Protocol

A pilot randomised trial exploring the intentions of people who smoke, to seek illicit tobacco if very low nicotine content cigarettes were the only tobacco available in New Zealand (VLNC tobacco use trial)

Trial Registration Number: Pending

Principal Investigator: Chris Bullen

Version 2.0

Pilot Trial Co-ordinating Centre

Postal address
School of Population Health
The University of Auckland
Private Bag 92019
Auckland Mail Centre
Auckland 1142
New Zealand
Tel: 64 9 373 7999
Email: c.bullen@auckland.ac.nz

Street address
Level 3 Building 507, School of Population Health
Grafton Campus
The University of Auckland
22-30 Park Road
Grafton
Auckland 1023
New Zealand

Steering Group Committee Members

Professor Chris Bullen Principal Investigator	General Practice and Primary Healthcare, School of Population Health University of Auckland, Private Bag 92019, Auckland 1142, New Zealand Tel: +64 9 923 4730 Emergency no: +64 21 415 267 Email: c.bullen@auckland.ac.nz
Dr Pyi Pyi Phyo Co-investigator (PhD student)	General Practice and Primary Healthcare, School of Population Health University of Auckland, Auckland 1142, New Zealand Tel: +64 2102247741 Email: pyi.pyi.phyo@auckland.ac.nz
Professor Natalie Walker Co-investigator	Until 28th March 2025: Social and Community Health School of Population Health University of Auckland, Private Bag 92019, Auckland 1142, New Zealand Tel: +64 9 923 9884 Emergency no: +64 21 028 62518 Email: n.walker@auckland.ac.nz From 31st March 2025 onwards: College of Medicine and Public Health Flinders University 1 Sturt Road, Bedford Park, Adelaide South Australia 5042 Australia Tel: pending Emergency no: pending Email: pending
Dr Alana Cavadino Co-investigator	Epidemiology and Biostatistics, School of Population Health, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand Tel: +64 9 923 1317 Email: a.cavadino@auckland.ac.nz
Dr Braden Te Ao	Health Systems,

Co-investigator	School of Population Health, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand Email: b.teao@auckland.ac.nz

Co-ordinating Centre Staff

Name	Position	Telephone	Email
Chris Bullen	Investigator	09 923 4730	c.bullen@auckland.ac.nz
Pyi Pyi Phyo	Co-Investigator	021 022 47741	pyi.pyi.phyo@auckland.ac.nz
Natalie Walker	Co-Investigator	09 923 9884	n.walker@auckland.ac.nz
Alana Cavadino	Co-Investigator	09923 1317	a.cavadino@auckland.ac.nz
Braden Te Ao	Co-Investigator		b.teao@auckland.ac.nz

Trial Sponsor

The University of Auckland is the trial sponsor. The design, conduct, analyses, and interpretation of pilot trial results will be independent of the sponsor.

Source of Trial Intervention

The very low nicotine content (VLNC) cigarettes used in this trial will be purchased at full cost from a Walgreens Store in the USA. The brand name of the purchased VLNC cigarettes is 'VLN King', and the cigarettes are manufactured by 22nd Century (a tobacco company).

Company Name	Company Contact Details
22nd Century Group (Purchased from Walgreens Store)	22nd Century Group, Inc. 500 Seneca Street, Suite 507 Buffalo, New York 14204 USA T: 716-270-1523

Signature Page

Author(s):

Authors Name	**Signature:**	**Date:**
Chris Bullen (PI)		

Department of General Practice and Primary Health Care	**Signature:**	**Date:**
Susan Wells		

Revision Chronology:	**Date**	**Type**
Protocol V1.0	18 Jan 2025	Original
Protocol V2.0	05 Feb 2025	Modification
Protocol V3.0	07 Mar 2025	Modification

Contents

1. Overview

Title of the study
Exploring the intentions of people who smoke, to seek illicit tobacco if very low nicotine content (VLNC) cigarettes were the only tobacco available in New Zealand.

Investigators and trial centre
This trial is part of a doctoral thesis being undertaken by Dr Pyi Pyi Phyo at the School of Population Health, Faculty of Medical and Health Sciences, University of Auckland, Auckland. The overall design and conduct of the trial are the responsibility of the Principal Investigator, supported by members of the Trial Steering Committee. Publication of data from this pilot trial will be the responsibility of all members of the Trial Steering Committee.

Trial period:
Trial start date: 1st March 2025, Trial end date: 30th April 2025 (2-months recruitment).

Assessment phase:
1st April 2025 to 31st July 2025

Aim:
To conduct a pilot study to assess the feasibility issues related to undertaking a randomised controlled trial exploring the intentions of people who smoke to seek illicit tobacco if VLNC cigarettes were the only tobacco available in New Zealand.

Duration of Intervention:
A maximum of 30 minutes is needed to allow adequate time for participants to smoke a single cigarette.

Trial design and methodology:
A three-arm, parallel group, randomised trial. Participants will be given a hypothetical scenario where all smoked tobacco legally available for purchase in New Zealand has 95% less nicotine than the tobacco they normally smoke. Participants will then be randomised to: 1) smoking a VLNC cigarette and viewing health messages about VLNC cigarettes, 2) smoking one of their own cigarettes and viewing health messages about VLNC cigarettes, or 3) smoking one of their own cigarettes. All data will be collected from each participant within an hour on one day.

Trial population:
Participants will be recruited from Auckland, using social media advertising with targeted promotion to reach Māori, Pacific, and low socio-economic groups, given their disproportionately higher smoking prevalence. Targeted promotion will be conducted to reach out to Māori and Pacific populations through social media advertising ads and through Pacific and Māori colleagues and organisations to spread the news to the specific populations. The study itself will provide a chance for eligible participants to participate on a first-come, first-serve basis, given that one of the outcomes is whether people can be recruited and how quickly they can be recruited with our advertisement and information-sharing approach in this pilot trial.

Number of subjects:
Thirty people will be randomised in this pilot trial (N=10 in each group).

Inclusion criteria:
Participants will be those who:

- Currently smoke (defined as people who have smoked more than 100 factory-made cigarettes and/or roll-your-own (RYO) cigarettes in their lifetime and currently smoke at least once a month(1))
- Live in New Zealand
- Are aged ≥18 years
- Are able to provide consent
- Are able to read and write English
- Are willing to smoke a VLNC cigarette
- Are willing to travel to the study site.

Exclusion criteria:
Participants will be excluded if they:

- Are pregnant/breastfeeding or are women trying to become pregnant in the next three months.
- Are currently using smoking cessation medication (including using e-cigarettes daily for the last month).
- Have ever smoked VLNC cigarettes.

Test products, dosages, and route of administration

- Smoking a VLNC cigarette and viewing health messages about VLNC cigarettes

Reference treatments:

- Smoking one of their own cigarettes and viewing health messages about VLNC cigarettes, OR
- Smoking one of their own cigarettes

Criteria for evaluation:
Primary focus
The main focus of the trial is to determine whether a larger trial would be feasible to conduct, specifically

1. Can people be recruited, and how quickly can they be recruited?
2. Do people attend the study site on their scheduled day and stay for their required time?
3. Are the study tasks and questionnaires understandable to participants, and are all questions answered?
4. Did participants highlight any difficulties with the trial?
5. Did participants face any adverse events or symptoms after smoking a VLNC cigarette?

Secondary focus

The secondary focus of the trial is to gather data on the likely impact of the tested interventions on potential participant behaviours. Specifically,

- Their likelihood of using illicit tobacco (i.e., tobacco with regular nicotine levels).
- Their likelihood of using VLNC cigarettes
- Their likelihood of using homegrown tobacco
- Their likelihood of using nicotine e-cigarettes
- Their likelihood of using heated tobacco products
- Their likelihood of using nicotine replacement therapy
- Their likelihood of using alcohol
- Their likelihood of using Cannabis/Marijuana/Tetrahydrocannabinol products
- Their likelihood of using other illicit drugs
- Their desire to quit smoking tobacco
- The maximum amount they are willing to pay per VLNC cigarette
- The maximum amount they are willing to pay per illicit cigarette
- The maximum time they would be prepared to travel to get illicit cigarettes
- Their reasons for seeking illicit cigarettes

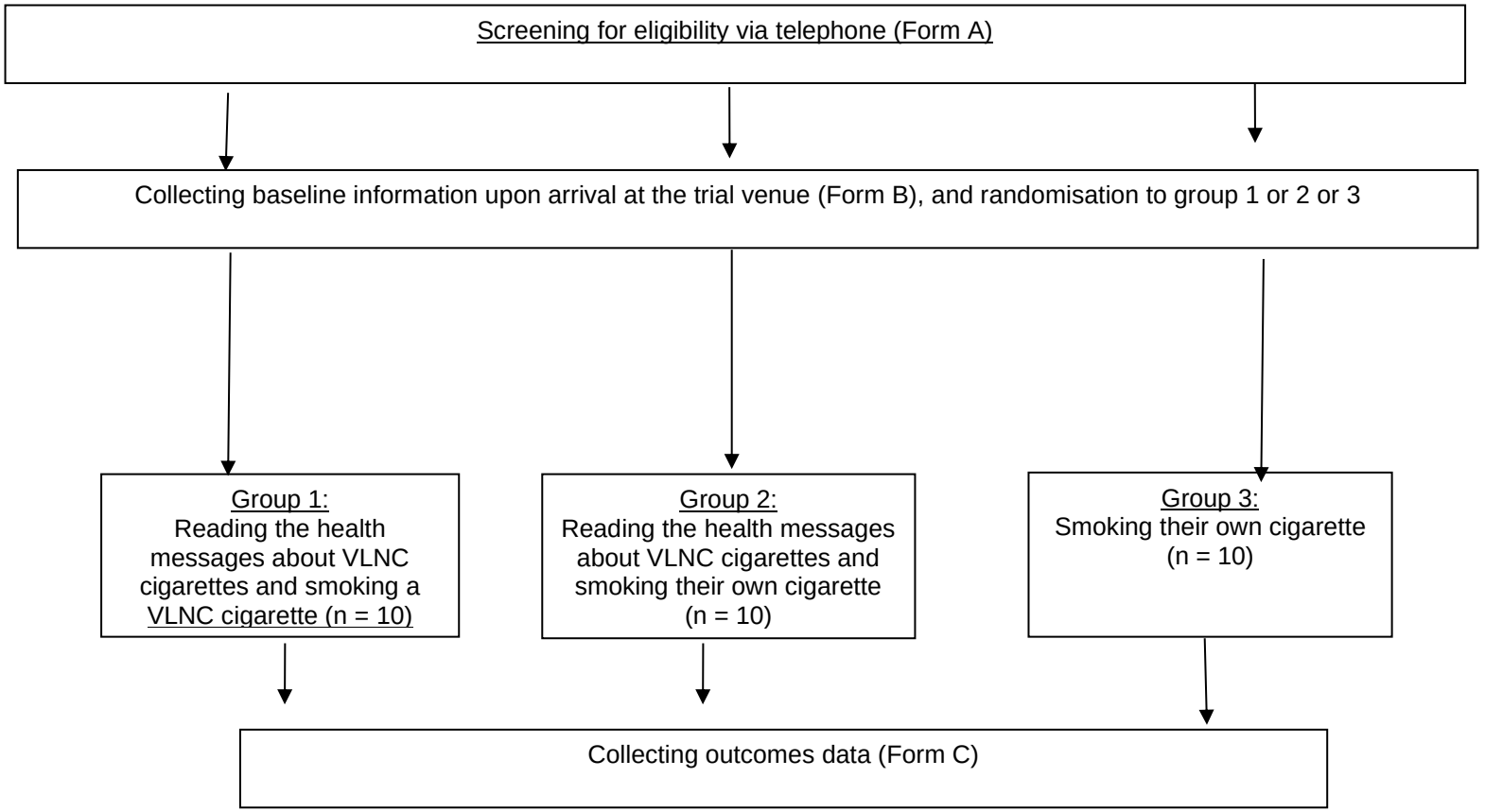
Statistical methods

Results will be presented using descriptive summaries within each group. Means and standard deviation or median and interquartile range will be used to describe continuous variables and number and percentage will be used to describe categorical variables. Missing data for all outcomes will be described.

Funding

No specific funding is provided for this study. The cigarettes were purchased from a retail store using research funds from the principal investigator.

2. Trial Plan Schematic



3. Background

3.1 Smoking in New Zealand

Tobacco claims the lives of half its users who do not quit, contributing to over 8 million deaths annually(2). The prevalence of smoking in New Zealand is declining, with 8.4% of adults (aged 15 years and above) identified as current smokers in 2023/24. However, smoking rates vary widely among different ethnic groups: 17.2% among Māori, 14.7% among Pacific peoples, 7.4% among New Zealand Europeans, and 5% among Asians. Smoking prevalence also varies significantly by neighbourhood deprivation, with 3.6% of people who were currently smoking in the least deprived neighbourhoods, compared to 15.9% in the most deprived. Therefore, smoking not only leads to premature deaths but also contributes to inequitable health outcomes across different populations in New Zealand(3).

3.2 Smokefree2025 and denicotinisation in New Zealand

New Zealand has set a smokefree 2025 goal of less than 5% of all adults aged ≥18 years smoking by 2025(4). The Smokefree Environments and Regulated Products (Smoked Tobacco) Amendment Act (SERPA) was introduced to achieve this goal. The three key policies in the SERPA were denicotinisation, reduction in tobacco retailers, and implementation of a smoke-free generation(5). Denicotinisation for New Zealand means to put the limit of the nicotine content in the tobacco for individual cigarettes to 0.8 mg/g(6). The denicotinisation policy was included to prompt current smokers to quit or switch to other less harmful nicotine products (7). However, in March 2024, the newly elected Coalition government repealed the SERPA, citing concerns that the illicit tobacco market would increase if these policies were implemented(8). Limiting the amount of nicotine in cigarettes in New Zealand could be an effective policy to reduce the smoking prevalence below 5% in almost all ethnicities except for Māori(9). Repealing such a policy could halt the actions to achieve smoke-free 2025 goals. Therefore, it is crucial to understand whether denicotinisation could drive current smokers to illicit tobacco use.

3.3 Denicotinisation and the likelihood of using illicit tobacco

VLNC cigarettes and full nicotine-strength illicit tobacco

There are a limited number of studies that directly investigate illicit tobacco use when there is a reduction in nicotine levels in cigarettes in the legal market. Two experimental studies conducted in the USA discovered that denicotinisation could be associated with a higher preference for illicit full nicotine-strength tobacco. In an online study with a convenient sample of 1712 adults who smoke tobacco, Hall et al. (2019) stated that people who smoke tobacco and were informed about the VLNC standard showed a higher likelihood of being very or extremely interested in buying regular cigarettes illicitly online, compared to those in the control group (24% vs. 16%, $p<0.001$)(10). In a study conducted by Dolan et al. (2023), the author explored how adults who smoke might shift their purchasing preferences when faced with reduced-nicotine content cigarettes. A total of 994 adult cigarette smokers participated in this study to examine their purchasing behaviors. They were asked to complete hypothetical

purchasing tasks for their usual-brand cigarettes, reduced-nicotine-containing cigarettes, and illicit normal-nicotine-containing cigarettes. They also completed tasks where reduced-nicotine content cigarettes were offered at different prices, while illicit normal-nicotine content cigarettes were consistently priced at $12 per pack. Additionally, participants were presented with scenarios where e-cigarettes were available at either $4 per pod or $12 per pod, alongside reduced-nicotine content and illicit normal-nicotine content cigarettes. The authors found

(a) compensatory smoking: The results show that demand for illicit normal-nicotine cigarettes is significantly lower than for reduced-nicotine cigarettes (log-Q0 = 0.77 vs. 0.96), but the availability of illicit cigarettes still reduces the demand for reduced-nicotine cigarettes (log-Q0 decreases to 0.87 in cross-commodity conditions). This suggests smokers might consider illicit cigarettes as a substitute when reduced-nicotine cigarettes are the only legal option, supporting the idea of compensatory behavior to maintain nicotine levels,

(b) willingness to engage in an illicit cigarette marketplace: The findings indicate that smokers are likely to purchase illicit cigarettes when they are available at a fixed price ($12/pack). This demonstrates a willingness to turn to the illicit market to bypass reduced-nicotine regulations and maintain nicotine consumption and

(c) economic independence: the price of reduced-nicotine cigarettes did not significantly predict illicit cigarette purchasing. This implies that illicit cigarettes could remain a consistent choice regardless of reduced-nicotine cigarette pricing, further emphasising the potential for an illicit marketplace(11).

In 2018, Tucker et al. (2018) explored how people who smoke tobacco might use VLNC cigarettes as substitutes for regular cigarettes and how their purchasing decisions change with price in New Zealand. In this study, each participant tried a VLNC cigarette and completed tasks to show how many regular and VLNC cigarettes they would buy at different prices. The study found that as the price of regular cigarettes increased, demand for VLNC cigarettes rose slightly, with an average cross-price elasticity of 0.32, meaning a 10% price increase in regular cigarettes led to a 3.2% rise in VLNC cigarette demand. However, this effect was only observed in 25% of participants, as the median cross-price elasticity was 0, indicating no increase in VLNC cigarette demand for most people(12).

Darredeau et al. (2013) conducted a study that examined how nicotine content information affects smokers' subjective and behavioral responses. Sixty participants (30 nicotine-dependent and 30 non-dependent) from Canada who had abstained from smoking for 12 hours took part in two laboratory sessions. Using a balanced placebo design, they smoked either nicotine-containing or nicotine-free cigarettes but were misinformed about the cigarette type in each session. Participants completed subjective assessments before and after taking three puffs from the assigned cigarette. The authors found

(a) nicotine expectations and subjective experiences: participants reported a greater increase in "head rush" when they were told the cigarette contained nicotine, regardless of the actual nicotine content ($p < 0.001$).

(b) effects of actual nicotine content: participants who smoked nicotine-containing cigarettes reported significant increases in "satisfaction" ($p < 0.001$) and "stimulation" ($p < 0.001$), regardless of the instructions they received.

(c) dependent smokers and pleasantness ratings: among nicotine-dependent smokers, pleasantness ratings increased only when the instructions about nicotine content matched the actual cigarette content ($p < 0.001$ for nicotine-containing cigarettes; $p < 0.01$ for nicotine-free cigarettes). Mismatched instructions did not lead to increased pleasantness. (13).

These findings suggest that VLNC cigarettes have some substitutability for full-strength nicotine cigarettes. At the same time, there is a need to examine the intentions of people who smoke to seek illicit tobacco if VLNC cigarettes were the only tobacco available in New Zealand.

Health messages and perceptions on VLNC cigarettes

In New Zealand, there is a common misunderstanding among adults that VLNC cigarettes are less harmful than regular cigarettes(14). Regarding the messages about VLNC cigarettes, the type and content of messages can greatly influence the perceived harmfulness and motivation for quitting, as well as the dissuasion of VLNC cigarettes (15). A USA randomised clinical trial conducted with 971 people who exclusively smoked cigarettes, 472 dual users of cigarettes and e-cigarettes, and 458 never-smokers aged 18-29, discovered that the effect of message condition on perceived absolute harm of VLNCs was significant. Specifically, VLNC messaging reduced the misperception that VLNCs are less harmful (16).

Intention to use illicit tobacco while introducing VLNC cigarettes in New Zealand

Phyo et al. (unpublished manuscript) analysed the likelihood of using illicit tobacco by people who currently smoke and whether the likelihood differs between populations with high smoking rates (specifically people with self-reported anxiety and/or depression, young people aged 18-30 years of low educational attainment, or individuals who report heavy alcohol and/or cannabis use) and populations with lower smoking rates. This study also explored the characteristics of populations likely to engage with illicit tobacco if the denicotinisation policy was introduced in New Zealand. The study analysed the Centre for the Evaluation of Nicotine in Cigarettes New Zealand Study (CENIC-NZ) cross-sectional survey data. The CENIC-NZ study is a mixed-methods, observational study exploring NZ adult smokers' perceptions, concerns, and intentions regarding a real-world plan to reduce nicotine content in smoked tobacco. Conducted in 2022 and 2024, the study surveyed participants, including ex-smokers and non-smokers, on their likelihood of using illicit tobacco if legal tobacco contained 95% less nicotine. The authors found that the key characteristics that influenced the likelihood of using illicit tobacco in this cohort of people were education, daily cigarette use, cannabis use, the desire to quit, the likelihood of using homegrown tobacco, the likelihood to drink alcohol, the likelihood of using cannabis and related products and intention to add nicotine low nicotine cigarettes or other smoked tobacco and perception on harms of VLNC cigarettes. They also found that relationships between these variables and the likelihood of illicit tobacco use did not differ in the priority and non-priority populations. In the CENIC-NZ study, the participants did not have a chance to taste the VLNC cigarette nor read the messages about VLNC cigarettes during the study.

4. Rationale for the Present Pilot Trial

Investigating the effects of denicotinisation on tobacco users' engagement with illicit tobacco offers important insights, particularly within the New Zealand context. It is important to explore whether sampling VLNC cigarettes, being exposed to health messages about VLNC products, or a combination of these interventions impacts the likelihood of people who smoke seeking illicit full-strength nicotine tobacco.

The existing graphic health warnings and text warnings on cigarette packages in New Zealand

Currently, in New Zealand, the following information are required to be displayed

- 14 pictorial health warnings in rotation covering the front and back of cigarette packets in New Zealand as specified in Schedule 2, Part 1 of the Smokefree Environments and Regulated Products Regulations 2021.
- the Quitline logo,
- freephone number, and
- other information about quitting smoking (17).

Proposed health warnings and health messages on VLNC cigarettes inside the pack (inserts)

Gendall et al. (2023) conducted an online survey with 710 participants to examine how people who smoked, people who formerly smoked and those who had never smoked regularly perceived messages about VLNC cigarettes in New Zealand. Participants were shown messages such as “Very Low Nicotine,” “90% Less Nicotine,” “Reduced Nicotine Content,” and “Minimally Addictive” alongside existing pictorial health warnings. The study found that 30% of respondents believed VLNC cigarettes to be less harmful than regular cigarettes. This perception was more common among former smokers (35%) and never-regular smokers (36%), compared to regular smokers (29%), though the differences were not statistically significant(14). The authors recommend that policymakers do not use brief messages about VLNC cigarettes to avoid misunderstandings but should consider the pack inserts on VLNC cigarettes to allow for expanded health messages that promote self-efficacy and support sustained smoking cessation.

Thrasher et al. (2023) conducted a 2×2 between-subject randomized trial (tobacco pack inserts with messages about quitting benefits and tips to quit vs. no inserts; large pictorial health warning labels vs. small text health warning labels) with 367 adults who smoked at least ten cigarettes a day in the USA. They found that participants who received packs with inserts were more likely to report skipping or extinguishing cigarettes early compared to those who did not receive inserts (adjusted odds ratio = 2.39, 95% confidence interval = 1.36, 4.20)(18).

Reynolds et al. (2022) conducted a discrete choice experiment with 1,763 USA adult participants. The participants included people who smoked tobacco, those who smoked and used e-cigarettes, former smokers, and people who had never smoked. The study tested different combinations of messages about VLNC cigarettes. Messages highlighting the specific harms and chemicals in VLNC cigarettes had the strongest effects.

These messages:

- Created the most negative attitudes toward a hypothetical denicotinisation policy.
- Increased the perception that VLNC cigarettes are harmful.
- Motivated participants to quit VLNC cigarettes.
- Reduced interest in trying VLNC cigarettes (15).

Exploring the intentions of people who smoke to seek illicit tobacco if very low nicotine content cigarettes were the only tobacco available in New Zealand

A randomised controlled trial is necessary to test the intentions of people who smoke to seek illicit tobacco if only VLNC cigarettes were available in New Zealand. We aim to determine the feasibility of conducting a randomized controlled trial to investigate health warnings by implementing a pilot trial. This pilot trial will help determine whether a full-scale randomised control is feasible for examining the beforementioned variables. While feasibility can be assessed in various ways, we will evaluate it by conducting a pilot randomised controlled trial (19). Feasibility will be measured by assessing whether the participants can be recruited and how quickly they can be recruited, whether the people attend the study site on their scheduled day and stay for their required day, whether the study tasks and questionaries are understandable to participants, whether all the questions are answered , whether participants highlight any difficulties in the trial and whether the participants face any adverse reaction or symptoms (20).

5. Trial Design

5.1 Aim

To conduct a pilot trial to identify the feasibility of undertaking a randomised controlled trial exploring the intentions of people who smoke, to seek illicit tobacco if VLNC cigarettes were the only tobacco available in New Zealand.

5.2 Inclusion criteria

Participants will be those who:

- Currently smoke (defined by people who have smoked more than 100 factory-made cigarettes and/or RYO cigarettes in their lifetime and currently smoke at least once a month(1))
- Live in New Zealand
- Are aged ≥18 years
- Are able to provide consent
- Are willing to smoke a VLNC cigarette
- Are willing to travel to the study site.
- Are able to read and write in English.

5.3 Exclusion criteria

Participants will be excluded if they:

- Are pregnant/breastfeeding or are women trying to become pregnant in the next three months.
- Are currently using smoking cessation medication (including using e-cigarettes daily for the last month).
- Have ever smoked VLNC cigarettes.

5.4 Recruitment

Participants will be recruited via social media advertisement (e.g., Facebook) and word of mouth. Potential participants will be asked to call a local telephone number to speak to a researcher who will briefly explain the study and offer to send the person a participant information sheet. Two or three days after sending out the participant information sheet, the researcher will call the potential participant again to discuss their interest and eligibility for the study. The researcher will schedule another call if potential participants need more time to decide. If the participants are eligible for the study and show interest, the researcher will inform them (via phone and email) about the specific study date and venue. Written consent will be obtained at the study site on the day of the study. If they participants are not eligible for the study, the written smoking cessation information in New Zealand will be provided (if they wish to receive it) as a part of our duty of care.

5.5 Baseline assessments

Eligible participants will be required to attend the study site on one of the scheduled study days. The site will be at the Grafton campus of the University of Auckland and a nearby outside space (for smoking a cigarette). Participants will be asked to bring a pack of their usual cigarettes to the study day, which they will give to a member of the study team (the pack will be returned to the participant at the end of the session). After participants have provided written consent, they will be assigned a unique registration number allocated by a central computer. The following baseline data will then be collected in a paper-based form.

- **Demographic information:** Age, gender, education level, and ethnicity.
- **Nicotine and Tobacco Use:** Smoking history; types of tobacco products smoked (factory-made, roll your own/ both, or others); the number of cigarettes smoked on a typical day; history of using Nicotine Replacement Therapy (NRT), nicotine-containing e-cigarettes(vapes), heated tobacco products, and illicit tobacco products.
- **Mental health:** Whether they have been diagnosed with 1) a mood disorder (and experienced symptoms in the last year) and/or 2) anxiety (and experienced symptoms in the past year). During the last 2 weeks, whether (1) they felt nervous, anxious, or on edge, (2) not being able to stop or control worrying, (3) Little interest or pleasure in doing things, and (4)Feeling down, depressed, or hopeless. As part of our duty of care, after answering these questions, information will be provided stating: If you have concerns about your mental health, feel free to call Free call or text 1737 any time for support from a trained counselor; Lifeline – 0800 543 354 (0800 LIFELINE) or free text 4357 (HELP).
- **Use of other dangerous consumptions:** Alcohol use will be measured by using the Alcohol Use Disorders Identification Test (AUDIT-C) score, designed to screen for risky alcohol use and potential alcohol use disorders. The AUDIT-C score focuses on three key questions about the frequency of alcohol consumption, the typical quantity of alcohol consumed, and the frequency of heavy drinking episodes (22). Cannabis use will be measured by how many days a week following the same measuring score as the CENIC-NZ study (21). As part of our duty of care, after answering these questions, information will be provided stating: “If you have concerns about your drinking, the Alcohol Drug Helpline provides free, friendly, non-judgmental, professional help and advice. 24 hours a day, 7

days a week. Call the Alcohol Drug Helpline on 0800 787 797 or text 8681 to speak with a trained counsellor or visit the alcohol drug helpline website to learn more."

- **Perceptions on general harms of tobacco and vaping:** The perceived harm of cigarettes, VLNC cigarettes, and e-cigarettes containing nicotine, and NRT will be measured on a five-point Likert scale (scores will range from 0 to 4, where 0 is "Not at all harmful" and 4 is "extremely harmful").
- **Perceptions of Harm: Regular vs. Reduced-Nicotine Cigarettes:** Participants' perceptions of harm will be recorded by asking whether they believe cigarettes with 95% less nicotine are more harmful or equally harmful or less harmful or if they don't know, compared to regular cigarettes.

5.6 Randomisation

Eligible participants will be randomised via computer (1:1:1 ratio) to one of three groups using block randomisation (using varying block sizes). The randomisation sequence will be generated by the trial statistician (Dr Alana Cavadino), and centrally managed and concealed until the point of randomisation.

5.7 Blinding

This is an open-label randomized controlled trial due to the infeasibility of blinding the interventions (smoking a VLNC cigarette or reading messages about VLNC cigarettes).

5.8 Trial intervention

Participants will be randomised into one of three groups, specifically:

1. *Smoking a VLNC cigarette and viewing health messages about VLNC cigarettes:* Participants will be given a VLNC cigarette pack and asked to read all information on and inside the pack. The pack will show the required 'lung cancer' graphic warnings and the words 'All cigarettes cause Lung cancer.' All other standard text about cigarettes will be added to the front and back of the pack following the existing standard, Appendix 3 (17). The pack will also clearly state the nicotine content of each cigarette (i.e., 0.41 mg of nicotine per gram of tobacco). Inside the pack will be an insert that states, "Imagine that all cigarettes in New Zealand have now been changed: the nicotine levels have been reduced by 95%. These cigarettes are no longer addictive, are less satisfying, and you can quit smoking more easily, but they still contain harmful chemicals like formaldehyde and arsenic. They may cause cancer.'' These messages are adapted from a paper by Reynolds et al. (2024)(15). The Participants will then be given one VLNC cigarette and asked to smoke it.

2. *Smoking one of their own cigarettes and viewing health messages about VLNC cigarettes:* Participants will be given the same VLNC cigarette pack and the exact instructions as

Group 1. Participants will be asked to remove a cigarette from their cigarette pack and smoke it.

3. *Control group: Smoking one of their own cigarettes:* Participants will be given back their usual cigarette pack and asked to read all information on the pack. The pack will show the existing graphic health warnings of New Zealand. Participants will then be asked to remove one of their cigarettes from the pack (17)and smoke it.

5.9 Withdrawal criteria

The following events are grounds for withdrawing.

- Any emergency due to an underlying medical condition or accident. In an emergency, the principal investigator will notify the appropriate ethical committee within 48 hours of becoming aware of the event. See below for guidelines for completing the form.
- If participants select to cease the intervention, i.e., they decline to smoke VLNC cigarette or their own tobacco or read health messages

5.10 Concomitant therapy

Throughout the trial, participants will be free to take whatever medications they wish.

5.11 Outcome data

Primary focus
The main focus of the trial is to determine whether a larger trial would be feasible to conduct, specifically.

1. Can people be recruited, and how quickly can they be recruited?
   This will be measured by
   - the number of participants recruited in a month
   - the number of participants in each ethnic group (NZ Europeans, Māori, Pacific people, Asian, Middle Eastern/Latin American/African and other ethnicity) as defined by Stat NZ (level 1 classification) (22)
   - the number and proportion of participants in priority and non-priority populations. Priority populations are defined as people with self-reported anxiety and/or depression, young people (aged 18-30 years) of low educational attainment or individuals who report heavy alcohol and/or cannabis use (following the same definitions as the CENIC-NZ study(21).

2. Do people attend the study site on their scheduled day and stay for their required time? This will be measured by using on-site attendance records.

3. Are the study tasks and questionnaires understandable to participants? Specific questions will be asked in the questionnaire.

4. Are all questions answered? This will be determined by counting the number of unanswered questions in the questionnaire.

5. Did participants highlight any difficulties with the trial?
   This will be measured by using the onsite records and feedback from the study participants.

6. Did participants face any adverse events or symptoms after smoking a VLNC cigarette?
   This will be measured by using the onsite records and feedback from the participants.

Secondary focus

The secondary focus of the trial is to gather data on the likely impact of the tested interventions on potential participant behaviours. The secondary outcome measures will be measured immediately after smoking and reading the health messages on VLNC cigarettes under the hypothetical scenario of all smoked tobacco legally available for purchase in New Zealand having 95% less nicotine than the tobacco they normally smoke. Specifically,

- Their likelihood of using specific harmful products, measured using a 7-point Likert scale ranging from 0 to 6, where 0 is 'very unlikely' and 6 'very likely'. These products include
    - VLNC cigarettes.
    - Illicit tobacco (i.e., tobacco with regular nicotine levels).
    - Homegrown tobacco (i.e., strictly self-grown tobacco. In New Zealand, individuals are allowed to manufacture up to 5kg of home-grown tobacco per adult per year for personal use. This amount translates to approximately 50 to 100 cigarettes per person daily, depending on the tobacco content per each cigarette. However, this tobacco is strictly for personal consumption and cannot be sold or shared(23).
    - Nicotine e-cigarette (vapes).
    - Heated tobacco products.
    - NRT (i.e., nicotine gum, patches, or nicotine lozenges or nicotine mouth spray).
    - Alcohol.
    - Cannabis/Marijuana/ Tetrahydrocannabinol products.
    - Other illicit drugs.
    - Their desire to quit smoking

- Their likelihood to add nicotine to low-nicotine cigarettes or other smoked tobacco was measured using a 5-point scale running from 0 to 4, where o is 'never' and 4 is 'daily'.
- The maximum amount they are willing to pay per VLNC cigarette is measured in New Zealand dollars.
- If the participants select 1 and above on the 7-point Likert scale for illicit tobacco, the following questions will be triggered
    - The maximum amount you are willing to pay per illicit cigarette, measured in New Zealand dollars.
    - The maximum time you would be prepared to travel to get illicit cigarettes, measured in minutes.
    - Their reasons for seeking illicit cigarettes to be collected in open field response

The following perception questions will be asked of all the participants.

- **Perceptions on general harms of tobacco and vaping:** The perceived harm of cigarettes, VLNC cigarettes, and e-cigarettes containing nicotine, and NRT will be

measured on a five-point Likert scale (scores will range from 0 to 4, where 0 is “Not at all harmful” and 4 is “extremely harmful”).

- **Perceptions of Harm: Regular vs. Reduced-Nicotine Cigarettes:** Participants' perceptions of harm will be recorded by asking whether they believe cigarettes with 95% less nicotine are more harmful or equally harmful or less harmful or if they don’t know, compared to regular cigarettes.

5.12 Study closure

Participants will spend approximately one hour attending the study day. At the end of their time in the study, they will be offered smoking cessation support consisting of: 1) a free ‘Advice to Client’ letter for low-cost NRT (subjectable to $5 copayment fees) (24) and 2) written information on smoking cessation support in New Zealand. Participants will then be given a $100 voucher to cover their time and travel costs (and will sign a document saying they received their payment). This amount is based on the estimated time commitment, which includes approximately one hour for the study and up to two hours for travel, in addition to covering travel-related costs. The compensation is aligned with the minimum wage in New Zealand from April 2025 ($23.50 per hour) to ensure fairness.

5.13 Risk of Coercion

The risk of coercion (25) is minimal for this study. Participation is voluntary, with no impact on access to services or support. We will provide smoking cessation support and a free ‘Advice to Client’ letter for low-cost NRT as part of our duty of care for eligible participants. During the course of the study, we will provide information on mental health support services, Alcohol and drug helpline as needed as part of our duty of care. Participants will receive a $100 NZD gift card as a token of appreciation for their time. This amount is based on the estimated time commitment, which includes approximately one hour for the study and up to two hours for travel, in addition to covering travel-related costs. The compensation is aligned with the minimum wage in New Zealand from April 2025 ($23.50 per hour) to ensure fairness. Participation is entirely voluntary, and individuals are free to decline or withdraw at any time without any consequences. The compensation is not intended to influence participation or responses in any way. Even if the participants decline participation, we will provide them with the opportunity to receive information on cessation support as part of our duty of care.

6. Statistical Considerations

6.1 Sample size

Since this is a pilot trial, no sample size calculations have been performed. Instead, the target sample size is based on feasibility and practical considerations. We anticipate that 30 participants will provide sufficient information to evaluate trial processes and provide enough data on the outcome measures to inform the development of a larger trial in the future.

6.2 Statistical analyses

6.2.1 *Baseline characteristics*

Demographics, nicotine and tobacco use, mental health, use of other dangerous consumptions, and perceptions on general harms and comparative will be summarised by group, and descriptive summary statistics will be provided. Since any differences between randomised groups at baseline could only have occurred by chance, no formal significance testing will be conducted.

6.2.2 *Treatment effects*

As this is a pilot study, treatment effects will not be compared using formal statistical testing. Instead, all outcomes will be presented using descriptive summaries within each group. Means and standard deviation or median and interquartile range will be used to describe continuous variables, and number and percentage will be used to describe categorical variables. Missing data will be described for all outcomes.

6.2.3 *Qualitative analyses*

The reasons for choosing illicit tobacco and the feedback on participating in the pilot trial will be analysed as conceptual content analysis and with manual coding. We will follow the following recommended steps in the conceptual content analysis of Columbia University Mailman School of Public Health (26).

The recommended steps are

- Decide the Level of Analysis
- Choose Concepts to Code
- Code for Existence or Frequency
- Distinguish Among Concepts
- Develop Coding Rules
- Handle Irrelevant Information
- Code the Text
- Analyse Results

7. Data Governance

7.1 Data collection

All data will be collected using a paper-based form, which will then be entered into a REDcap database after the data collection. Validation rules for each variable will be specified by the PhD student in collaboration with the study statistician. These rules will include range checks so that inaccuracies in data collection can be identified early. A query will be raised as soon as any values are entered that are outside the allowed range or if data are missing. The data will be stored securely on a secure University of Auckland-approved electronic system/server. Data will be stored on the University of Auckland Research Drive for researchers during data collection as it has unlimited storage.

7.2 Data Management

Refer to the separate Trial Data Management Plan, which describes identifiable and non-identifiable data and how these data are captured, transmitted, and stored securely.

7.3 Data sharing

7.3.1 *Availability of data and materials*

All requests for de-identified individual participant data or trial documents will be considered, where the proposed use aligns with the ethical approval and participant consenting for the trial, aligns with public good purposes, does not conflict with other requests, or planned use by the Trial Steering Committee, and the requestor is willing to sign a data access agreement and has sought relevant ethical approvals. All requests for data access require approval from the principal investigator of the study.

7.3.2 *Data-sharing for Indigenous communities*

To ensure data sovereignty in light of, for example, the global directives on Indigenous rights and local treaties such as Te Tiriti o Waitangi in Aotearoa/New Zealand, we do not make Indigenous data available in public repositories but will consider requests where the proposal meets the agreement with Dr. Braden Te Ao (Kaitiaki [Guardian] of the trial data) to ensure that datasets are analysed in accordance with Tikanga Māori.

8. Ethical Approval and Consent

8.1 National ethics approval

Ethical approval for the study will be sought from the Human Participants Ethics Committee (UAHPEC).

8.2 SCOTT Regulatory Approval

SCOTT approval is not required for this study as VLNC cigarettes are not classified as a medicine and this study is not investigating the potential therapeutic value of the VLNC cigarettes.

8.3 Informed consent

This study will conform to standards of good clinical practice. Maintenance of confidentiality and compliance with the Privacy Act will be emphasised to all study participants. Participants will be healthy volunteers and will be provided with a written participation information sheet describing the study so that they can make an informed decision about their participation. Written consent will be obtained from all participants at the study site on the day of the study.

9. Assessment of Safety / Adverse Event Reporting

9.1 Adverse events (AE)

9.1.1 *Definition of an adverse event*

An adverse event includes any illness, sign or symptom, or clinically significant abnormality that has appeared or worsened during the course of the study.

9.1.2 *Management of the Adverse Events*

All the adverse events will be recorded using the adverse event form (Form X).

9.1.3 *Emergency*

No serious adverse event is expected in the trial as the participants are people who currently smoke, and the intervention will be either their regular tobacco or VLNC cigarettes. The unlikely event of life-threatening emergencies will be handled by dialling '111' and summoning emergency services.

9.2 Reporting safety information

Any serious adverse events that occur during the study period will be reported to the University of Auckland Human Participant Ethics Committee within seven working days. Any emergency will be reported to the University of Auckland Human Participant Ethics Committee within 3 working days.

10. Clinical Supplies

10.1 Trial intervention identification

The following trial interventions will be used in this study:

SUPPLIER	TREATMENT	INGREDIENTS	DESCRIPTION
22nd Century Group (bought through the US market)	VLN king	Nicotine (0.41 mg of nicotine per gram of tobacco)	Cigarettes (20 per pack)

10.2 Handling and dispensing of trial treatment

All trial cigarettes will be under the direct responsibility of the principal investigator. The VLNC cigarettes will be stored at ambient room temperature at the Department of General Practice and Primary Healthcare, School of Population Health, University of Auckland.

10.3 Packaging and labelling

The VLN king cigarettes will be removed from their original packets, and the pack will show lung cancer required graphic warnings for all New Zealand tobacco products and the words 'All cigarettes cause Lung cancer.' All other standard text will be added to the front and back of the pack following the existing standard, Appendix 3 (17). The pack will also clearly state the nicotine content of each cigarette (i.e., 0.41 mg of nicotine per gram of tobacco).

10.4 Treatment supply records

The PhD student will be responsible for ensuring that an inventory of the VLNC cigarettes is maintained at the Department of General Practice and Primary Healthcare.
Records or logs will include:

- Amount placed in inventory at the Department of General Practice and Primary Healthcare.
- Dates of treatment inventory movement.
- Initials of the PhD student

10.5 Trial treatment on completion of trial

Unused VLNC cigarettes will be returned to the Department of General Practice and Primary Healthcare, where they will be stored.

11. Relevance to Health

Tobacco claims the lives of half its users who do not quit, contributing to over 8 million deaths annually(2). The prevalence of smoking in New Zealand is declining, with 8.4% of adults (aged 15 years and above) identified as current smokers in 2023/24. However, smoking rates vary widely among different ethnic groups: 17.2% among Māori, 14.7% among Pacific peoples, 7.4% among New Zealand Europeans, and 5% among Asians. Smoking prevalence also varies significantly by neighbourhood deprivation, with 3.6% among those in the least deprived neighbourhoods compared to 15.9 % in the most deprived. Therefore, smoking not only leads to premature deaths but also contributes to inequitable health outcomes across different populations in New Zealand(3). Reducing the nicotine in cigarettes and smoked tobacco could encourage current smokers to quit or switch to other less harmful nicotine products (7).

While there are concerns that tobacco endgame policies in New Zealand would drive the people who smoke tobacco to the illicit market, limited numbers of studies directly investigate illicit tobacco use when there is a reduction in cigarettes in the legal market. Illicit tobacco users have significantly worse health conditions than smokers who only smoke legal tobacco (27).
While evidence indicates the proposed denicotinisation strategy would likely enhance quitting(7), is crucial to investigate whether the denicotinisation would impact the tobacco users' interaction with the illicit tobacco market.

11.1 Relevance to Māori Health

The rate of smoking has been declining among Māori populations in the past ten years, from 40.3% in 2011/12 to 17.2% in 2023/24 (3). While the denicotinisation policy was to promote quitting, illicit tobacco could hinder the policy. Such an impact would be larger among populations with higher smoking rates.

12. Dissemination of Results

To ensure the findings have the greatest possible impact, the dissemination strategy will focus on key messages, target audiences, appropriate communication channels, activities and timing, and measures of success. Pathways include:

- Academic and professional colleagues will be informed about the study via articles submitted to a peer-reviewed journal, such as Tobacco Control, Addiction, Psychopharmacology, and the Society for Research on Nicotine and Tobacco Journal.
- An oral presentation to a local, national and/or international audience will be actively pursued.
- Dissemination of findings to Māori and Pacific organisations, media, and community groups as guided by Dr. Braden Te Ao.

13. Administrative Section

13.1 Adherence to the protocol

Except for a change that is intended to eliminate an immediate hazard to participants, the approved protocol will be conducted as described. Any significant protocol deviation will be documented.

13.2 Protocol revision procedures

All revisions will be discussed with, and approved by, the Study Personal. If the revision is an “administrative letter,” the principal investigator will submit it to the appropriate Ethics Committee for their information. If the revision is an “amendment,” the principal investigator will sign it. The principal investigator will submit the amendment to the appropriate Ethics Committee for review and approval or favourable opinion prior to implementation. Documentation of approval signed by the chairperson or designee of the Ethics Committee will be sent to the principal investigator.

If an amendment substantially alters the study design or increases the potential risk to the subject the consent form will be revised and submitted to the Ethics Committee for review and approval or favourable opinion.

13.3 Case report form procedures

All questionnaire information will be recorded on the paper-based forms.

13.4 Data confidentiality and security

Data will be stored in the University of Auckland-owned storage and servers. Data stored on The University of Auckland storage and servers will be managed in accordance with appropriate New Zealand Information Security Manual (NZISM) guidelines and relevant legislation, including the Privacy Act 1994.

13.5 Record retention policy

The principal investigator will retain trial treatment disposition records and source documents for the maximum period required by the Privacy Legislation and the Health (Retention of Health Information) Regulations 1996 (6 years from the termination of trial). Staff involved in the trial will not destroy any records associated with the trial without the prior approval of the Principal Investigator. If the Principal Investigator or a co-investigator withdraws from the trial (e.g., relocation, retirement), any records they hold will be transferred to a mutually agreed upon designee (e.g., another co-investigator). Notice of such transfer will be given in writing to the Department Head of the Department of General Practice and Primary Care.

13.6 Insurance

This research is not conducted principally for the benefit of the manufacturer or distributor of VLNC cigarettes. Therefore, participants may be entitled to compensation from the Accident Compensation Corporation (ACC) for personal injury suffered as a result of treatment given as part of the study (section 32 (4) of the Injury, Prevention, Rehabilitation and Compensation Act 2001 and section 13 of the Injury, Prevention, Rehabilitation and Compensation Amendment Act (No 2) 2005).

13.7 Ownership of data and publication policy

Individual study data will remain the property of individual study participants. The study team will be responsible for the storage, protection, and retrieval of study data. The Steering Committee will be responsible for the safe guardianship and use of the data. All access, analyses and dissemination of Māori-specific data will be the joint responsibility of the Steering Committee.

All publications will be approved by members of the Steering Committee, who will be named on all reports. Study participants and the research team will be acknowledged in the final report and all publications and presentations resulting from this study.

14. References

1.Ministry of Health NZ. New Zealand Health Survey: Methodology Report (2023/24). Ministry of Health, New Zealand 2024.

2.World Health Organization. Fact Sheets: Tobacco. 2023; Available at: https://www.who.int/news-room/fact-sheets/detail/tobacco. Accessed April 25, 2024.

3.Ministry of Health NZ. New Zealand Health Survey . 2024; Available at: https://www.health.govt.nz/nz-health-statistics/surveys/new-zealand-health-survey#method. Accessed December 02, 2024.

4.Ministry of Health New Zealand. Smokefree Aotearoa 2025 Action Plan - Auahi Kore Aotearoa Mahere Rautaki 2025. 2021; Available at: https://www.health.govt.nz/publication/smokefree-aotearoa-2025-action-plan-auahi-kore-aotearoa-mahere-rautaki-2025.

5.Ministry of Health NZ. Smokefree Environments and Regulated Products (Smoked Tobacco) Amendment Act. 2023; Available at: https://www.health.govt.nz/our-work/regulation-health-and-disability-system/smoked-tobacco-products/smokefree-environments-and-regulated-products-smoked-tobacco-amendment-act. Accessed Jan 13, 2024.

6.Ministry of Health NZ. Smokefree Environments and Regulated Products Act 1990. 2023 Jan 01.

7.Health Coalition Aotearoa. Key facts – Smoking and the Smokefree Environments and Regulated Products (Smoked Tobacco) Amendment Act (SERPA). 2023; Available at: https://www.healthcoalition.org.nz/wp-content/uploads/2024/04/SERPA-Information-Current-and-updated-as-of-20-12-23.pdf.

8.Edwards R, Hoek J, Waa A. New Zealand: Ground-breaking action plan may help country achieve its Smokefree 2025 goal. 2022; Available at: https://blogs.bmj.com/tc/2022/01/12/new-zealand-ground-breaking-action-plan-may-help-country-achieve-its-smokefree-2025-goal/.

9.Wilson N. Modelling the impacts of tobacco denicotinisation on achieving the Smokefree 2025 goal in Aotearoa New Zealand. New Zealand medical journal 2022 Jan 21;135(1548):65–76.

10.Hall MG, Byron MJ, Brewer NT, Noar SM, Ribisl KM. Interest in Illicit Purchase of Cigarettes Under a Very Low Nicotine Content Product Standard. Nicotine & tobacco research 2019 Dec 23;21(Supplement_1):S128–S132.

11.Dolan SB, Bradley MK, Johnson MW. E-cigarette Price Impacts legal and Black-Market Cigarette Purchasing Under a Hypothetical Reduced-Nicotine Cigarette Standard. Nicotine & tobacco research 2023 Aug 19;25(9):1556–1564.

12.Tucker MR, Laugesen M, Grace RC. Estimating Demand and Cross-Price Elasticity for Very Low Nicotine Content (VLNC) Cigarettes Using a Simulated Demand Task. Nicotine & tobacco research 2018 Jun 7;20(7):843–850.

13.Darredeau C, Stewart SH, Barrett SP. The effects of nicotine content information on subjective and behavioural responses to nicotine-containing and denicotinized cigarettes. Behavioural pharmacology 2013 Aug;24(4):291–297.

14.Gendall P, Popova L, Thrasher J, Hoek J. Nicotine beliefs and perceptions of low nicotine labels and mitigating statements among people who do and do not smoke: a cross-sectional study from Aotearoa New Zealand. Tob Control 2024 Jan 9:tc–058353.

15.Reynolds RM, Popova L, Ashley DL, Henderson KC, Ntansah CA, Yang B, et al. Messaging about very low nicotine cigarettes (VLNCs) to influence policy attitudes, harm perceptions and smoking motivations: a discrete choice experiment. Tob Control 2024 May 1;33(3):325–332.

16.Pei D, Reynolds RM, Ntansah CA, Hackworth EE, Henderson KC, Yang B, et al. Independent and combined effects of very low nicotine cigarette messages and e-cigarette messages: a randomised clinical trial. Tob Control 2024 Apr 25:tc–058556.

17.Ministry of Health NZ. Smokefree background information. 2023; Available at: https://www.health.govt.nz/strategies-initiatives/programmes-and-initiatives/smokefree-2025/smokefree-history/smokefree-background-information. Accessed Dec 12, 2024.

18.Thrasher JF, Ferguson SG, Hackworth EE, Wu C, Lambert VC, Porticella N, et al. Combining Inserts With Warning Labels on Cigarette Packs to Promote Smoking Cessation: A 2-Week Randomized Trial. Annals of behavioral medicine 2024 Jan 1;58(1):56–66.

19.Eldridge SM, Lancaster GA, Campbell MJ, Thabane L, Hopewell S, Coleman CL, et al. Defining Feasibility and Pilot Studies in Preparation for Randomised Controlled Trials: Development of a Conceptual Framework. PloS one 2016 Mar 15;11(3):e0150205.

20.Thabane L, Ma J, Chu R, Cheng J, Ismaila A, Rios LP, et al. A tutorial on pilot studies: the what, why and how. BMC Medical Research Methodology 2010 Jan 6;10(1):1–1.

21.Wake field University School of Medicine & University of Auckland. CENIC II New Zealand Supplement: Perceptions, Concerns, Needs, and Intentions Related to Reducing Nicotine in Combusted Tobacco.

22.Stats NZ. Place and ethnic group summaries user guide. 2024 November.

23.New Zealand Customs Service. Tobacco : FAQs. 2023; Available at: https://www.customs.govt.nz/business/import/tobacco/faqs/. Accessed Nov 7, 2024.

24.Health New Zealand. Health-services-and-programmes. 2024 Aug 28.

25.Klitzman R. How IRBs view and make decisions about coercion and undue influence. Journal of medical ethics 2013 Apr 1;39(4):224–229.

26.Columbia University Mailman School of Public Health. Content Analysis. 2024; Available at: https://www.publichealth.columbia.edu/research/population-health-methods/content-analysis. Accessed Dec 12, 2024.

27.Aitken CK, Fry TRL, Farrell L, Pellegrini B. Smokers of illicit tobacco report significantly worse health than other smokers. Nicotine & tobacco research 2009 Aug 1;11(8):996–1001.

15. Trial Acknowledgement

TRIAL ACKNOWLEDGMENT

I have read the protocol and agree that it contains all necessary details for carrying out the trial as described. I will conduct this protocol as outlined therein and will make a reasonable effort to complete the trial within the time designated.

I will provide copies of the protocol and access to all information to trial personnel under my supervision. I will discuss this material with them to ensure that they are fully informed about the treatment and the trial.

I understand that the trial may be terminated or enrolment suspended at any time if it becomes necessary to protect the best interests of the trial participants.

Chris Bullen

_____

Investigator's printed name and signature Date

Address of trial site:

Building 507, School of Population Health, Grafton Campus, The University of Auckland, 22-30 Park Road, Grafton, Auckland 1023, New Zealand

16. Appendix 1 – Proposed Timeline

Study year	1 year											
Actual year	2025											
Months	J	F	M	A	M	J	J	A	S	O	N	D
Ethics Approval												
Trial recruitment												
Assessment												
Data cleaning and data lock												
Analysis												
Writing and dissemination												

17. Appendix 2 – Graphic health warning

To comply with New Zealand regulations around tobacco(17), the graphic health warning below will be added to the VLNC tobacco packs.

Smoking causes over 80% of lung cancers
NEKE ATU I TE 80% O NGĀ MATE PUKUPUKU KI NGĀ PŪKAHUKAHU I AHU MAI I TE KAI PAIPA

18. Appendix 3 – Summary of Protocol Amendments

Page	Section heading	Amendment
