Statistical Analysis Plan (Addendum)

An Electronic Brief Alcohol Intervention for Women Attending a Breast Screening Service (Health4Her-Automated)

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Study rationale and design

Alcohol is a major modifiable risk factor for female breast cancer, even in very low amounts. Yet, awareness of this risk remains low and is not systematically addressed in healthcare settings. Embedding a brief alcohol intervention within lifestyle information offered to all women attending breast screening provides the opportunity to address harmful drinking in a discrete, non-judgmental way, to prevent alcohol-attributable breast cancer among this at-risk population.

Building on a previous randomised controlled trial of a prototype brief e-health intervention (which included alcohol-related questions asked by a researcher, and an animation viewed on an iPad that was activated by the researcher), the aim of the current pragmatic, single-site, double-blind, parallel group randomised controlled trial is to test the effectiveness of a co-designed, automated brief alcohol intervention (Health4Her-Automated) in reducing women's drinking intentions, improving alcohol literacy, and reducing consumption.

Women attending Maroondah BreastScreen for routine mammography completed a baseline assessment before being randomised to receive alcohol brief intervention plus lifestyle health promotion, or lifestyle health promotion only. Participants received an iPad and earphones to self-complete interventions. Alcohol and/or lifestyle information was delivered by way of an animation on an iPad, alongside self-completed activities that reinforced intervention content. Follow-up assessments were completed after intervention completion (i.e. immediately post-randomisation; drinking intentions outcome only) and at 4-weeks post-randomisation.

This study also included a pilot arm – active arm but completed post-screening offsite (i.e. at home on own device). The pilot arm did not form part of the planned randomised controlled trial or power and sample size calculation, but was included based on findings from the previous phase of this research (e.g. women not having time to complete the intervention onsite, some breast screening services not having space or resources to deliver the intervention onsite).

Statistical Analysis Plan (SAP)

This plan, or SAP Addendum, provides additional detail to the statistical considerations that were documented in the statistical analysis plan in Health4Her-Automated Protocol_V4_11 08 2023 (available via the trial record on ClinicalTrials.gov).

Additional analyses not specified in the published protocol or this addendum will be regarded as exploratory.

Statistical software

Analyses will be conducted using the most appropriate procedures in programs such as GenStat, R, SAS, or Stata.

Analytic approach

Data will be collated, cleaned, and validated using programmed edit checks.

The analysis will take place based on the intention to treat (ITT) principle (i.e. subjects' data are analysed as randomised) after all subjects, not known to have withdrawn or not deemed lost to follow-up, have had their 4-week assessments.

Outcome variables with repeated measurements will be analysed by fitting Generalised Linear Mixed Models (GLMMs) with an appropriate link function (e.g. gaussian for continuous outcomes or outcomes treated as continuous [e.g. 5-point Likert scales] and logit for binary outcomes). Inferences about the effect of the Health4Her intervention on the outcomes will be based on a comparison, between treatment groups, of change in outcomes from baseline to immediate post-intervention (i.e. immediately post-randomisation) and/or 4-weeks post-randomisation. Models will estimate fixed effects for treatment and time, and their interaction, and random effects for subjects and assessments within subjects. If necessary, suitable variance-covariance structures for the repeated measures will be compared using Akaike's Information Criterion and/or Bayesian Information Criterion. In the case that GLMMs have estimation/convergence difficulties regression models may be estimated via Generalised Estimating Equations (with an appropriate link function). A Wald test (or equivalent approach) will be used to test for an overall group by time interaction in outcomes.

Outcome variables without a baseline assessment will be examined using Generalised Linear Models (i.e. the non-mixed model version). Inferences about the effect of the Health4Her intervention on these outcomes will be based on a comparison between treatment groups of outcomes assessed at 4-weeks post-randomisation. Models will estimate fixed effects for treatment.

All statistical tests will be two-tailed with the alpha level set to 0.05.

Pilot Arm – active arm but completed post-screening (i.e. offsite on own device)

Inferences about the effect of the Health4Her intervention completed post-screening (i.e. offsite on own device) on outcomes will be based on based on: 1) a comparison of change, in the pilot arm only, from baseline to immediate post-intervention (i.e. immediately post-randomisation) and/or 4-weeks post-randomisation, and 2) a comparison, between treatment groups (i.e. pilot arm vs control; pilot arm vs intervention; acknowledging that assignment to the pilot arm was not randomised), of change from baseline to immediate post-intervention (i.e. immediately post-randomisation) and/or 4-weeks post-randomisation. The analytic methods described above will be implemented here.

Missing data

Where appropriate, missing values will be addressed through maximum likelihood estimation (i.e. in a mixed model) or using multiple imputation.

Sensitivity analyses

Several sensitivity analyses may be performed:

- Using a per-protocol approach, defined as those who received all elements of the intervention.

- Stratified by participants based on those who: a) report drinking any alcohol in the past month, and b) are identified to be drinking at a level exceeding current national guidelines for weekly and/or single day consumption.
- Including relevant covariates (e.g. age, education, CALD, LGBTIQA+) as adjustments. Covariates may also be used to stratify analyses.
- Models to examine the robustness of missing data modelling decisions (e.g. including auxiliary variables in models or in complete case data).

Primary Outcome

1) Change in next-month drinking intentions (immediate post-intervention)

Secondary Outcomes

1) Change in next-month drinking intentions (4-weeks post-randomisation)

2) Change in intended number of standard drinks consumed over the next month (4-weeks post-randomisation)

3) Proportion of participants intending to reduce their next-month alcohol consumption (immediate post-intervention)

4) Proportion of participants intending to reduce their next-month alcohol consumption (4-weeks post-randomisation)

5) Proportion of participants accurately identifying alcohol as a clear risk factor for breast cancer (4-weeks post-randomisation)

6) Proportion of participants accurately identifying i) the increased breast cancer risk associated with drinking one average restaurant serve of wine a day; ii) the number of standard drinks in an average restaurant serve of red wine; iii) the maximum number of standard drinks per week recommended by current Australian Alcohol Guidelines (4-weeks post-randomisation)

7) Proportion of participants accurately identifying inactivity and excess weight as risk factors for breast cancer (4-weeks post-randomisation)

8) Proportion of participants sharing the information they learned with others (4-weeks post-randomisation)

Potential additional exploratory outcomes

Potential additional exploratory outcomes include (but are not limited to): change in next-month: physical activity intentions, vegetable consumption intentions; change in: physical activity frequency/amount, vegetable consumption frequency; change in physical activity / diet-related health literacy.