Statistical Analysis Plan

WARNING! Study Stage 3

WARNING! Study - Developing and Testing Alcohol Warning Labels in adult New Zealanders who purchase and consume alcohol.

Principal Investigator

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STATISTICAL ANALYSIS PLAN APPROVAL SHEET

Study: WARNING (Stage 3)

Title: WARNING! Study - Developing and Testing Alcohol Warning Labels in adult New Zealanders who purchase and consume alcohol.

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The undersigned have reviewed this document and find it to be consistent with the requirements of the protocol as it applies to their respective areas. The author/reviewer also finds this document to be in compliance with ICH-E9.

Yannan Jiang Trial Statistician	Date
	28/03/24
Principal Investigator	Date

PREFACE

The purpose of this Statistical Analysis Plan (SAP) is to provide a detailed statement of the intended statistical analyses that will be performed in the analysis of data from the WARNING study (stage 3). This document is intended to be stand-alone from the protocol and adhere to the main points in the analysis summary specified in the protocol. Please note that the scope of this SAP is intended to cover ONLY those main analyses described in the protocol.

Please refer to the study protocol for a full description of the study design.

1. STUDY OVERVIEW

1.1. Study Objective

To determine the impact of three selected warning labels versus a 'no label' control condition, on consumers' online alcohol purchase behaviour.

1.2. Study Design

A four-arm, parallel, randomised controlled trial, undertaken online.

Participants will be recruited via a market research company's (Dynata and partners) national online panel. Panel members are invited by email to take a web-based survey hosted by Dynata, which includes a hyperlink to a participant information sheet (which can be downloaded) on the study website. Interested participants will be asked to complete a series of online questions to ascertain their eligibility. The participant information sheet will also be available in Te Reo Māori.

Three different warning labels have been developed, based on findings from Stages 1 and 2 of the WARNING study, stakeholder feedback and published research. These labels relate to liver cancer, violence, and heart attack/stroke, and utilise both a pictogram/image with text (Figure 1).

Figure 1: Tested alcohol warning labels

Liver cancer	Violence	Heart / stroke
		

These labels will be shown on an alcoholic drink and beside the product and tested against a no-label control (i.e., the product will only display the mandatory pregnancy and % alcohol labels). Participants will have the choice to view the text of the test warning labels (shown in Figure 1) in English only, or English and Te Reo Māori.

1.3. Study Population

Participants will be adults (≥18 years); report purchasing and consuming any alcohol from an off-license retailer (e.g. supermarket, bottle store, uber eats, etc, but excluding drinking at a bar, pub, or restaurant) in the past week; are able to read English; have access to the internet, reside in NZ; and have not previously undertaken a Dynata survey about alcohol. Only people who have drunk beer, wine, spirits or ready-to-drink (RTD) products in the last week will be eligible

1.4. Sample size

A sample size of 1,000 participants (250 per arm) will have >90% power at the 5% overall significance level (two-sided) to detect an effect size of 0.33 Standard Deviations (SD) on the primary outcome, between any one of three label groups and the control, with adjustment for multiple comparisons. An approximately equal sample size per ethnic group will provide 90% power at 5% significance to detect a group difference of 0.5 SD in subgroup analysis.

1.5. Randomisation

Participants will be randomly allocated (1:1:1:1 ratio) within the Dynata platform to view an image of an alcoholic drink (based on their response to the 'drink of choice' question) with one of the three warning labels, or no warning label (control), on the product.

Randomisation will be stratified by ethnicity (Māori and/or Pacific; non-Māori/non-Pacific) and alcohol use (light to moderate; heavy) using block randomisation with variable block sizes of 4 or 8. The randomisation sequence will be generated by the trial statistician, and centrally managed by Dynata and concealed until the point of randomisation.

1.6. Blinding

Due to the nature of the study, participants will be aware of the treatment allocation post-randomisation. Study investigators and the trial statistician will remain blinded until the end of the trial.

1.7. Baseline Data

After screening, eligible participants will be asked to provide baseline data via the online platform. Baseline questions will include:

- **Socio-demographics**: Age group, sex, gender, ethnicity, whether they would classify their place of residence as 'urban' or 'rural', and highest educational level (as a measure of socio-economic position).
- **Existing health conditions**: Participants will be asked if they have ever been told by a doctor that they have any of nine listed health conditions. These conditions will be those where alcohol is a risk factor. This question is asked because participants with an alcohol-related health condition may respond to the questions in a different way and may be more likely to support mandated alcohol warning labels.
- **Voting behaviour**: (this is an outcome routinely collected by Dynata). This question is asked because it is possible that more conservative participants may be less likely to support mandated alcohol warning labels.
- **Alcohol use and misuse**: assessed using the AUDIT-C.
- **Drink of choice** (i.e., the drink they purchase most of and drink): Beer, wine, spirit, or RTD products.

- **Average 'regular', weekly number of alcoholic drinks purchased**: Participants will be asked to estimate their average, weekly number of alcoholic drinks purchased from an off-license retailer (e.g. supermarket, bottle store, uber eats, etc, but excluding drinking at a bar, pub, or restaurant).
- **Average 'regular', weekly spend on alcoholic drinks:** Participants will also be asked to estimate their average, weekly spend on alcoholic drinks purchased from an off-license retailer (e.g. supermarket, bottle store, uber eats, etc, but excluding drinking at a bar, pub, or restaurant).

1.8. Outcome Assessments

Primary outcome:

Participants will be asked about their 'likely intent' to purchase and drink the viewed alcoholic drink, based on an 11-point Juster probability scale, where zero represents 'not likely at all to purchase and drink' and 10 represents 'very likely to purchase and drink'.

Secondary outcomes:

Participants will be asked to imagine that they are completing their regular, weekly shop for alcohol and to choose how many (from a drop-down menu of 0-100) of this particular alcoholic drink they would buy and drink. The participants will be advised to assume the drink is in the same price range as their usual drink of choice.

Participants will then proceed to the next page (without the ability to return/back-click), and will be asked a series of questions:

- Unprompted recall: Participants will be asked if they noticed anything about the image. Those who select 'yes' will be asked to explain their answer in a free-text field.

- Prompted recall: Participants will be asked if they noticed any warning labels (Yes/No).

- Comprehension: Participants will be asked to explain what message(s) the label(s) was providing. Answers will be collected using a free-text field.

- Behaviour (unprompted): Participants will be asked to explain what the label(s) was wanting them to do, with responses captured in a free-text field.

- Behaviour (prompted): Participants will be asked if the presence of the warning labels influenced the number of drinks they selected to purchase and drink in the previous section (assessed on a 5-point scale, where '1' is 'No, not at all' and '5' is 'Yes, very much'). Participants will also be asked if they are likely to discuss the labels with family and/or friends (assessed on a 5-point scale where '1' is 'No, not likely at all' and '5' is 'Yes, very likely').

- Judgement: Participants will be asked if the message provided by the warning label(s) was believable, measured on a 5-point likert scale, where '0' is 'Not believable at all' and '5' is 'Very believable', and to explain their answer in a free-text field.

- Support for health warning labels: Participants will be asked how strongly they agree or disagree with the following statement: “Alcohol health warning labels should be required on all alcoholic drinks?” Responses will be measured on a likert scale of 1 to 7, where 1 is strongly disagree and 7 is strongly agree. Participants will also be asked to explain their response to the above question in a free-text field.

2. VARIABLE DEFINITIONS

2.1. AUDIT-C scores

For eligible participants, alcohol use will be assessed using the three AUDIT-C questions (see below) and sex at birth (male/female). The score for each question is indicated in the bracket.

Q1. How often did you have a drink containing alcohol in the past year?

- Monthly or less (1)
- 2-4 times a month (2)
- 2-3 times a week (3)
- 4 or more times a week (4)

Q2. How many standard drinks containing alcohol did you have on a typical day when you were drinking in the past year?

- 1 or 2 (0)
- 3 or 4 (1)
- 5 or 6 (2)
- 7 to 9 (3)
- 10 or more (4)

Q3. How often did you have six or more drinks on one occasion in the past year?

- Never (0)
- Less than monthly (1)
- Monthly (2)
- Weekly (3)
- Daily or almost daily (4)

A total score out of 12 will be calculated by summing the three AUDIT-C question scores. Higher scores indicate an increased likelihood of alcohol dependence.

Mild to moderate alcohol use is indicated by an AUDIT-C score of <3 for women and <4 for men, whilst **heavy alcohol use** is indicated by an AUDIT-C score of ≥3 for women and ≥4 for men. These two categories are used to define the stratification factor “alcohol use” in randomisation.

2.2. Prioritised ethnicity

Each participant will complete a question on which ethnic groups they belong to (tick all that apply):

a. New Zealand European
b. Māori
c. Samoan

d. Cook Islands Māori
e. Tongan
f. Niuean
g. Chinese
h. Indian
i. Other, e.g., Dutch, Japanese, Tokelauan (please state): _____

Those who tick (b) and/or any of (c)-(f) will be in the ethnic group "Māori and/or Pacific". Those who don't tick any of these options will be in the ethnic group "non-Māori/non-Pacific". These two categories are used to define the stratification factor "ethnicity" in randomisation.

For analysis purposes, we will also summarise Māori and Pacific participants separately. Those who tick (b) will be in the ethnic group "Māori". Those who didn't tick (b) but ticked any of (c)-(f) will be in the ethnic group "Pacific".

2.3. Primary outcome measure

Each participant will indicate how likely they are to purchase and drink the alcoholic drink, after viewing the product with or without the warning label in the group they are randomised to.

Their 'likely intent' to purchase and drink this alcoholic drink, is measured on an 11-point Juster probability scale, where zero represents "not likely at all to purchase and drink" and 10 represents "very likely to purchase and drink".

(not likely at all) (very likely to purchase)

0	1	2	3	4	5	6	7	8	9	10

This outcome will be summarised as a continuous variable in analysis.

3. STATISTICAL ANALYSIS

All statistical analyses will be performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). All statistical tests will be two-tailed and at 5% significance level throughout the analyses.

Summaries of continuous variables will be presented as numbers observed, mean and standard deviations (SD), while categorical variables will be presented as frequencies and percentages. The amount of missing data will be reported. All results will be presented in a figure and tables based on the analyses stated below. The CONSORT 2010 statement will be used as the guideline for reporting.

3.1. Participant accountability

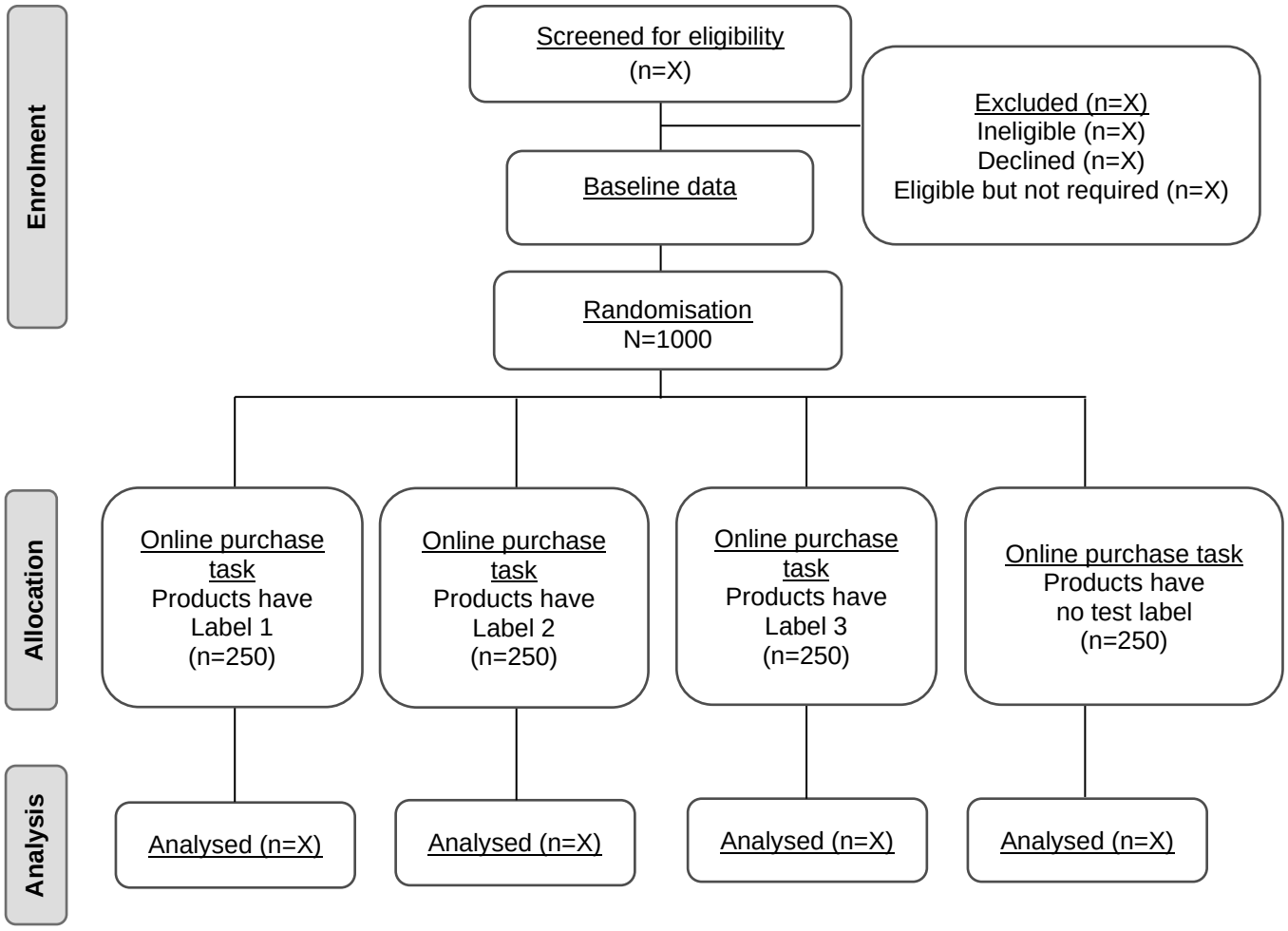
The number of participants who were registered, fulfilled eligibility criterion, together with reasons for exclusion will be summarised. The CONSORT diagram will be used to present the flow chart of all study participants (Figure 2).

3.2. Baseline characteristics

Baseline characteristics of all randomised participants will be summarised descriptively for each intervention and control groups. Since any differences between the groups at baseline could only have occurred by chance, no formal significance testing will be conducted.

As a pre-planned subgroup analysis that is considered in randomisation and the recruitment target, separate baseline summaries will be provided for Māori/Pacific and non-Māori/non-Pacific participants. If we recruit enough number of participants, all Māori and Pacific participants will also be summarised separately.

Figure 2: Participant flow diagram



3.3. Efficacy Analysis

Treatment evaluation will be performed on the principle of intention-to-treat (ITT), including all randomised participants in the group they were randomised to. Since all eligible participants will receive the intervention and complete the questionnaire online, no per protocol analyses are planned.

The primary outcome will be analysed using linear regression model, adjusting for stratification factors (ethnicity and alcohol use) and the type of alcohol the participant chose (beer, wine, spirit or RTD), and controlling for multiple comparisons with the control group. Other baseline characteristics (e.g. sex and age group, pre-existing alcohol-related health conditions) will be considered in the model if deemed important. Model-adjusted mean difference between the groups will be estimated with 95% confidence interval and p-value.

As a pre-planned subgroup analysis, the consistency of intervention effects on the primary outcome will be tested between ethnic groups using an interaction term between randomised group and ethnicity in the main model. Separate subgroup analyses will also be conducted, and the results will be presented if equal recruitment targets are met.

Generalised linear regression models will be used to analyse secondary outcomes using a link function appropriate to the distribution of outcome variable. Similar model adjustments will be considered as in the primary outcome analysis. Model-adjusted group differences will be presented with 95% confidence intervals and p-values.