatments, it may be tentatively suggested that CBT may have limited effectiveness in reducing impulsivity as measured by the DDT. CM and CM+CBT has been found to be more effective than CBT alone in facilitating abstinence in adolescent smokers (Krishnan-Sarin et al., 2013). Results did not differ between CM and CM+CBT, suggesting that CM may be the component
responsible for the results. CBT may be less likely to reduce impulsivity as the intervention skills taught are complex and may be less effective for smokers during the initial stages of quitting. Alternatively, the six sessions of CBT may not have been sufficient for smokers to sufficiently learn the skills to result in significant decreases in impulsivity.

The two studies in the review examining cognitive training reported conflicting results. The cognitive training in Loughead et al. (2016) targeted domains of working memory, attention, and executive functioning and yielded nonsignificant results between groups across time on the non-cued GNG task and CPT. Their findings contrast with that of Adams, Mokrysz, et al. (2017) who reported increased impulsivity following response inhibition training as measured by both non-cued and smoking-cued GNG tasks. While this finding is counterintuitive to the intervention’s intended purpose, there are three possible explanations for these results. Firstly, by using the GNG task as both the training task and measurement of response inhibition, it is suggested that the task may have obscured the training effects post-intervention by encouraging pre-potent responding whereby contingencies of “no-go” trials decreased from 50% in the training to 25% in the test measure. Secondly, the decrease in inhibitory control may be the consequence of participant fatigue given that all tests and the 30-minute training session were completed on the same day. This is supported by increases in self-reported anxiety, cigarette craving, and drowsiness at post-intervention. These findings are congruent with previous research indicated that mental fatigue following sustained duration of a cognitive task can result in increased reaction time and error rates (Kato, Endo, & Kizuka, 2009; Lorist, Boksem, & Ridderinkhof, 2005). Thirdly, participants were non-treatment seeking
whose low levels of motivation to change may have prevented the training from reducing their impulsivity.

The findings of this review suggest that the type of impulsivity measure may influence the likelihood of detecting changes in impulsivity. Namely, nonsignificant results could be due to the use of a non-cued GNG task and CPT as measurements of impulsivity. The two studies using one or both of these two measures (Bradstreet et al., 2014; Loughead et al., 2016) may have reported null findings as these measures lack motivationally relevant stimuli that would induce approach behaviour. That is, the standard non-cued versions of the GNG and CPT tasks would be less sensitive in detecting deficits in impulsivity and any subsequent changes post-intervention. In contrast, smoking-cued versions of tasks or delay discounting measures that include monetary or cigarette rewards appear to be more sensitive. This is congruent with Stevens et al.’s (2014) argument in their meta-analysis that neurocognitive tasks that incorporate appetitive elements are better predictors of substance use relapse. Indeed, although the changes in impulsivity in Adams, Mokrysz, et al.’s (2017) study were in the opposite direction to what was expected, the effect sizes yielded by the smoking-cued GNG task was larger than the non-cued task in measuring commission errors. The importance of relevant stimuli is further supported by the findings of Yi et al. (2008) who reported that participants discounted cigarette rewards more steeply than monetary rewards, consistent with other literature demonstrating that substance users discount their drug of use or other primary, consumable reinforcers such as food, at a greater rate than money (Jiga-Boy, Storey, & Buehner, 2013; Johnson et al., 2010; Johnson, Bruner, & Johnson, 2015; Odum & Baumann, 2007; Odum & Rainaud, 2003). As such, smoking-cued cognitive tasks
may be more likely to find significant effects due to the appetitive relevance of the cues and may thus be more valid assessment tools for investigating the link between impulsivity and smoking cessation outcomes.

Interestingly, there were no studies examining trait impulsivity as measured by self-report that met the criteria for inclusion in this review. This may be the result of literature suggesting that behavioural measures of impulsivity are superior predictors of smoking relapse (Krishnan-Sarin et al., 2007; Powell et al., 2010) and as such, research has tended to focus on those aspects in respect to change post-intervention as opposed to trait impulsivity as assessed by self-report measures.

**8.4.3 Durability of changes in impulsivity**

Three studies conducted follow-up assessments of impulsivity following the post-intervention time-point. Significant decreases as measured by the DDT were reported by Weidberg, Landes, López-Núñez, et al. (2015) and Weidberg, Landes, García-Rodríguez, et al. (2015) at six-month follow-up and Secades-Villa et al. (2014) at 12-month follow-up in abstinent participants only. Weidberg et al. examined a combination of CM and CBT, and Secades-Villa et al. examined CBT only. In contrast, nonsignificant results were reported at six-month follow-up by Loughead et al. (2016) who examined a combination of cognitive training and NRT, using the GNG and CPT as impulsivity measures. It is important to note that this nonsignificant finding at follow-up is not unsurprising as no significant changes were reported at post-intervention. These results suggest that the DDT may be a more sensitive measure at detecting change in impulsivity across time.
8.4.4 Association between impulsivity and smoking outcomes

In regards to the second aim, three studies (Secades-Villa et al., 2014; Weidberg, Landes, García-Rodríguez, et al., 2015; Yoon et al., 2007) examined the association between changes in impulsivity and smoking outcome. Secades-Villa et al. (2014) reported abstainers at 12-month follow-up displayed greater improvements on the DDT, a significant interaction not evident at post-intervention. Conversely, studies by Weidberg, Landes, García-Rodríguez, et al. (2015) and Yoon et al. (2007) reported no significant relationships, although Yoon et al. was the relapse prevention study that had reported nonsignificant changes in impulsivity at post-intervention. Weidberg et al., who examined the association using the DDT at post-intervention and six-month follow-up, suggested that significant results may only be yielded following a longer follow-up period, as in Secades-Villa et al.’s study.

In considering possible explanations of this relationship, it has been theorised that sustained abstinence results in avoidance or reduced attentional bias of smoking cues (Littel & Franken, 2007; Munafò, Mogg, Roberts, Bradley, & Murphy, 2003; Peuker & Bizarro, 2014) which has been associated with decreased delay discounting rates (Field, Christiansen, Cole, & Goudie, 2007; Murphy & Garavan, 2011). Alternatively, factors unrelated to treatment may be responsible, whereby prolonged abstinence from smoking results in engagement in other healthy behaviours, such as exercise and healthy diets (Jang et al., 2012; Nagaya, Yoshida, Takahashi, & Kawai, 2007), which has also been associated with decreased rates of delay discounting (Bradford, 2010). Thus, while there is some evidence to suggest that decreases in impulsivity may only be significantly associated with smoking outcomes following a sustained period of abstinence in
smoking cessation studies, further research is required in exploring these mechanisms and their proposed role in the association between impulsivity and smoking outcome.

### 8.4.5 Clinical implications

The findings of the present review are mixed regarding the primary question of whether impulsivity levels reduce following smoking cessation treatments. In this respect, it is premature to draw clinical implications from this review. While it may be hypothesised that smoking cessation treatment explicitly targeting impulsivity constructs would be more effective in reducing impulsivity, only one such treatment was included in this review (Adams, Mokrysz, et al., 2017) and this reported an increase in impulsivity and no significant effects on smoking outcome following intervention. There needs to be further investigations into such treatments to expand the scope of the evidence base.

Broader knowledge of the specific impulsivity-related constructs that reduce following treatment may translate to significant improvements in treatment planning. However, compared with interventions targeting behavioural aspects of impulsivity, substance use treatments directly targeting trait impulsivity are fewer, with established treatments often focusing instead on other factors that would significantly impact the manifestation of impulsivity. For instance, aligning with literature arguing that mindfulness and impulsivity are inversely correlated (Murphy & MacKillop, 2012; Peters, Erisman, Upton, Baer, & Roemer, 2011), mindfulness-based therapies have been found to reduce rash impulsivity in substance users (Himelstein, 2011; Margolin et al., 2007). This may in turn decrease future substance use given the significant role rash impulsivity plays in substance use (Balevich et al., 2013; Chase & Hogarth, 2011; Dissabandara et al.,
2014; Doran et al., 2007; Gullo, Ward, Dawe, Powell, & Jackson, 2011); although this has yet to be systematically investigated. Similarly, treatments that target or include modules of emotion regulation or distress tolerance may also reduce substance use in response to negative emotions that often predict impulsive behaviour (Greenberg, Martindale, Fils-Aimé, & Dolan, 2016; Schreiber, Grant, & Odlaug, 2012). For example, Brooks et al. (2017) examined four weeks of regular dialectical behavioural therapy sessions in inpatients with methamphetamine use disorder. Results reported significant improvements in impulsivity across the lack of self-control, lack of attention, and cognitive instability subscales of the Barratt Impulsiveness Scale, yielding large effect sizes ($d = 1.18$-$1.45$). However, these interventions often include multiple components or examine comorbid disorders, and as such, it is difficult to identify the key element that led to significant decreases in impulsivity. It is clear that further research is needed to determine whether a central focus on trait impulsivity or targeting it via other characteristics will lead to clinically significant substance use outcomes.

### 8.4.6 Limitations and future research

Several limitations of the present review should be considered. Due to the methodological variation and small number of studies, a meta-analysis could not be performed. Given the limited number of studies in this review, particularly treatment efficacy studies, it is difficult to draw clear conclusions with respect to decreased levels of impulsivity post-intervention and generalisability of findings is limited. Furthermore, as previously noted, an important consideration is that the small sample sizes in a number of studies may have resulted in them being underpowered.
Despite the clinical relevance of impulsivity to smoking, there is currently limited empirical research examining changes in impulsivity levels within a treatment context, with much of the literature measuring impulsivity as a characterisation of participants or a predictor of treatment outcome. Future studies should continue to contribute to this expanding field and explore other types of smoking cessation treatments and impulsivity-related constructs, given that currently a majority of studies examine CM using a delay discounting measure. In particular, impulsivity traits as assessed by self-report measurements warrant additional research attention as contrary to previous beliefs that these are enduring personality traits, research evidence suggests that they are amenable to change following substance use treatment (Hershberger et al., 2017). Compared with behavioural measures, they represent largely different constructs of impulsivity (Cyders & Coskunpinar, 2011; Reynolds et al., 2006) and would thus index unique facets that would contribute additional information relating to changes in the construct of impulsivity following smoking treatments. There is also a need for more empirical studies utilising a longitudinal design to understand the trajectory of impulsivity levels following treatment, particularly in relation to its relationship with smoking cessation outcomes.

8.5 Chapter Summary

This systematic review yields mixed results regarding whether psychosocial treatments targeting smoking can result in reduced impulsivity post-intervention. There is some evidence to suggest that CM results in decreased impulsivity as measured by delay discounting measures. There is also tentative evidence to suggest that decreases in impulsivity may also be associated with improved smoking outcomes when measured after prolonged abstinence at a
distant follow-up time-point after the intervention period. However, these findings should be interpreted with caution given the small number of studies published and the limited range of treatment types and impulsivity constructs examined. Further research is required to expand upon this evidence base to understand this clinically relevant relationship and the utility of targeting impulsivity in smoking cessation treatment.

INST will further contribute to this domain of literature as a multi-session cognitive training program targeting impulsivity. Furthermore, it uses smoking-cued cognitive tasks that would be sensitive in capturing decreases in impulsivity over time. Given that this thesis has been focused on the development and piloting of intervention, the relationship between impulsivity and smoking cessation outcomes will be further explored in future investigations of INST.

With the completion of both components of the thesis, the following chapter will present the general discussion which summarises the findings of this thesis and examines the important directions for future research in addition to the clinical implications of INST.
Chapter Nine: General Discussion

The first part of this thesis reported on the development of the first web-based response inhibition training for smokers (INST). This is a significant contribution to the field of smoking cessation interventions given that smoking remains a pressing health issue worldwide and there is a need to continue to develop and offer effective treatments in order to increase rates of abstinence and reduce tobacco-related diseases and deaths. Given that response inhibition has been found to predict relapse to smoking (Powell et al., 2010), it was argued that this is an important target for novel treatments. The development of INST was informed by careful consideration of the literature, following which three empirical studies were conducted to further support this process.

The second part of this thesis presented a systematic review that investigated the relationship between the broader construct of impulsivity and interventions aimed to assist in smoking cessation. Given that impulsivity has consistently been identified as a significant factor in nicotine dependence and smoking relapse (Flory & Manuck, 2009; Kale et al., 2018; Loree et al., 2015; Stevens et al., 2014), it was argued that levels of impulsivity should reduce following effective interventions and such decreases would further be associated with smoking cessation outcomes.

This chapter reviews the aims and results of the two parts of this thesis. It discusses the future directions of this research and the clinical implications of the collective findings. Following this, limitations of the research are examined before the concluding remarks.
9.1 Summary of Results

9.1.1. Development and piloting of the INST program

This first part of the thesis outlined the conceptualisation, development, and piloting of INST which utilised a smoking-cued Go/No-Go (GNG) task. Considerations in the development of the intervention and protocol were informed by extensive reviews of the literature. An empirical study was conducted to validate the stimuli to be incorporated into the smoking-cued training task and an additional smoking-cued response inhibition measure. A sample of smokers were used in the validation process to ensure that the stimuli selected would be ecologically valid and have appetitive relevance to the target population as they are an essential component of the training task.

Following this, INST was piloted in two studies where the primary aims were to investigate the feasibility and acceptability of the program in samples of smokers. A secondary aim of the second pilot study was to examine the effects of the training on smoking outcomes. All results were presented descriptively given the nature of pilot studies and that the small samples prohibited any statistical analysis. The first study recruited 16 smokers from the community to complete the four-week training program. This involved completing a total of 14 training sessions; five sessions a week for the first two weeks and two sessions a week for the last two weeks. Participants reported that INST was a feasible intervention, with the program as a whole deemed acceptable and well-run. Data supported feedback that the GNG training was easy to complete, with participants yielding an accuracy percentage of approximately 98% in training sessions. Barriers to completing the intervention related to prioritising other commitments and not being able to access the intervention on a mobile device. Adherence was generally
positive, although there was a large number of potential participants who were eligible but did not participate.

A second pilot study was conducted with 13 smokers following modifications to the training protocol as informed by participant feedback and examination of adherence data. The primary modification was the reduction of the overall duration of the intervention from four weeks to two weeks. Results relating to smoking outcomes were also explored as a technical error in the training in the first pilot study meant that this could not occur.

Similar to the first study, participants in the second study reported the training program to be feasible and demonstrated high accuracy when completing the GNG training. Drop-out rates were lower compared to that of the first study, most likely due to modifications in recruitment strategy, shorter length of the training, and possible differences in sample characteristics. Preliminary results suggested that INST may be effective in reducing the number of cigarettes smoked. At two-week follow-up, three participants reported reductions in their smoking and one participant reported abstinence. Several participants specified that the training had resulted in real-life behavioural change where they would envision the training and consciously reject smoking cigarettes. Craving levels were found to have decreased following each training session from pre-session levels. Both quantitative and qualitative data also indicated that cravings decreased from baseline to post-intervention, a factor identified by some participants as playing an important role in their reduction in smoking following the intervention.

A majority of participants correctly identified the mechanisms of the intervention (i.e. consistent mapping of the “no-go” cue on smoking stimuli), with
a few participants specifying that they believed the intervention aimed to form a negative association with cigarettes. All eight participants who completed the stimulus evaluation test at all three time-points reported a decreased rating of wanting to engage in the smoking behaviours depicted in the stimuli. Of the five participants who provided valid Stop Signal Task (SST) data for at least two time-points, the results of four participants indicated that there was an improvement in inhibitory control at post-intervention or follow-up. Overall, the results suggested that INST is a highly promising treatment option that could aid in assisting meaningful reductions in smoking.

9.1.2 Systematic review

This study aimed to investigate whether levels of impulsivity decrease following smoking cessation treatment and whether such decreases were related to smoking outcomes. Studies were included if the treatment entailed a behavioural, affective, cognitive, and/or social component targeting smoking. A systematic review of 10 studies (nine independent studies) yielded mixed results. Study treatments were categorised and compared in four categories: behavioural therapy, cognitive training, psychotherapy, and combined therapies. Findings suggested that there was only consistent evidence in relation to contingency management (CM) interventions reducing impulsivity as measured by delay discounting measurements. In relation to the second aim, there was tentative evidence to suggest that reduced impulsivity is associated with improved smoking outcomes when measured at a distal follow-up time-point after prolonged abstinence. However, further research is required due to the small sample size of studies and the limited range of treatments and impulsivity measures investigated.
This is the first review to investigate the impulsivity changes in any substance as assessed by both self-report and behavioural measures, despite a large body of evidence indicating that impulsivity is significantly associated with problematic substance use (Jentsch et al., 2014; Littlefield & Sher, 2014; Loree et al., 2015; Müller, Weijers, Böning, & Wiesbeck, 2008; Stevens et al., 2014). This highlights the need for further research in this area to determine the clinical relevance of decreasing impulsivity levels in smoking cessation treatment.

9.2 Future Directions

There are a number of significant research implications following the investigations of this thesis. The favourable results of the pilot studies indicate that a larger research trial is warranted. Given the scale of this proposed trial, this will include statistical analyses relating to moderators and mediators of training effects. The results of this trial will contribute to: 1) the evidence base for web-based response inhibition training, 2) the literature on substance use interventions targeting implicit processes, and 3) the literature examining the association between impulsivity and smoking outcome. Each of these points is examined in greater detail below.

First and foremost, the findings of this thesis provide the necessary empirical support to conduct a larger effectiveness trial. The details of this trial are provided in Appendix C in the form of a research protocol paper on which the writer was the lead student investigator. This double-blinded randomised controlled trial (RCT) will constitute the first multi-session web-based study examining the effectiveness of response inhibition training in smokers. The RCT will compare the intervention training with the active control training to assess its effectiveness within a rigorous protocol informed by the findings of the pilot
studies presented in this thesis. The follow-up time-point will also be extended to provide necessary information regarding the stability of training effects.

The scale of the RCT allows for the investigations of preregistered moderators in considering that response inhibition training may not be effective for all smokers and the size of its effects may vary according to individual differences. In food-cued training studies, intervention effects are most pronounced in individuals who have high levels of dietary restraint or are currently dieting (Houben & Jansen, 2011; Lawrence, Verbruggen, et al., 2015; Veling et al., 2011). This has been theorised to be due to a greater motivation to change behaviour (Jones et al., 2016). Additionally, the significance of dietary restraint may be accounted for by stronger appetitive approach tendencies (Houben, Roefs, & Jansen, 2012) given that larger training effects have been yielded by individuals with high appetite (Veling et al., 2013b). Similarly, having a high body mass index (BMI) has been found to result in greater training effects (Veling et al., 2014), possibly due the impulse-modifying nature of the training. In contrast, moderating variables have yet to be examined in alcohol training studies. Investigations of INST could examine baseline levels of response inhibition as a moderator given that weaker inhibitory control has been identified as a predictor of larger training effects (Houben, 2011). As an extension of this, self-reported trait levels of impulsivity may also moderate changes in response inhibition training as these two constructs of impulsivity are positively correlated (Pettiford et al., 2007). Additionally, severity of tobacco dependence would be a potential moderator of interest given its association with enhanced appetitive response and motivational salience towards smoking cues (Claus, Blaine, Filbey, Mayer, & Hutchison, 2013). These analyses could yield valuable information regarding
which subgroups of smokers may obtain the greatest benefits from response inhibition training.

Mediators of training effects as informed by current theories in the field will also be investigated in the RCT to gain a further understanding of the mechanisms of the intervention. Changes in inhibitory control will be measured using the SST as an independent measure of response inhibition; this is an important question of interest considering the conflicting results yielded by previous studies that also used GNG training (Alcorn et al., 2017; Houben, Havermans, et al., 2012). Additionally, examination of stimulus devaluation will add to the existing knowledge base in response inhibition training literature relating to the devaluation hypothesis (Jones et al., 2016). The second pilot study is one of the few studies that has used a measure of explicit stimulus evaluation to investigate the mechanisms of the training as proposed by this hypothesis, with results indicating that there were decreased positive evaluations towards smoking across time-points. This supports evidence indicating that explicit measures are a viable method of capturing the occurrence of stimulus devaluation and will thus be used in the RCT to further investigate this potential mediator.

Future examination of stimuli devaluation may also yield related information regarding moderators of training effects. A recent study by Chen, Veling, Dijkstra, and Holland (2018) investigating assumptions of the devaluation-based Behaviour Stimulus Interaction theory reported that individuals with greater response inhibition deficits did not experience larger devaluation effects following a single session of food-cued GNG training. However, response inhibition was assessed with a non-cued SST; this measurement of general response inhibition may not be significantly related to the food-cued response
inhibition required by the GNG training (see Houben, Nederkoorn, & Jansen, 2014), particularly in a non-clinical sample of university students of normal body weight. Further research into this question could include stimulus-specific measures of response inhibition in order to adequately predict the effectiveness of the training. Additionally, while craving of substances is a crucial component of substance use, it had not previously been explored in substance use training studies. Given past research indicating that craving and positive evaluations about smoking are positively correlated (Huijding & de Jong, 2006; Palfai, 2002; Waters et al., 2007), research on how these variables interact in the context of a substance use intervention could expand upon theoretical hypotheses regarding the mechanisms of response inhibition training.

**9.2.1 Research implications of the RCT**

The results of the RCT will have a number of notable research implications. Firstly, it will contribute to the body of evidence examining web-based response inhibition training as a method of decreasing problematic health behaviours. Of note, since the completion of this thesis, an RCT by Jones et al. (in press) had been published examining web-based response inhibition training in problem drinkers ($n = 246$). There were four experimental conditions: 1) modified GNG task where the “no-go” cue was consistently paired with alcohol stimuli, 2) modified SST where stop signals were paired with 50% of trials with alcohol stimuli, 3) general SST with no alcohol stimuli, and 4) a control group that completed a categorising task with no inhibition required. Participants completed up to 14 training sessions in a four-week period. There were significant reductions in alcohol consumption across all groups, with no differences between training groups, or between the training groups and control group. Their results contrast
with previous studies in food training that had reported a significant specific
effect of web-based GNG training (Lawrence, O'Sullivan, et al., 2015; Veling et
al., 2014). Given that two meta-analyses have reported no difference in training
effects between the two domains of food and alcohol (Allom et al., 2015; Jones et
al., 2016), it is thought that the lack of specific effects in Jones et al. may be the
result of 1) a brief intervention administered pre-training that aimed to increase
motivation to change drinking levels through psychoeducation and goal-setting,
and 2) regular self-monitoring of alcohol consumption that may be an intervention
technique in itself. These factors may have obscured any effects that would have
been yielded by the training paradigms. Moreover, the GNG training task used in
the study did not include filler stimuli. It is likely that the task was too easy to
complete with only two categories of stimuli and insufficient attentional
engagement with the task prevented improvement of inhibitory control or
modifications of stimulus evaluations. Indeed, evidence has indicated that
individuals only learn stimulus-stop associations when adequate attention is paid
to the task (Best, Lawrence, Logan, McLaren, & Verbruggen, 2016).
Nevertheless, it is clear that the web-based format of response inhibition training
would benefit from further empirical evidence in relation to whether it generates
significant treatment effects in a real-world context.

Secondly, the findings of INST will contribute to the evidence base for the
class of substance use interventions targeting implicit processes. Aside from
response inhibition training, primary examples of such interventions are cognitive
bias modification interventions, training tasks used to modify maladaptive
cognitive biases such as attentional bias and approach bias in problematic
substance use (Kakoschke, Kemps, & Tiggemann, 2017; Wiers, Gladwin,
From the perspective of the dual process Reflective-Impulsive model reviewed in Chapter Two, both response inhibition training and cognitive bias modification target implicit processes that influence reactions to stimuli that may not occur within smokers’ conscious control (Verdejo-Garcia, 2016). It is argued that by weakening the impulsive processes that influence substance use, the necessity of effortful control as exerted by the reflective system is diminished and approach behaviour toward substance use is decreased (Friese et al., 2011). As such, further investigations of this method of targeting implicit processes would be advantageous given the theoretical and clinical implications for substance use.

Lastly, INST will contribute to the understanding of the relationship between impulsivity and smoking outcome. Preliminary results of the pilot studies align with growing literature highlighting impulsivity as a viable treatment target across different substances (e.g. Hershberger et al., 2017). Despite the significant role impulsivity plays in smoking, there has been limited research investigating treatments specifically targeting impulsivity, as evidenced by the small number of papers included in the systematic review in Chapter Eight. The focus on behavioural measures of state impulsivity indicate that there is a disproportionate focus on state impulsivity as clinical outcomes while neglecting trait forms of impulsivity. Furthermore, with the exception of the response inhibition training study by Adams, Mokrysz, et al. (2017), none of the interventions targeted impulsivity directly. In this respect, research using the INST program will contribute to the understanding of which specific impulsivity-related traits decrease following treatment which can further translate to more targeted and effective treatment planning to improve outcomes.
9.2.2 Beyond the RCT

Should results of the RCT be significant, future research should assess conditions under which INST would be most effective by investigating variables of the training schedule such as frequency and duration. This could yield information regarding dose-response effects and its role in moderating treatment outcome, which would contribute uniquely to the response inhibition training literature given the currently limited knowledge regarding the association between quantity of training sessions and effectiveness. An additional variable of interest is the timing of quitting or reducing smoking during the intervention period. Changes in smoking behaviour have been shown to impact on neurocognitive abilities due to the pharmacological effects of nicotine. A meta-analysis reported that smokers who were abstinent for at least eight hours had significantly poorer response inhibition compared with satiated smokers as measured by the GNG task or SST (Grabski et al., 2016). Clear guidance and planning of how smokers will change their smoking behaviours could assist in systematically analysing how the timing of these changes interact with intervention effects.

It would be important to examine the application of the intervention outside the bounds of a structured program whereby smokers can access an unlimited amount of sessions while having minimal interaction with researchers (i.e. no face to face meeting, no SMS reminders). This would provide information regarding how INST as an intervention could be independently completed by smokers should it be made widely available on the internet. Part of this process would necessitate the introduction of modifications to improve engagement and address low adherence commonly reported in web-based smoking interventions (Taylor et al., 2017). INST could allow for the personalisation of certain features
given that this has been identified in literature as an imperative aspect of engagement and subsequent effectiveness (Hutton et al., 2011). For instance, pilot study participants suggested that smokers could have the ability to insert their own images of alternative behaviours to smoking into the training task; this may increase the effectiveness of the training given the personal salience of the behaviours. Other versions of INST may introduce game-like elements into the training to further increase engagement and motivation to complete the training (Boendermaker, Prins, & Wiers, 2015; Gladwin, Figner, Crone, & Wiers, 2011). However, it should be noted that research in cognitive bias modification training for alcohol misuse suggest that this gamification needs to be executed with careful consideration to prevent decreasing engagement due to features being experienced as disappointing or distracting (Boendermaker, Sanchez Maceiras, Boffo, & Wiers, 2016).

Additionally, the development of a mobile or tablet app version of the intervention would be an important extension of INST if results of the computer-based version are favourable. Participant feedback indicated that this would improve feasibility of the intervention due to increased convenience. However, there would need to be considerations that the mobile version would likely be used in a larger variety of environments or “on the go” where there would be more external distractions that may interfere with people’s ability to engage meaningfully with the intervention. Indeed, feedback and participant results suggest that being attentive to the images during the training is a critical aspect of the training in facilitating change.

The INST training could also be used adjunct to other smoking cessation treatments to maximise effectiveness. In accordance to a dual process model
perspective, substance use behaviour has been proposed to result from conflict between the reflective and impulsive systems. As such, it has been argued that addictions can be addressed through targeting both the reflective and impulsive systems to facilitate behavioural change throughout the different stages of addiction (Friese et al., 2011). This would involve strengthening the reflective system to ensure that it possesses adequate resources and is sufficiently engaged to overcome the urges of the impulsive system (Grenard et al., 2008; Strack & Deutsch, 2004; Thush et al., 2008). In conjunction with this, the impulsive system would be addressed by modifying basic cognitive aspects such as inhibitory control, attentional biases, automatic associations, or approach tendencies towards the problematic behaviour (Friese et al., 2011; Hofmann et al., 2008; Wiers & Gladwin, 2017).

This approach of targeting both systems has previously been explored in food response inhibition training studies. For example, van Koningsbruggen and colleagues (2014) examined single sessions of a food-cued GNG training task and implementation intentions, both of which had an active and control condition. Participants who received the control conditions of the interventions served themselves significantly more sweets post-intervention than those who received one or both active interventions. However, using one active condition of either intervention appeared to be more effective than using both active conditions. It may be that using both interventions did not yield additional effects given that they both aim to reduce the impulse-provoking nature of palatable food cues. Veling et al. (2014) extended this study by administering the two interventions online once a week over a four-week period to examine treatment effects. Results indicated that both types of interventions significantly facilitated weight loss, with
the largest effect size yielded by participants who completed the intervention conditions of both interventions; however, there were no interaction effects of the two interventions.

Forman and colleagues (2016) examined a single session of mindful decision making training and four sessions of a food-cued SST. Participants received either one of the interventions, a combination of both interventions, or psychoeducation only. While exploratory analyses indicated that participants in the combination condition yielded the greatest reduction in snack consumption from baseline to post-intervention when compared to the psychoeducation group, they reported no synergistic additive effects of the combined condition. It was suggested that this may be due to a ceiling effect given that the combined condition had already significantly decreased snack consumption. However, it could also be that the use of the SST diminished training effects as it may not have been sufficient in significantly increasing inhibitory control due to the inconsistent stop signals (Jones et al., 2016). Aside from methodological considerations, the efficacy of this combined intervention of targeting both explicit top-down and implicit bottom-up inhibitory control may be dependent on the severity of impulsivity levels; that is, those with high levels of impulsivity at baseline would yield the greatest treatment outcomes, in line with response inhibition literature (Houben, 2011). As such, this dual approach may yield larger effects in a clinical sample of smokers given the high levels of impulsivity exhibited in this population.

**9.2.3 Broader implications**

It is important to note that findings from further investigating the variables of interest outlined above would benefit the broader literature of response
inhibition training. As reviewed, while variables such as moderators and mediators have been examined, research systematically examining the translation of the training from structured, laboratory-based protocols to real-world contexts remains in its infancy. Indeed, this is particularly relevant to response inhibition training for substance users, where there are important considerations of abstinence and neurocognitive implications in optimising the training while maintaining feasibility. More broadly, the results of the empirical investigations into INST would also contribute to the body of evidence for web-based interventions addressing a range of health-related issues such as physical exercise, diet, and sleep. These have examined similar considerations including personalisation (e.g. Storm et al., 2016), dose-response effects (e.g. Schweier et al., 2014) and usage (e.g. Kelders, Van Gemert-Pijnen, Werkman, Nijland, & Seydel, 2011). By investigating such pertinent issues, INST would yield highly relevant evidence to the general field of interventions targeting a wide spectrum of health behaviours.

9.3 Clinical Implications

The findings of the present thesis provide a vital foundation upon which future research on INST will contribute to response inhibition training literature targeting substance use. The examination of moderators as outlined in the previous section could yield valuable empirical evidence identifying specific subgroups that would benefit most from the training. It converges with previous arguments that treatments could be matched with substances users based on individual factors such as personality traits, including impulsivity (Staiger et al., 2007; Tomko et al., 2016). This tailoring of treatment to individual profiles could assist in maximising treatment response and entail more efficient use of resources.
As a web-based intervention, INST is an accessible and cost-effective treatment option. It aligns with other smoking cessation treatments of this modality (e.g. Hutton et al., 2011) that have been developed in response to modern society’s increasing preference for technological and mobile mediums. Its convenience to a wide community of smokers at minimal costs is a significant benefit given that lack of funding is the biggest challenge identified in tobacco control efforts (Leischow, Okamoto, McIntosh, Ossip, & Lando, 2017).

Considering the burden that smoking poses on the health system, statistically significant effects of even a small effect size could accumulate to have an immense impact in the public health sphere. As the training can be completed independently, this would mitigate the strain on treatment resources and enable providers to reserve the availability of more resource-intensive treatments (e.g. psychotherapy) for smokers who prefer or require an intervention with face-to-face interpersonal contact. Thus, INST has the potential to facilitate clinically significant changes in smoking behaviour and impact upon tobacco-related outcomes and health services on a global scale.

9.4 Limitations

As the limitations of the systematic review have been discussed in depth in Chapter Eight, this section will only examine limitations relating to the first part of the thesis that developed the INST program. As previously stated in Chapter Seven, the pilot studies were conducted using small sample sizes and the results may not be wholly reflective of the general population of smokers. This may have ramifications for the design of the intervention and program protocol given that modifications were based on the quantitative results and qualitative
feedback obtained from these samples. Furthermore, participants included in the pilot studies were generally very motivated to quit smoking, which may have led them to deem the intervention more feasible and acceptable than smokers who have low to moderate levels of motivation.

While all efforts were made to develop an empirically-sound intervention protocol, it should be noted that there are several potential limitations in the design. The control training task to be used as a comparison to the intervention training does not incorporate smoking stimuli. While the lack of target stimuli in control training has been suggested to be most conservative (Adams, Mokrysz, et al., 2017) and hence preferable, it could be argued that any training effects may be confounded by the intervention group’s consistent exposure to smoking cues. As such, the inclusion of an additional control training group to match for cue exposure may assist to further increase the validity of findings. This may take the form of control groups that receive the same images as the intervention group, but either passively observe and do not respond to any trials (e.g. Adams, Lawrence, et al., 2017) or inhibit their responses on 50% of smoking trials (e.g. Adams, Mokrysz, et al., 2017; Houben, 2011). However, limitations for both these approaches have been noted. An observe group would be engaging in a form of response inhibition training by not approaching appetitive stimuli (Adams, Lawrence, et al., 2017), as supported by evidence indicating that this condition results in devaluation of stimuli (Chen et al., 2016). Conversely, inconsistent mapping on the target stimuli may increase attentional salience and subsequent engagement in the behaviour (Anselme et al., 2013). Indeed, findings in food training studies show that such groups displayed a greater consumption of calories compared with a condition where unhealthy foods were consistently mapped with
“go” cues (Houben, 2011; Houben & Jansen, 2011). It may thus be difficult to determine a true control training condition that is able to control for cue exposure.

Secondly, the primary outcome measurement is self-reported number of cigarettes in the form of the Timeline Followback (TLFB). While this is generally considered a valid assessment, it may nevertheless yield inaccurate results in the absence of biochemical verification due to misreporting. Another limitation relating to smoking outcome is that the current protocol attempts to balance structured parameters on smoking reduction/quittrig within the intervention with participant autonomy to choose how they change their smoking. However, analysis of the data may be complicated by the range of possible changes in smoking behaviour (i.e. abstinence or reduction at different points during the intervention). Additionally, the variation in smoking changes means that it would be difficult to discern how the pharmacological effects of changes in smoking behaviour and nicotine withdrawal interact with the training. As such, it may be that a more consistent approach would ultimately be more beneficial in providing uniformity.

Thirdly, as an independent measure of response inhibition training, the SST indexes a different form of response inhibition that requires “action cancellation” and is related to top-down inhibitory control, contrary to the GNG task that elicits “action restraint” and engages bottom-up processes (Verbruggen & Logan, 2008). As previously reviewed, other studies have also used this approach and yielded conflicting results (Alcorn et al., 2017; Houben, Havermans, et al., 2012). As such, it is acknowledged that this may not adequately capture changes in response inhibition as facilitated by GNG training.
9.5 Conclusions

This thesis primarily examined the development and piloting of the first web-based smoking-cued response inhibition training for smokers who wish to quit. Conceptualisation and development of the intervention was informed by reviews of the literature and an empirical study validating stimuli incorporated into the training task. Findings from two pilot studies indicate that it is a highly feasible and acceptable intervention, with preliminary results suggesting that it is a promising intervention that could assist smokers in reducing the number of cigarettes smoked.

In the second part of this thesis, results of a systematic review found that there was some evidence to support the hypothesis that impulsivity reduced following non-pharmacological treatments targeting smoking behaviour, although this was only consistently demonstrated in CM treatments using delay discounting measures. Additionally, the relationship between reduced impulsivity and smoking outcomes only appears to be significant when measured at a longer follow-up time-point. However, further research is required before definitive conclusions can be drawn given the limited amount of literature in this area.

The results of this thesis yield several research implications for future directions. Given the favourable findings of feasibility and preliminary results, INST will now be examined in a double-blinded RCT by the research team to provide further evidence for its effectiveness under more rigorous conditions and in a larger sample size. Results from this trial will not only contribute to the growing literature examining response inhibition training across problematic health behaviours, but also expand upon the knowledge base of the clinically significant relationship between impulsivity and smoking. Should INST be found
to yield significant results, it would be a cost-effective and accessible intervention option for smokers that can be widely disseminated. It has important clinical implications if made available to the wider public and has the potential to significantly reduce the health and financial burden of tobacco-related outcomes worldwide.
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Appendices
Appendix A

Pilot Study 1: Qualitative Feedback Interview

Post-intervention: Qualitative questions

<table>
<thead>
<tr>
<th>Participant number:</th>
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<tr>
<td>Number of sessions completed:</td>
<td>Week 1 – Week 2 – Week 3 – Week 4 –</td>
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<tr>
<td>Meeting date:</td>
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<tr>
<td>Chosen quit date:</td>
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<td>Date:</td>
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This phone call will take about 20-30 minutes. We will first estimate how many cigarettes you smoked over the past month and then I’ll ask you some questions about how you found the intervention. After that I’ll send you the link to do the same online questionnaires you did at our face-to-face meeting.

**Timeline Followback**

*Complete TLFB*

Did you start using nicotine replacement therapy during this time? E.g. patches, gum

*If yes, complete a TLFB*
Since our last meeting, did you try to use any other methods aside from our intervention to help you quit smoking?

**Experience of intervention**

Now I’ll ask you some questions about your experience of the intervention and what you did and didn’t find helpful. Your feedback is really important in helping us refine our program so please be as honest as you can.

How did you find doing the intervention?

Could you rate from 0 (not at all effective) to 10 (really effective) how effective it was in helping you give up smoking?

What did you think the intervention was training you to do? What made you think that?

Did you think that that actually helped/had any impact on your smoking in any way?

Did the task made you want to smoke more because you were looking at pictures of cigarettes?

What was the impact of being asked when you last smoked each time before you did a training session?
Could you rate from 0 to 10 how feasible it was for you to do the training session 14 times over a month?

Is there anything you would suggest in terms of the number of sessions – more/less or not having a strict structure?

As you know, the program required you to do two intensive weeks of 5 sessions a week, and then only 2 sessions a week in the last two weeks. Do you think these last two weeks were helpful or necessary in maintaining the effects of the first two weeks?

Were there any barriers or difficulties?

What were your expectations of the intervention?

Did it meet expectations?

What are your expectations of regarding your smoking at the end of the intervention? E.g. quit/smoking less

As you might remember, at our meeting you set a quit date for yourself. As I mentioned, a quit date was something we are also investigating, as we were not sure whether it was better to let participants set their own quit dates or
whether to ask participants to quit at the start or at the end. Did you have any thoughts about that?

Aids in Adherence

Now I’ll move onto some questions about things we put in place to encourage people to do as many training sessions as possible.

We decided to meet people to show them the training session and make sure they understood how to do it before having them complete it at home. Do you think that was necessary/helpful?

Could you rate from 0 to 10 how helpful or necessary you think the face-to-face meeting was?

Could you rate from 0 to 10 how helpful or necessary you think the training calendar and card were?

Could you rate from 0 to 10 how helpful or necessary you think the SMS reminders were?

What frequency would you find helpful?

Can you think of anything else that would have helped?
Other Feedback

Is there anything you would change about the intervention?

Any other feedback?

Remind them re: follow up call in 2 weeks (shorter phone call next time)

Email them the online link to the post-intervention questionnaires:

http://psych.hosted-sites.deakin.edu.au/inst/post

Request that they try and do it all in one sitting, or at the very least in one day
Two-week follow-up

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This phone call is to follow-up with how your smoking has been in the past two weeks, so it should only take about 5-10 minutes. After that, I’ll send you the link to do the same online questionnaires you did at our last follow-up.

**Timeline Followback**

*[Complete TLFB]*

Did you start using nicotine replacement therapy during this time? E.g. patches, gum?

*If yes, complete a TLFB*

Since our phone call, did you try to use any other methods aside from our intervention to help you quit smoking?

Comments/observations regarding their smoking:

Email them the online link to the follow-up questionnaires: [http://psych.hosted-sites.deakin.edu.au/inst/follow-up](http://psych.hosted-sites.deakin.edu.au/inst/follow-up)

Request that they try and do it all in one sitting, or at the very least in one day
Appendix B
Pilot Study 2: Qualitative Feedback Interview

Post-intervention: Qualitative questions

<table>
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<td>Meeting date:</td>
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<td>Chosen quit date:</td>
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This phone call will take about 15 minutes. We will first estimate how many cigarettes you smoked over the two weeks and then I’ll ask you some questions about how you found the intervention. After that I’ll send you the link to do the same online questionnaires you did at our face-to-face meeting.

**Timeline Followback**

[Complete TLFB]

Did you start using nicotine replacement therapy during this time? E.g. patches, gum

*If yes, complete a TLFB*
Since our last meeting, did you try to use any other methods aside from our intervention to help you quit smoking?

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Experience of intervention

Now I'll ask you some questions about your experience of the intervention and what you did and didn’t find helpful. Your feedback is really important in helping us refine our program so please be as honest as you can.

How did you find doing the intervention?

Could you rate from 0 (not at all effective) to 10 (really effective) how effective it was in helping you give up smoking?

What did you think the intervention was training you to do? What made you think that?

*For those who do not know, explain that purpose (implicitly training brain to have better control over impulses to smoke) and ask the next question*

Did you think that helped/had any impact on your smoking in any way?

Did it have any impact on your smoking during more stressful situations?

Did you notice any changes in your craving levels?

Could you rate from 0 to 10 how feasible it was for you to do the training session every day for 2 weeks?
Is there anything you would suggest in terms of the number of sessions – more/less?

Were there any barriers or difficulties?

What are your expectations regarding your smoking at the end of the intervention? E.g. quit/smoking less

You may remember that at the meeting you set your quit date as _______. How did you go with that?

**Other Feedback**

Is there anything you would change about the intervention?

Any other feedback?

*Remind them re: follow up call in 2 weeks*

Email them the online link to the post-intervention questionnaires:


Request that they try and do it all in one sitting, or at the very least in one day
Two-week follow-up

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This phone call is to follow-up with how your smoking has been in the past two weeks, so it should only take about 5-10 minutes. After that, I’ll send you the link to do the same online questionnaires you did at our last follow-up.

**Timeline Followback**

[Complete TLFB]

Did you start using nicotine replacement therapy during this time? E.g. patches, gum?

*If yes, complete a TLFB*

Since our phone call, did you try to use any other methods aside from our intervention to help you quit smoking?

*Comments/observations regarding their smoking:*
Email them the online link to the follow-up questionnaires: [http://psych.hosted-sites.deakin.edu.au/inst/pilot3/followup1/](http://psych.hosted-sites.deakin.edu.au/inst/pilot3/followup1/)

Request that they try and do it all in one sitting, or at the very least in one day
Appendix C

Manuscript Submitted to BMC Public Health on the Study Protocol of a
Randomised Controlled Trial of INST

A Randomised Controlled Trial Examining the Efficacy of Smoking-related
Response Inhibition Training in Smokers: A Study Protocol

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Abstract

Background

Smoking is one of the leading preventable causes of illness and premature death worldwide. Despite a variety of effective treatments, relapse rates remain high, and novel, innovative interventions are needed in order to reduce the global prevalence of smoking. Research has indicated that deficits in the ability to inhibit a response (referred to as response inhibition) is a predictor of relapse and subsequently, targeting this potentially modifiable risk factor may lead to improvements in smoking outcomes. Indeed, in recent years, stimulus-specific response inhibition training has emerged as a potentially efficacious intervention to reduce unwanted/unhealthy behaviours such as alcohol and unhealthy food consumption. As such, the present trial aims to evaluate the efficacy of response inhibition smoking training (INST) in a sample of adult smokers.

Methods/Design

This randomised controlled trial recruited nicotine dependent smokers aged between 18 and 60 using social media and advertisements in Victoria, Australia. The sample target was 150 to account for drop out and non-adherence. Once informed consent had been obtained, participants completed a range of baseline measures during a face to face interview. Participants were then randomly allocated to one of two online training conditions: an intervention
training group (INST), which requires participants to exercise response inhibition
towards smoking-related stimuli; or an active control group, which requires
participants to exercise response inhibition towards household items and does not
include any smoking-related stimuli. They complete the first training session
during the interview to ensure the training protocol is clear. Both groups were
then instructed to complete a further 13 training sessions (1 per day) at home on
their computer and follow-up phone calls will be conducted at three time points:
post-intervention, one-month and three months. The primary outcome is a
reduction in the quantity of daily smoking at post-intervention, one and three
months follow-up.

Discussion

There is a pressing need to develop novel and innovative smoking
interventions. If proven to be effective, INST could make a highly cost-effective
contribution to improvements in smoking cessation outcomes.

Trial Registration

The trial was prospectively registered with the Australian New Zealand Clinical

Keywords: Smoking cessation, response inhibition, inhibitory control, cognitive
training, devaluation, eHealth, craving, intervention
Background

Tobacco smoking is one of the leading preventable causes of illness and premature death worldwide. It is the second largest contributor to the burden of disease globally, with 134.2 million years lost to disability, illness and premature death [1]. In 2013, 6.1 million people died globally as a result of tobacco use [1], and, if trends persist, this number will exceed eight million by the year 2030 [2]. Furthermore, tobacco use has been found to cost the global economy more than US$1 trillion each year in healthcare expenditures and lost productivity [3]. As smoking remains at unacceptable levels across the world [4, 5], examinations of effective and accessible smoking cessation treatments are crucial in reducing the global burden of smoking on public health.

Currently, pharmacological and psychosocial interventions have the most support as efficacious treatments for the cessation of smoking [6-10]. However, despite the positive outcomes associated with these interventions, most smokers do not seek formal treatment to reduce smoking [11] and existing treatments can entail several limitations. First, smokers have reported concerns regarding adverse side-effects of pharmacological treatments which have impacted treatment uptake and long-term adherence [12-14]. Second, the long-term cost of pharmacological and psychosocial interventions, which can be more expensive than cigarettes themselves, often prohibit individuals from accessing smoking cessation treatments. This is particularly relevant given that: 1) the financial costs of tobacco are one of the primary reasons underpinning quit intentions and attempts [4, 15, 16] and; 2) the incidence of smoking is increasing most rapidly in developing nations who have the lowest levels of disposable income [5]. Therefore, there is a critical need for accessible and cost-efficient interventions for
smoking cessation. Third, relapse rates remain consistently high following treatment [17] and, the vast majority will relapse within five to ten days of treatment cessation [18, 19]. Thus, a substantial proportion of individuals attempting to quit smoking fail to achieve long-term abstinence, inviting the question: what modifiable risk factors for smoking relapse may be targeted to increase abstinence rates?

Previous research indicates that deficits in response inhibition are a strong predictor of relapse for smokers following a quit attempt [20, 21]. Research suggests that recently abstinent smokers experience heightened difficulties with response inhibition [22, 23], indicating that targeting this may assist in preventing relapse. Importantly, a meta-analysis [23] supports evidence showing that individuals dependent on substances such as cocaine and alcohol may experience deficits in response inhibition. Furthermore, Yin and colleagues [24] found that a group of smokers reported response inhibition deficits on the GNG task. Taken together this provides some evidence that smokers may experience difficulties with response inhibition. Of significance is that individuals who reported higher nicotine dependence experienced greater deficits in response inhibition than those of lower use or dependence [25, 26]. Given that heavier smokers find it more difficult to quit [27, 28], response inhibition deficits may be an effective target for treatment in these individuals.

Indeed, response inhibition training interventions utilising tasks such as the go/no-go (GNG) task and stop signal task (SST) focus on training successful inhibition of a habitual or pre-potent response by pairing pictorial cues of the targeted behaviour with stop signals or no/go cues [29]. The GNG task targets automatic bottom-up response inhibition (or action restraint) by consistently
pairing no-go cues with the target stimuli [30, 31], while the SST targets top-down inhibitory control (or action cancellation) as stop signals occur after an initiated response and are mapped only to a proportion of target stimuli [32]. These tasks have recently been examined to reduce alcohol and food intake, yielding efficacious results [33]. For example, Houben, Havermans, Nederkoorn, and Jansen [34] randomly assigned 57 heavy alcohol drinkers to receive one of two training conditions: a beer/no-go condition, where alcohol-related stimuli were consistently paired with a stopping response, or a beer/go condition, where participants always responded to alcohol-related stimuli. Compared to participants in the beer/go condition, those who were trained to inhibit their response towards alcohol-related stimuli (beer/no-go) reported significantly less alcohol intake. Similar findings were reported by Jones and Field [35]. In their study, following motor inhibition training utilising a modified SST, heavy social drinkers were found to consume significantly less alcohol in a subsequent ad libitum taste test.

More recently Lawrence et al. [36] implemented an internet-delivered response inhibition training intervention for food among 83 overweight and obese adult participants. Participants were randomly allocated to receive four 10-minute training sessions completed online. In the intervention group, high-calorie foods were consistently paired with no-go signals and in the control group, non-food stimuli were consistently paired with no-go signals. At one-week follow-up, participants in the food no-go condition consumed significantly less food, showed significant weight loss, and had decreased positive evaluations towards high calorie foods compared to controls. At six month follow-up, participants in the intervention group displayed significantly higher average weight loss (2.21kg) compared to controls (0.36kg). These findings are consistent with a previous trial.
that compared two interventions for losing weight: an implementation intention intervention that instructed participants to plan reminders for dieting and a response inhibition intervention that paired no-go responses with food-related stimuli. Findings indicated that participants who completed only the response inhibition training reported significant weight loss after four training sessions. Together, these results indicate that response inhibition training can be effectively delivered online, promoting greater accessibility and cost-efficiency of these types of interventions.

Two meta-analyses have found that inhibitory control training resulted in an overall significant effect (albeit a small effect size), with GNG training yielding larger (medium) effect sizes than SST training [29, 33]. According to the Behaviour Stimulus Interaction (BSI) theory [38] behavioural changes induced by the GNG training are mediated by changes in evaluations of the stimuli used in the task. That is, positively regarded stimuli will become associated with negative affect as a result of consistently being paired with no-go cues. This is thought to devalue the stimuli and minimise the likelihood of approach behaviours occurring towards the stimuli in real life. This theory has been supported by evidence in studies targeting alcohol consumption that suggest a mediating effect of changes in implicit attitudes on alcohol intake [34, 39]. In the food domain, there is evidence of devaluation of trained no-go food stimuli as assessed by visual analogue scales [36, 40, 41]. Another proposed mechanism of response inhibition training is the automatic inhibition hypothesis (AIH) [32], which posits that automatic response inhibition can develop over practice if stimuli are consistently associated with stopping [42, 43].
Given that significant effects of the GNG task were found despite the use of non-clinical samples, it was expected that these interventions would be particularly effective with smokers as smoking receives the most frequent reinforcement compared with other dependent populations, with multiple smoking sessions each day. Furthermore, it would be particularly beneficial for heavy smokers who report the greatest difficulty in maintaining abstinence, particularly within the first month of quitting [4]. This is suggested by findings that stronger nicotine dependence is associated with poorer inhibitory control [44]. Thus, this was the first study to use the GNG task in a sample of individuals who have a Tobacco Use Disorder according to DSM-5 criteria and who wish to quit.

As previous studies have found response inhibition training to be effective even when administered over the internet [36, 37], this study also delivered the training paradigm online. This enabled the intervention to be accessible, convenient and cost-efficient for individuals and further contribute to reducing the burden on other treatment services and resources. The study was a randomised controlled trial (RCT) examining the efficacy of response inhibition training in reducing smoking. It was implemented in accordance with CONSORT guidelines, and involved collecting follow-up data from participants at one month and three months post-intervention.

**Primary hypothesis**

1. Smokers who receive smoking-related response inhibition training (INST program) would smoke significantly less compared to smokers in the control condition at the end of the intervention, one month and three months post-intervention.
Secondary hypotheses

1. Smokers who received smoking-related response inhibition training (INST program) would report significantly less craving for cigarettes compared to smokers in the control condition at the end of the intervention and one month and three months post-intervention.

2. Smokers who received smoking-related response inhibition training (INST program) would report significantly lower levels of nicotine dependence compared to smokers in the control condition at the end of the intervention and one month and three months post-intervention.

Predictor/moderator hypotheses

1. Individuals reporting high levels of impulsivity would report significantly improved outcomes from the intervention training compared to those with lower levels of impulsivity.

2. Individuals who completed a greater number of sessions (i.e., dose) would report significantly improved outcomes from the intervention training compared to those who completed less sessions.

The following exploratory hypotheses are proposed:

1. Smokers who received smoking-related response inhibition training (INST program) would report significantly higher levels of self-confidence and motivation to reduce smoking compared to smokers in the control condition at the end of the intervention, one month and three months post-intervention.
2. The effects of INST training on level of smoking would be mediated by devaluation of smoking stimuli as measured by a devaluation of smoking images task.

3. The effects of INST training on level of smoking would be mediated by an independent measure of response inhibition (SST).

Methods/Design

Design

This is a triple-blind randomised controlled trial testing the efficacy of an intervention compared to an active control training. The intervention training is a smoking version of the food GNG training task in Lawrence et al. [36]. The active control training is identical to the control training in Lawrence et al. [36], with no-go training to household items. The Deakin University Human Research Ethics Committee (DUHREC) reviewed and approved all relevant study materials (Project ID: 2015-298) and approved all study protocol amendments. The trial was registered with the Australian New Zealand Clinical Trials Registry (Trial ID: ACTRN12617000252314).

Procedure

The following sections describe the study procedure. See Figure 1 for an overview.

Initial screening
Participants were adult smokers aged between 18 and 60 years, recruited through social media and advertisements in Victoria, Australia. They were individuals who reported a wish to quit smoking.

**Inclusion criteria**

- Aged between 18-60 years.
- Smoke, on average, a minimum of ten cigarettes per day.
- Meet criteria for moderate or above Tobacco Use Disorder defined by the DSM-5 [45].
- Regular smoker for at least the past 12 months.
- Be motivated to make a quit attempt during the training stage of the intervention.
- Completed at least Year 9 (or equivalent) schooling.
- Have computer and internet access during the intervention phase of the study.

**Exclusion criteria**

- Primarily uses electronic cigarettes on a daily basis.
- Non-smoking period of two weeks or more in the past 3 months.
- Currently using anti-craving medication.
- Using nicotine-replacement therapy during the intervention period.
- Self-reported problematic alcohol or drug(s) use other than tobacco.
- Reported a traumatic or acquired brain injury or a loss of consciousness for more than 30 minutes.
• Reported current use of psychotropic medication such as anti-depressant, anti-psychotic and/or anxiolytic medication.

Interested participants were invited to contact the research team via email. They were screened over the phone/online to determine their eligibility. Participants who met the inclusion criteria were invited to participate in the study and attended a face to face interview in order to sign the consent form, collect baseline measures and participate in the first online training session.

**Baseline assessment (T1)**

At the beginning of the baseline interview session, participants read the plain language statement and completed the consent form. They were requested to report any adverse events or consequences and were informed that they were able to withdraw from the study at any time. They were asked to indicate whether they would like to receive a summary of the trial findings following completion of data analyses. Participants were informed that they would receive one of two brain training tasks as the aim of the study was to investigate which one was more effective. While they were informed that the task incorporated a “variety of visual images”, the types of images were not specified to prevent participants from identifying if they were in the control group and hence we propose that it is a triple-blind design.

Participants completed a battery of questionnaires (outlined in Table 1), and completed ratings of their craving, motivation and self-efficacy. Following the completion of the questionnaires, participants completed ratings of stimulus
evaluation test and a smoking stop signal task (SST), an independent measure of response inhibition separate to the response inhibition training.

[Insert Table 1; see pages 35-39]

**Randomisation**

Immediately following the completion of the baseline assessment, participants began the online training task. Participants were automatically randomised to either the intervention or the control training task via a pre-computed randomisation procedure. A permuted block randomisation procedure was utilised [46] whereby participants were allocated to the intervention or control group through the use of a randomly generated number. The permuted blocks were organised in groups of ten, the details of which were not known by investigators involved with the administration of the trial. The use of the permuted block randomisation process ensures that intervention group numbers will be balanced at the end of each block and is thus the recommended process in studies with smaller samples.

Upon finishing this task participants were instructed to complete the online training task once per day for the next 13 days, totalling 14 sessions. They were asked to rate their smoking craving level before and after each training session. Twice per week, participants were sent text reminders to complete the training. All data from the online training task and outcome measures were securely stored on the Deakin University server and linked to an anonymous participant ID number such that only de-identified data were available to researchers. The data was checked for training task performance accuracy and
participant adherence to the training protocol by a research assistant who was
independent from investigators and not involved in data collection or analyses.

**Inhibition training task**

The intervention is an online GNG training task as developed by Lawrence et al. [36], modified to incorporate images of smoking. The task included nine smoking images (or household items in the control group), nine relaxation images (or household items in the control group) and 18 neutral filler images presented on the left or right of the computer screen (see Figure 1). Each image was presented for 1250ms followed by a 1250ms inter-stimulus interval. Participants were instructed to indicate whether the image is located to the left or the right of the screen using the keys “C” and “M” respectively on their keyboard. On half of the trials, the frame around the picture was bolded and the participants were required to not respond (no-go trials). On the other half of the trials the frame was not bolded (go trials) and the participant were required to respond as quickly as possible. During each training session participants completed 6 training blocks, with each of the 36 images presented once per block. At the end of each block, participants were provided with feedback on their accuracy and mean correct go reaction time and will be encouraged to continue trying to beat their own score. Each training session will last for approximately 10 minutes. Participants were asked to complete the training at home in a quiet place and preferably, when they experienced cravings for a cigarette.

[Insert Figure 1]
**Intervention group**

The intervention consisted of nine smoking-related images, nine relaxing images (i.e. depicting relaxing/enjoyable activities), and 18 neutral filler pictures (e.g. clothing). For the intervention group, the smoking-related pictures were always “no-go” trials and the non-smoking pictures were always “go” trials. The neutral pictures were equally “go” and “no-go” trials (see Figure 2). The neutral filler pictures were incorporated to prevent participants from easily identifying the associative rules of the task and to ensure the task remains challenging and engaging.

**Control group**

In the control group, participants completed an identical task to the smoking intervention group except that 18 images of household objects replace the 18 smoking and relaxation images. The nine “go” images will consist of stationery items and the nine “no-go” images will consist of furniture.

**Post-intervention (T2)**

At the completion of the two-week intervention period, participants were contacted via phone by a researcher naïve to the group randomisation (i.e. a different researcher to the one who conducted the baseline interview). They received a text message reminder 24-hours prior to confirm the time of the phone call. During these phone interviews, participants were asked to provide details about their use of cigarettes and nicotine replacement therapies or anti-craving medications over the previous two weeks. At the conclusion of this interview,
participants were emailed a link to complete the same battery of questionnaires, ratings of their craving, motivation and self-efficacy and SST (completed last) as completed at baseline (T1).

One-month and three-months follow-up (T3 and T4)

Follow-up at one month (T3) and three months (T4) are conducted in the same manner as T2. The two follow-up time points were identical with the exception that the SST was not completed at T3. At the completion of each time point, participants were mailed a $20 Coles/Myer gift card. At the conclusion of the data collection period, participants in the control group are offered the opportunity to complete the smoking-related response inhibition training.

Measures

This study used information from a face-to-face interview session (T1) and phone interviews (T2, T3 and T4), in addition to self-report questionnaires, a cognitive task and a stimulus evaluation test. A list of measures used at each assessment point is provided in Table 1. Demographic information, such as age, gender, socioeconomic status and number of years of smoking, were collected at baseline.

Researcher-administered measures:

Timeline Follow-Back (TLFB) [47, 48]

The TLFB is a calendar-based assessment of daily cigarette use for periods of time ranging from 1 to 12 months prior to assessment. Initially developed to
assess alcohol consumption, the TLFB has since been utilised to assess a variety of substance use inclusive of cigarette use [47]. Memory aids are used to enhance recall of certain time-periods in order to retrospectively estimate number of cigarettes used for each date. The cigarette TLFB has shown high test-retest reliability and temporal stability across both clinical and non-clinical participants [47].

Self-report measures:

**Fagerström Test for Nicotine Dependence (FTND) [49]**

The FTND is a six-item self-report questionnaire of nicotine dependence. Dichotomous items (yes or no) are scored as 0-1, and options for categorical items are scored 0-3. The FTND has a maximum score of 10, with higher scores indicating greater nicotine dependence. The FTND demonstrates moderate internal consistency ($\alpha = .61$) and has been validated in smokers from the general population [48] and in a clinical sample [50].

**Craving for Cigarettes**

A one-item question utilising a 100mm slider scale measures craving from “not at all” to “extremely”. Participants respond to the question “How much are you currently craving a cigarette”. A slider bar is presented at the left end of the scale and participants will click and drag the bar along the scale to indicate their response. It has been found that a single measure of craving is just as reliable and sensitive as self-report questionnaires for measuring craving for smoking [51, 52].
Slider scales are considered to be an engaging type of interface [53] and are regarded as a psychometrically acceptable measurement [54].

*Depression, Anxiety and Stress Scale (DASS-21) [55]*

The DASS-21 is a 21-item measure consisting of three subscales: depression, anxiety, and stress. Participants are asked to use a four-point Likert scale to rate the extent to which they have experienced the state described over the past week. The DASS has excellent internal consistency for the total scale ($\alpha = .97$), and each subscale (Depression = .96; Anxiety = .92; Stress = .95) has high test-retest reliability and acceptable construct and convergent validity [56].

*Alcohol Use Disorders Identification Test (AUDIT) [57]*

The AUDIT is a 10-item measure of alcohol problems. Questions relate to frequency and quantity of consumption, and alcohol-related problems. Participants are asked to rate items from 0-4 and can receive a maximum possible score of 40, with higher scores indicative of more hazardous drinking. AUDIT is highly reliable and valid for use across a range of populations [58].

*Barratt Impulsiveness Scale (BIS-11) [59]*

The BIS-11 is a 30-item questionnaire assessing trait impulsivity. Each item is scored on a four-point Likert scale that ranges from “rarely/never” to “almost always”. Scores are summed to yield an overall total score ranging from 30 to 120, with higher scores indicating greater trait impulsivity. The BIS-11 also provides scores on three subscales: attentional impulsiveness, motor impulsiveness, and non-planning impulsiveness. The BIS-11 is widely used in
research and clinical contexts and has been shown to demonstrate good reliability [59, 60].

Ratings of motivation and self-efficacy

Participants are asked to rate their motivation (“currently, how motivated are you to reduce or quit smoking?”) and self-efficacy (“currently, how confident are you in your ability to quit or reduce smoking?”) on slider scales. The scale is a 100mm line with the left anchor labelled “not at all” and the right anchor labelled “extremely”. Similar to the craving slider scale, participants indicate their response by clicking and dragging the slider bar along the scale.

Stimulus evaluation test (ratings of likeability of smoking and relaxing images)

Slider scales are used for the likeability ratings of the smoking and relaxing images used in the inhibition training task. Participants are presented with the question, “how much would you like to do this activity right now?” and rate the images from “not at all” to “extremely”. The slider bar is presented in the middle of the scale and participants click and drag the slider bar to indicate their response.

Cognitive task:

Stop Signal Task (SST) [32, 61, 62]

A smoking-specific version of the SST [30, 32, 61-63] is utilised. The SST contains images of smoking-related stimuli that are different images from those used in the intervention task. Participants are presented with a fixation cross in the
centre of a screen on a white background for 500ms. A smoking-related image (go-stimulus) then appears for 1000ms, followed by a blank white screen for 1000ms (inter-stimulus interval). The 16 images used in the SST are comprised of 8 pairs of images, where one image of the pair is a cigarette pointing to the left, and the second image is its mirror image pointing to the right. As such, the presentation of stimuli pointing left or right will be equally balanced. Each of the 16 images is presented a total of 12 times.

Participants are instructed to indicate whether the cigarette is pointing left or right by pressing the computer keys “C” or “M” respectively (Figure 2). The stop signal is a pair of red lines across the image and will appear on 25% of trials. It appears at a short delay (Stop Signal Delay or SSD) after the onset of the go stimulus and stays on screen until the inter-stimulus interval. Participants are instructed to respond as quickly as possible but to not respond when the red lines appear. This delay between the onset of the go signal and the stop signal begins at 250ms on the first stop trial, and then adjusted by 50ms in a staircase manner.

Successful inhibition on stop trials results in the SSD increasing for the next stop trial, while unsuccessful inhibition, where the participant responds on a stop trial, will shorten this delay by 50ms. The SST consists of one practice block of 10 trials followed by the experimental block of 192 trials. The SSD will be used to calculate the stop signal reaction time (SSRT) as a measure of response inhibition and the reaction time on go trials will be a measure of behavioural impulsivity [62].

[Insert Figure 2]
**Analysis plan**

All participants will be included in the intent-to-treat analyses for the primary and secondary hypotheses. Per protocol analysis will include those who complete at least four sessions of the training (as per Lawrence et al. [36]) and achieve a training accuracy of at least 70%. SST data will be included for those who yield an accuracy of 40-60% on stop trials and at least 70% on go trials. Prior to analyses, all variables will be examined through IBM Statistical Package for Social Sciences (SPSS Version 25) for accuracy of data entry, missing values and fit between their distributions and the assumptions of multivariate analysis. Any violations will be addressed as per standard protocols [64].

Missing data will be managed using SPSS. First, a missing value analysis will be conducted to determine the percentage and pattern of missing data. If missing data are found to relate to a measured participant variable, those variables will be included as covariates in the analyses. If appropriate, multiple imputation will be used to replace missing values and the imputation model will include baseline covariates and outcome data. Missing data will be imputed using the Markov Chain Monte Carlo method or the Monotone method, contingent upon the pattern of missing data. A minimum of five imputed datasets will be produced [65]; however, depending on the percentage of missing data, a minimum of 20 imputed datasets may be required [66]. Wherever possible, results from the complete case analysis will be compared with results based on imputed data. If there are important differences, explanations will be offered.

The primary and secondary hypotheses will be analysed using separate mixed-design ANOVAs. For each analysis, group (i.e., intervention or control) will be included as the between-subjects factor. For the primary hypothesis, the
repeated-measures factor will be the average number of cigarettes smoked per day at each timepoint (i.e., baseline, post-intervention, one month and three months post intervention). For the secondary hypotheses, the repeated-measures factor will be craving or nicotine dependence at each timepoint. The predictor hypotheses will be examined using separate moderated regression analyses, with group as the predictor variable, impulsivity and dose as the moderator variable and change in smoking as the dependent variable.

The exploratory hypotheses related to self-confidence and motivation will be examined using a separate mixed-design ANOVA, with group included as the between subjects factor and self-confidence and motivation at each timepoint included as the repeated-measures factor. Two mediation analyses utilising a linear mixed model approach will be conducted to examine whether the effects of INST training on level of smoking will be mediated by devaluation of smoking stimuli or an independent measure of response inhibition (SSRT).

Separate mixed-design ANOVAs will be performed on “go” reaction times and “no-go” accuracy to examine stimulus-specific learning effects (100% stimuli vs. 50% stimuli) over time (first vs. fourth training session as per the analysis by Lawrence and colleagues to allow comparability). Evidence of learning will be indicated by faster reaction time on 100% go stimuli and fewer errors on 100% no-go stimuli. A between-subjects factor of group will be included to examine whether active and control groups show similar task performance, stimulus-specific learning and improvements over time. Any further exploratory analyses will be labelled as such in the publication.

*Power analysis*
Power analysis was calculated for the primary hypothesis and indicated that an overall sample size of 92 is required to detect a medium effect size (approximately .50) at the .05 alpha level using linear techniques (power = .80).

Given that it is expected that approximately 25% will be lost to follow-up and up to 30% would not complete a minimum of 4 sessions, the target of the current study was set at 150 at the time of registration. However, estimated attrition was revised in light of low rates of attrition in a pilot of this study resulted in an amended target sample of 120.

Discussion

The widespread prevalence of tobacco smoking means that many people would benefit from interventions to assist in maintaining abstinence following a quit attempt. However, pharmacological and psychosocial interventions for smoking are restricted in accessibility due to the high, long-term cost of these interventions. This trial has been designed to deliver an internet-based response inhibition training in order to offer a simple, low-cost, and easily accessible smoking cessation intervention. As such, even small effect sizes of the intervention may translate to cumulatively large gains to public health. The current study protocol has been designed to examine the efficacy of response inhibition training to reduce cigarette use among smokers.

The intervention has several strengths regarding its timing, delivery and content. Firstly, the intervention maximises the use of being an internet-based program, which capitalises on the ability to have a wide reach within the community at a relatively low cost. This ensures that the intervention is both convenient and highly accessible given that the majority of the population have
access to a computer. Secondly, while there is currently limited evidence to suggest that training response inhibition to smoking cues reduces cigarette use or craving [67], previous studies suggest that online response inhibition training to energy-dense food images helps individuals reduce their food intake, weight and food liking [36, 37, 68]. Thirdly, it has been suggested [69] that the best test of stimulus-specific response inhibition training is to use real-world studies that adopt a mixed between- and within-subjects design with repeated-measures (pre to post-intervention). This allows changes from baseline to be computed for meaningful/ecologically valid outcome measures.

While the usual process in translational research is to conduct “proof of concept” studies in the lab before attempting trials in the real-world, we decided to proceed straight to a real-world RCT of smoking-related response inhibition training based on the promising findings in eating behaviour and weight change. This is because laboratory studies can only measure acute training effects that may have little application or predictive value for real-world effects, and because laboratory studies typically adopt a single-session, between-groups design with the dependent variable often being measured only once post-training. This design is limited by confounds such as only one group being exposed to smoking cues during training. Furthermore, if the training relies on changing stimulus-response associations [43], it may be more effective at inducing behavioural change when conducted in real-world contexts associated with smoking (such as the home or workplace) than when conducted in a neutral laboratory setting.

A number of limitations need to be considered. Ongoing studies need to include an objective measure of nicotine use and larger samples in order to adequately power mediation analyses.
Considerations for future research

If this trial suggests positive effects of smoking-related response inhibition training, future research will need to determine how to optimise it for smokers. Furthermore, research could include examining which aspects of the intervention will produce particular effects. This is both in terms of the training schedule (frequency, duration, timing and location of the training) and the mode of delivery (e.g. online vs. smartphone delivery). Smartphone apps and digital interventions to assist with smoking cessation are very popular but are largely lacking in evidence [70]. This RCT aims to contribute to the evidence-base for the development of a new digital intervention for smoking.
List of abbreviations

AIH: Automatic Inhibition Hypothesis
ANOVA: Analysis of Variance
AUDIT: Alcohol Use Disorders Identification Test
BIS-11: Barratt Impulsiveness Scale
BSI: Behaviour Stimulus Interaction
CONSORT: Consolidated Standards of Reporting Trials
DASS-21: Depression, Anxiety and Stress Scale
DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
DUHREC: The Deakin University Human Research Ethics Committee
FTND: Fagerström Test for Nicotine Dependence
GNG: Go/No-go
ID: Identification
INST: Inhibition Smoking Training
NRT: Nicotine Replacement Therapy
RCT: Randomised Controlled Trial
SSD: Stop Signal Delay
SSRT: Stop Signal Reaction Time
SST: Stop Signal Task
T1: Time 1 (baseline assessment)
T2: Time 2 (post-intervention)
T3: Time 3 (one month follow-up)
T4: Time 4 (three months follow-up)
TLFB: Timeline Follow-Back
Declarations

Ethics approval and consent to participate
Ethics for this study was approved by the Deakin University Human Research Ethics Committee (DUHREC) on 2nd February 2016 (Project ID: 2015-298). All participants consented to participating.

Consent for publication
Not applicable.

Availability of data and material
The syntax and full analysis plan will be made available on the Open Science Framework and the dataset made available by contacting the first author.

Competing interests
The authors declare that they have no competing interests.

Funding
This research is wholly funded by Deakin University. This funding source had no role in the design of the study and collection, analysis, interpretation of data or writing of the manuscript. No external funding or sponsorship was sought, and therefore has not been peer-reviewed by an external body.

Authors' contributions
PS is the project lead who has overall responsibility for the design and content of the intervention, and wrote the draft of the manuscript. MH is co-lead on this
project and has shared responsibility for the design and content of the intervention and wrote the discussion section. KG is a Doctorate of Clinical Psychology Candidate and led the piloting of the intervention. LH is a PhD student and along with JB, who is a Doctorate of Clinical Psychology Candidate, contributed to the intervention design, the trial design, and will collect and analyse the data. NL is the expert advisor on the response inhibition training intervention and provided all aspects of the control intervention and had input into the design. All authors contributed to the development of the protocol and writing of this paper.

Acknowledgements

The authors would like to thank the following people for their expertise and input: Ron Borland, Robert Dvorak, Peter Enticott, Denise Foley, Ben Richardson, and Adrian Shatte.


44. Pettiford J, Kozink RV, Lutz AM, Kollins SH, Rose JE, McClernon FJ. Increases in impulsivity following smoking abstinence are related to baseline nicotine intake and boredom susceptibility. Addict Behav. 2007; 32:2351-7.


Figure 1. Overview of the “go” and “no-go” trials in the treatment condition of the GNG task.
Figure 2. Overview of the “go” and “stop” trials in the Stop Signal Task illustrating correct responding.
Table 1

SPIRIT Flow Diagram of the schedule for participants and data collection for the INST study

<table>
<thead>
<tr>
<th>ENROLMENT:</th>
<th></th>
<th>STUDY PERIOD</th>
<th>Follow-Up Period</th>
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<td>1-Month Post-Intervention Training Period (T3)</td>
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**INTERVENTION**

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  - Control training: X X

**ASSESSMENTS:**

- Demographic Questions: X
- TLFB: X X X X X
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<td>3-Months Post-Intervention (T4)</td>
<td>Close-out</td>
<td></td>
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</table>

**STUDY PERIOD**

TLFB = Timeline Follow-Back interview, FTND = Fagerström Test of Nicotine Dependence, DASS = Depression Anxiety and Stress Scale, AUDIT = Alcohol Use Disorders Identification Test, BIS-11 = Barrett Impulsiveness Scale, SST = Stop Signal Task.

t is in days (from t<sub>1</sub> onwards).
# Appendix D

## PRISMA 2009 Checklist

<table>
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<th>Section/topic</th>
<th>#</th>
<th>Checklist item</th>
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<tr>
<td>Title</td>
<td>1</td>
<td>Identify the report as a systematic review, meta-analysis, or both.</td>
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<tr>
<td><strong>ABSTRACT</strong></td>
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<tr>
<td>Structured summary</td>
<td>2</td>
<td>Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.</td>
<td>N/A</td>
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<td><strong>INTRODUCTION</strong></td>
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<tr>
<td>Rationale</td>
<td>3</td>
<td>Describe the rationale for the review in the context of what is already known.</td>
<td>153-158</td>
</tr>
<tr>
<td>Objectives</td>
<td>4</td>
<td>Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).</td>
<td>158-159</td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
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<td></td>
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<tr>
<td>Protocol and registration</td>
<td>5</td>
<td>Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.</td>
<td>N/A</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>6</td>
<td>Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.</td>
<td>159-160</td>
</tr>
<tr>
<td>Information sources</td>
<td>7</td>
<td>Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.</td>
<td>160-161</td>
</tr>
<tr>
<td>Search</td>
<td>8</td>
<td>Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.</td>
<td>340</td>
</tr>
<tr>
<td>Study selection</td>
<td>9</td>
<td>State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).</td>
<td>161</td>
</tr>
<tr>
<td>Data collection process</td>
<td>10</td>
<td>Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.</td>
<td>161</td>
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<tr>
<td>Data items</td>
<td>11</td>
<td>List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.</td>
<td>163-164</td>
</tr>
<tr>
<td>Risk of bias in individual studies</td>
<td>12</td>
<td>Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.</td>
<td>161</td>
</tr>
<tr>
<td>Summary measures</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td>178-186</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis.</td>
<td>176-177</td>
</tr>
</tbody>
</table>

Appendix E

Full search strategy for MEDLINE Complete

TI (impulsiv* OR disinhibit* or "sensation seek*" OR "novelty seek*" or "reward seek*" or "reward sensitiv*" or "reward dependen*" or “reward drive” or premeditation or “behavi* approach” or “behavi* activation” or BAS or urgency or “positive urgency” or perseverance or “boredom proneness” or “boredom susceptibility” or "response inhibit*" or "motor inhibit*" or "cognitive inhibit*" or "inhibitory control" or "delay discounting" or interference or "exec* *function*" or "exec* *control*" or "attention* bias")

OR

AB (impulsiv* OR disinhibit* or "sensation seek*" OR "novelty seek*" or "reward seek*" or "reward sensitiv*" or "reward dependen*" or “reward drive” or premeditation or “behavi* approach” or “behavi* activation” or BAS or urgency or “positive urgency” or perseverance or “boredom proneness” or “boredom susceptibility” or "response inhibit*" or "motor inhibit*" or "cognitive inhibit*" or "inhibitory control" or "delay discounting" or interference or "exec* *function*" or "exec* *control*" or "attention* bias")

OR

(MH "Impulsive Behavior") OR (MH "Inhibition (Psychology)+") OR (MH "Delay Discounting") OR (MH "Executive Function") OR (MH "Attentional Bias")

AND
TI (smoking or smoker* or “nicotine use*” or “nicotine abuse*” or “nicotine addict*” or “nicotine dependen*” or “tobacco use*” or “tobacco abuse*” or “tobacco dependen*” or “tobacco addict*”)

OR

AB (smoking or smoker* or “nicotine use*” or “nicotine abuse*” or “nicotine addict*” or “nicotine dependen*” or “tobacco use*” or “tobacco abuse*” or “tobacco dependen*” or “tobacco addict*”)

OR

(MH “Tobacco Use+”)

AND

TI (treatment or intervention or therapy or “response inhibition training” or “inhibitory control training”)

OR

AB (treatment or intervention or therapy or “response inhibition training” or “inhibitory control training”)

OR

(MH "Psychotherapy+") OR (MH "Tobacco Use Cessation+")

Limiters - Human; Age Related: Adolescent: 13-18 years, Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Middle Aged + Aged: 45 + years, Aged: 65+ years, Aged, 80 and over, All Adult: 19+ years