

Reporting Summary

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Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a Confirmed

- ☐ ☒ The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
- ☐ ☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- ☐ ☒ The statistical test(s) used AND whether they are one- or two-sided
Only common tests should be described solely by name; describe more complex techniques in the Methods section.
- ☐ ☒ A description of all covariates tested
- ☐ ☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- ☐ ☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- ☐ ☒ For null hypothesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
Give P values as exact values whenever suitable.
- ☒ ☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- ☐ ☒ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- ☐ ☒ Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection The web developers who built the intervention website built a bespoke questionnaire platform for data collection, housed within the intervention website.

Data analysis R Studio version 2022.12.0+353 was used for analysis. Regressions were performed using the lmer, glmer, glmmTMB packages. Plots were developed using the ggplot2 package. SMDs were calculated with the countES package.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

De-identified participant data will be made available to researchers on request to Dr Katrina Champion (katrina.champion@sydney.edu.au) and with appropriate

reason when accompanied by study protocol and analysis plan. Data will be shared after the approval of a proposal by a committee of the current research team with a signed data access agreement.

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender

Students reported their gender identity, with options of “male”, “female”, “non-binary/gender fluid”, “different identity”, and “prefer not to say.” Selection of different identity prompted an open-ended text box where participants specified their identity. Two researchers (SS and another researcher with expertise in gender identities and health) independently reviewed “different identity” responses and recoded phony answers (such as “helicopter”) to missing. The two recoded datasets were then compared, combined and merged into the main datafile. Following this process, participants that identified as non-binary, gender fluid, or a genuine different identity were combined into one group. While sex at birth was also captured in the questionnaire, gender identity has been used for analysis, recognising the fact that non-binary and gender diverse young people have unique experiences that are often associated with unique social and health outcomes.

Population characteristics

As randomisation was stratified by school sex ratio (single sex versus co-educational) and school region (NSW regional, NSW major city, WA and QLD), these were included as covariates in all models. However, gender identity was chosen over sex at birth for the aforementioned reasons. As both the Big 6 and mental health are also known to be associated with socioeconomic status and cultural and linguistic diversity, sensitivity analyses were conducted to determine whether model fit improved when adjusting for relative family affluence and cultural and linguistic diversity.

Recruitment

As is standard practice for school-based cRCTs, schools were recruited through convenience and purposive sampling, with 519 schools approached across NSW, QLD and WA. A-priori power analysis was conducted for primary outcomes but not for secondary outcomes.²⁵ The methodology proposed by Heo and Leon was used.³⁶ Power was set at 0.80; the correlation among level 1 data (repeated measurements over time within one student) was set at 0.60 and the number of timepoints was set at five. A mean of 70 students per school from 72 schools was estimated and a minimum detectable effect size was set at 0.158, based on alcohol use, which was the targeted risk behaviour with the lowest anticipated prevalence at baseline. A total of 72 schools would have enabled analysis within each trial site separately (8 intervention and 8 control in each of the four trial sites); however, this sample size was not achieved due to school withdrawal. The final sample of 6639 students from 71 schools provided sufficient power for primary outcome analysis in the overall sample but not by trial site.

It is possible that bias may have occurred at the school-level, however every effort was made to reduce barriers to participation that may have biased the types of schools that could participate. For example, participation was free, had no teacher training required and took minimal preparation for teachers outside of class time (the program was online and “plug and play”). Given the randomized design and adjustments during analysis for clustering, any school-level factors should not have impacted between-group differences identified. However, we are transparent in the limitations section that findings may not be generalizable as the sample was not population-representative, which is a standard challenge in school-based research.

Ethics oversight

The trial was approved by ethics boards from the University of Sydney (HREC2018/882), Curtin University (HRE2019-0083), University of Queensland (2019000037), NSW Department of Education (SERAP 2019006), and relevant Catholic Diocese.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description

Quantitative experimental design - cluster randomised controlled trial.

Research sample

Participants are Australian secondary school students from 71 schools in three Australian states (New South Wales, Queensland, and Western Australia). A total of 6,639 students completed the baseline survey (Mean age=12.7 years, SD=0.50; 50.6% male). Almost all students (N=6,454; 97.2%) completed at least one follow-up survey and 5,698 (85.8%) completed two or more follow-up surveys. Retention was 76% at 24-month follow up (N=5,014, Mean age=14.7, SD=0.82). All Year 7 students at participating schools at baseline were eligible, but participation required active student consent and either passive or active parental consent, depending on ethics board requirements.

Sampling strategy

As is standard practice for school-based cRCTs, schools were recruited through convenience and purposive sampling, with 519 schools approached across NSW, QLD and WA. A-priori power analysis was conducted for primary outcomes but not for secondary

outcomes.²⁵ The methodology proposed by Heo and Leon was used.³⁶ Power was set at 0.80; the correlation among level 1 data (repeated measurements over time within one student) was set at 0.60 and the number of timepoints was set at five. A mean of 70 students per school from 72 schools was estimated and a minimum detectable effect size was set at 0.158, based on alcohol use, which was the targeted risk behaviour with the lowest anticipated prevalence at baseline. A total of 72 schools would have enabled analysis within each trial site separately (8 intervention and 8 control in each of the four trial sites); however, this sample size was not achieved due to school withdrawal. The final sample of 6639 students from 71 schools provided sufficient power for primary outcome analysis in the overall sample but not by trial site.

Post-hoc power analysis for the present study was conducted, again using the methodology from Heo and Leon.³⁶ Power was set at 0.80, the correlation among level 1 data set at 0.6, alpha at 0.05, and the number of timepoints set to four. The actual mean number of students at participating schools (n=93) was used. Effect sizes of 0.17 and 0.16 were set for depression and anxiety symptoms respectively, consistent with mean effects identified in a 2021 meta-analysis of universal school-based prevention interventions.⁵ The psychological distress effect size was set at 0.13, consistent with mean effects of psychoeducation-focussed universal prevention interventions in another meta-analysis.³⁷ Post-hoc power analysis confirmed that the present study is sufficient powered to detect these effect sizes, with 10 schools (5 intervention, 5 control) required for anxiety and depressive symptoms and 16 schools (8 intervention, 8 control) required for psychological distress.

Data collection	Students completed online questionnaires during class on the intervention website. Hard copy surveys or research-assistant-administered in-person surveys were offered to facilitate feasibility and accessibility. Where students were absent from class for follow-up occasions, they were able to complete the online or hard copy survey at home.
Timing	Baseline data was collected in the mid-late 2019, post-intervention follow up was collected 6-8 weeks after baseline, also in 2019. 12 month follow up was collected in mid-late 2020. 24-month follow up was collected in mid-late 2021.
Data exclusions	The only data excluded from analyses were phony responses to gender identity. Responses were double screened by two researchers to determine valid versus phony responses and phony responses were recoded to missing.
Non-participation	A detailed CONSORT diagram is provided in the manuscript. Briefly, total of 6,639 students completed the baseline survey. Almost all students (N=6,454; 97.2%) completed at least one follow-up survey and 5,698 (85.8%) completed two or more follow-up surveys. Retention was 76% at 24-month follow up (N=5,014).
Randomization	A biostatistician with no role in school recruitment performed randomisation using the Blockrand function in R. Stratification was applied during randomisation based on school region (NSW major city, NSW regional, WA, and QLD), and school gender composition (coeducational, predominately male [>60%], or predominately female [>60%]). As is routine for school-based interventions, researchers, students and teachers were not blind to allocation.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration	ACTRN12619000431123
Study protocol	Teesson M, Champion KE, Newton NC, Kay-Lambkin F, Chapman C, Thornton L, et al. Study protocol of the Health4Life initiative: a cluster randomised controlled trial of an eHealth school-based program targeting multiple lifestyle risk behaviours among young Australians. <i>BMJ Open</i> . 2020;10(7):e035662.
Data collection	Data was collected in secondary schools in three Australian States: New South Wales, Queensland and Western Australia. Recruitment commenced in early 2019, baseline data was collected in the mid-late 2019, post-intervention follow up was collected 6-8 weeks after baseline, also in 2019. 12 month follow up was collected in mid-late 2020. 24-month follow up was collected in mid-late 2021.
Outcomes	As the Health4Life trial tested a MHBC intervention spanning six lifestyle behaviours and mental health, it has numerous pre-

registered primary and secondary outcomes (ANZCTR trial registration: ACTRN12619000431123). As such, the results of the Health4Life intervention against the pre-registered primary outcomes (six primary behaviour change outcomes for the Big 6 behaviours) and a number of Big-6-related secondary outcomes have been published elsewhere. The present study examines three further pre-registered secondary outcomes related to mental health; depressive symptoms (Patient Health Questionnaire), anxiety symptoms (PROMIS-A) and psychological distress (Kessler 6) symptoms.