Statistical analysis plan (SAP): Sun-D Trial

Working title	The effect of high SPF sunscreen application on vitamin D production: The Sun-D Trial		
Date of plan	26 July 2024		
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Overview			
Aims	Our **primary aim** is to determine whether randomisation to routine application of high SPF sunscreen (versus discretionary use) on all days when the ultraviolet (UV) index is forecast to be ≥3 leads to a decrease in serum 25-hydroxyvitamin D (25(OH)D) concentration from baseline. Our **secondary aims** are to determine whether randomisation to routine application of high SPF sunscreen on all days when the UV index is forecast to be ≥3 (versus discretionary use) leads to a decrease in serum 25(OH)D concentration from baseline: • Within categories of: (a) baseline serum 25(OH)D concentration; (b) residential UV radiation zone; (c) skin exposure; and (d) personal UV radiation exposure.[1] • Taking into account adherence with the study protocol in the intervention group and contamination from off-study sunscreen use in the control group (referred to in this SAP as the per-protocol analysis). • In participants who took no vitamin D supplements during the trial. [1] Additional details regarding the stratification variables can be found in the Participants and Data section (Stratification Variables), and in Appendix E		
Outcomes	The outcome of interest is the difference in serum 25(OH)D concentration from baseline and was measured at two post-baseline time points.		
Outcome measurement	Participants were asked to provide 3 blood samples at the following timepoints: Sample 1 (baseline): Jun 2022 to Nov 2022 Sample 2 (summer): Jan 2023 to Mar 2023 Sample 3 (winter): Jun 2023 to Aug 2023 STable 1 shows the number of samples returned by month and randomisation group at each of the 3 time points for all randomised participants. Serum 25(OH)D concentration was quantified for all 3 samples using liquid chromatography with tandem mass spectroscopy at the end of the intervention phase.		

Documentation	
Analysis packages	SAS version 9.4 R version 4.3.2 Stata version 18.0
Participants and data	
Participants and eligibility	We will include all randomised participants except 11 who provided a blood sample at baseline only. The sample size will be 628 (312 in the intervention group and 316 in the control group).
Exposure variable	Randomisation group
Randomisation stratification variables	The following variables were used to stratify randomisation to the intervention and control groups. These variables will be included as covariates in all analysis models. • Age group at baseline: 18 to <45 years; ≥45 to 70 years • Sex: Male; Female • State of residence at baseline: NSW/ACT; QLD; TAS; VIC
UV index data	The Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) provided ground-based UV index data for Kingston (Hobart), Melbourne, Canberra, Sydney, Newcastle, Gold Coast, Brisbane, Emerald, and Townsville. These datasets included actual and expected daily maximum UV index, and 10-minute average actual UV index for each day and location during the period 01/07/2022 to 30/09/2023.
Sunscreen use data	Participants were asked to report their sunscreen use (study sunscreen and off-study sunscreen use) in monthly surveys.
Use of vitamin D supplements	Participants were asked to report their intake of vitamin D supplements in monthly surveys. They were also asked to report changes to vitamin D supplementation by phone or email as they occurred.
Calculated variables	
Stratification variables	Baseline serum 25(OH)D concentration Participants' baseline serum 25(OH)D concentrations will be categorised into three groups (<50 nmol/L, 50 to <75 nmol/L, ≥75 nmol/L). Residential UV radiation zone We calculated the total daily standard erythemal dose (SED) for each site using the 10-minute average actual UV index data. We compared the average total daily SED during the period 01/09/2022 to 31/08/2023 (i.e., over a one year period), and grouped sites into low, medium and high UV radiation zones (Appendix E, Table A). • Low UV radiation zone: Hobart and Melbourne; • Medium UV radiation zone: Canberra, Sydney, and Newcastle; • High UV radiation zone: Gold Coast, Brisbane, Emerald, and Townsville. Participants were assigned the ARPANSA monitoring site closest to their place of residence at baseline, thereby assigning them a residential UV radiation zone (i.e., low, medium, or high).

	For more details see Appendix E – Residential UV radiation Zone Skin exposure category Skin exposure is a function of time spent outdoors between 8am and 4pm and clothing worn while outdoors (i.e., amount of skin exposed). A skin exposure score was calculated for each month that a participant was in the trial. The final skin exposure score was calculated by averaging the monthly skin exposure scores from November 2022 to May 2023 inclusive (NB these months were chosen as they encompassed the period where all participants had been recruited and none had finished the trial). We then categorised the final score into low, medium, or high based on cohort-wide tertiles. Personal UV radiation exposure category We reclassified the nine ARPANSA monitoring sites into two residential UV zones: lower UV radiation (Hobart and Melbourne); and higher UV radiation (Canberra, Sydney, Newcastle, Gold Coast, Brisbane, Emerald, and Townsville). We dichotomised the skin exposure score (based on the cohort-wide median) into lower skin exposure and higher skin exposure. These two variables were combined to create a four-category variable representing all possible combinations of dichotomised skin exposure and residential UV zone. For further details on the derivation of these variables, refer to Appendix E.
Adherence and contamination	We used the expected daily maximum UV index to calculate the number of days per month that the UV index was expected to be ≥3 at each site (i.e., the number of days when sunscreen would be required). Adherence to the study protocol in the intervention group and contamination from off-study sunscreen use in the control group were calculated based on UV index data and reports of sunscreen use based on monthly survey data. Consistent with the skin exposure score, the overall adherence/contamination score was calculated by averaging the monthly score from November 2022 to May 2023 inclusive. For further details on the derivation of adherence and contamination, refer to Appendix E.
Data cleaning and missing data	
Data cleaning	The Sun-D Trial REDCap database was constructed using conditional logic which minimised inconsistencies in survey data. Vitamin D intake was checked and cleaned by phone or email with participants during the trial period.
Handling missing data	Four participants are missing some baseline data used to calculate inverse probability weights that are used in the per-protocol analysis and the analysis accounting for vitamin D supplementation. We will not impute these data; rather, we will exclude these participants from those analyses. Skin exposure, adherence and contamination scores relied on data captured in monthly surveys. Where relevant data were completely missing or insufficient we did not compute the score for that month. We used all available* data during the period November 2022 to May 2023 to calculate the final score. * If fewer than 7 months of data were available, we used the data from all available months in the relevant time period. Supplementary methods Table E & Table F in Appendix E show how much data was available to calculate the final score in each case.
Maintaining blinding	An analyst will produce statistical code for all analyses reporting the link between randomisation group and serum 25(OH)D concentration based on a data set with simulated participant identifiers and randomisation allocation. Once all co-authors approve the

	analysis plan including all tables and figures, the analyst will be provided with the actual group assignments to complete the final analyses.
Analysis details	
Main analysis	We will describe participant flow using a CONSORT diagram (Figure 1). We will describe the baseline characteristics by randomisation group (restricted to those included in the analysis) (Table 1). We will visualise the distribution of serum 25(OH)D concentration (using an outlier box and whisker plot), and report the number (%) of participants within categories of serum 25(OH)D concentration (<50 nmol/L, 50 to <75 nmol/L, ≥75 nmol/L), at each time point according to randomisation group (Figure 2, STable 2). We will fit a linear mixed model and model the change in serum 25(OH)D concentration from baseline (Table 2). The model will include randomisation group, baseline serum 25(OH)D concentration, post-baseline time point (summer and winter, coded as 0 and 1), sex, age group, state, and interaction terms between time point and: (i) randomisation group; and (ii) baseline serum 25(OH)D concentration. A significant interaction between randomisation group and time point would indicate that the effect of the intervention changes over time. The interaction between baseline serum 25(OH)D concentration and time point may improve the fit of the model by accounting for a potential relationship between baseline concentration and change from baseline.
Sensitivity analysis	There are some variables that are not perfectly balanced between study groups. We will fit a linear mixed model that includes variables with a standardised mean difference of ≥0.15 (with the exception of alcohol consumption which is strongly associated with self-reported overall health) to investigate whether their inclusion alters the estimates of interest (STable 3). Variables included will be self-reported overall health and tendency to sunburn.
Analysis for secondary aims	*Stratified analysis – intention to treat analysis* We will conduct subgroup analyses (Figure 3) by: (a) baseline serum 25(OH)D concentration; (b) residential UV zone; (c) skin exposure category; and (d) personal UV radiation exposure category. *Per-protocol analysis* The per-protocol analysis will restrict the analysis to those in the intervention group who were adherent and those in the control group who were not contaminated (by use of their own sunscreen). Adherence and contamination are described in detail in Appendix E. Participants in the intervention group will be classified as adherent if their adherence to sunscreen was ≥70%, and non-adherent otherwise. Participants in the control group will be classified as non-contaminated if they used sunscreen on fewer than 3 days per week, and as contaminated otherwise. Dropping participants from the analysis can introduce bias. To address this, we will use logistic regression models to estimate propensity scores separately in each group (i.e., probability of being adherent in the intervention group, and probability of remaining non-contaminated in the control group). We will use the propensity scores to calculate inverse probability weights (IPWs). We will compare characteristics of adherent/non-contaminated participants according to randomisation group before and after applying the IPWs (STable 4, SFigure 1). We will then apply the IPWs to the cohort comprising only those participants who were adherent (intervention group) or non-contaminated (control group), and rerun the linear mixed model (STable 5). This weighted model will include randomisation group and any characteristics that remain imbalanced after reweighting, provided that the characteristic is also associated with serum 25(OH)D concentration.

	Accounting for vitamin D supplementation This analysis will follow the same general approach as the per-protocol analysis. Briefly, we will exclude participants who took any supplement containing vitamin D at any time during the trial, using IPWs to account for the potential bias introduced by restricting the analysis to a subset of participants (STable 6, STable 7, SFigure 2). *Stratified analyses: per protocol and vitamin D-free analyses* We will perform subgroup analyses only if we find a clinically relevant effect (difference in serum 25(OH)D from baseline of 10 nmol/L or more) in the overall analysis. If performed, the results will be presented as supplementary figures consistent with Figure 3.
Additional supplementary tables and figures	We will present supplementary figures showing the distribution of serum 25(OH)D concentration at each time point for the entire cohort within categories of: • Baseline serum 25(OH)D concentration (SFigure 3); • Residential UV zone (SFigure 4); • Skin exposure (SFigure 5); and • Personal UV radiation exposure (SFigure 6) We will present supplementary tables showing overall adherence (STable 8), contamination (STable 9), and the distribution of skin exposure score by residential UV radiation zone (STable 10).

Appendix A: Planned Main Figures

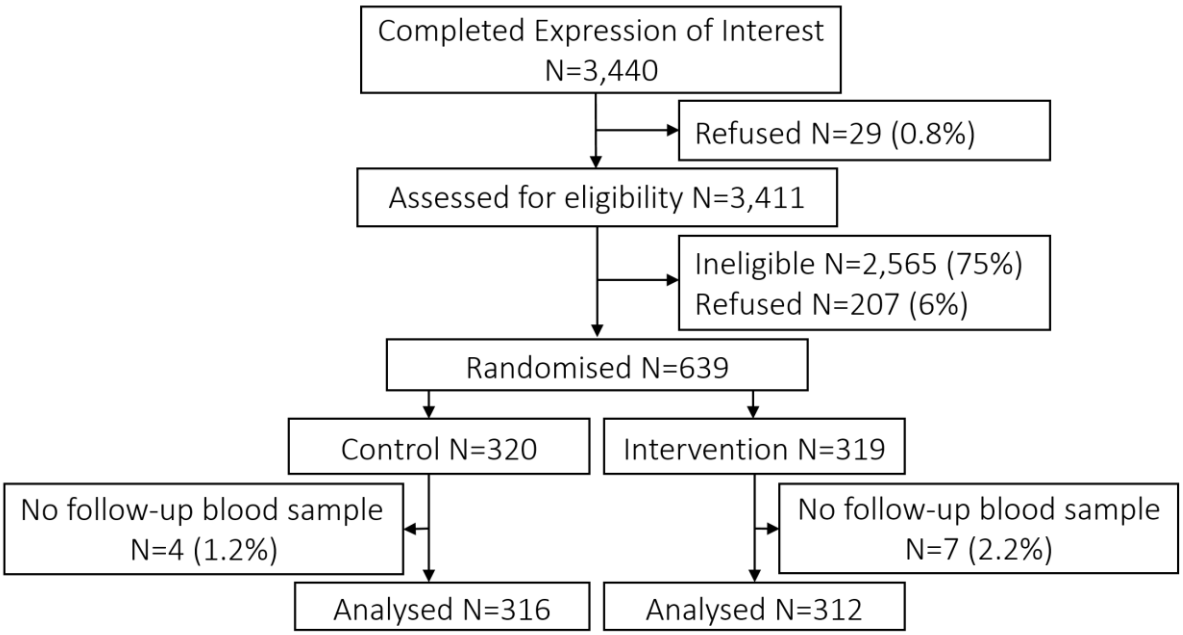


Figure 1. Participant flowchart

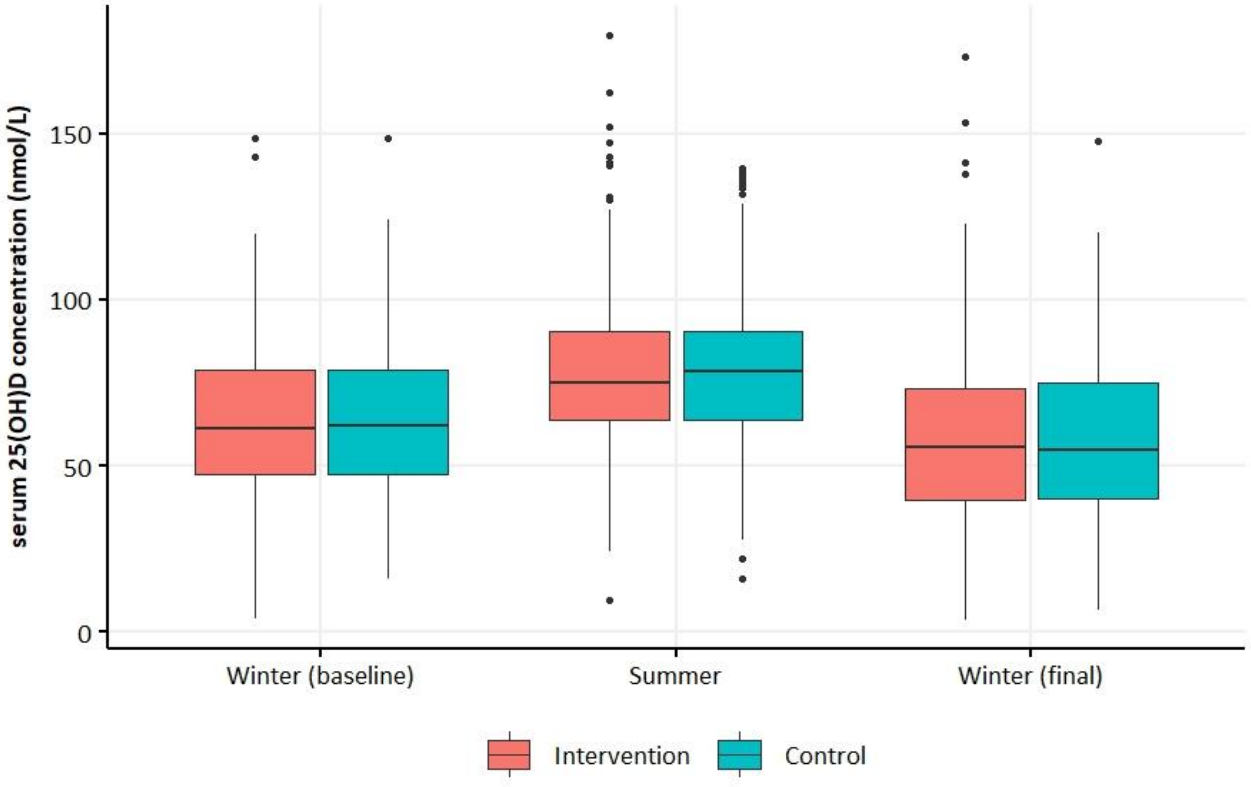


Figure 2. Outlier box plot of the serum 25-hydroxyvitamin D concentration at each time point within the entire cohort, by randomisation group (NB randomisation group has been simulated for the purposes of the SAP).

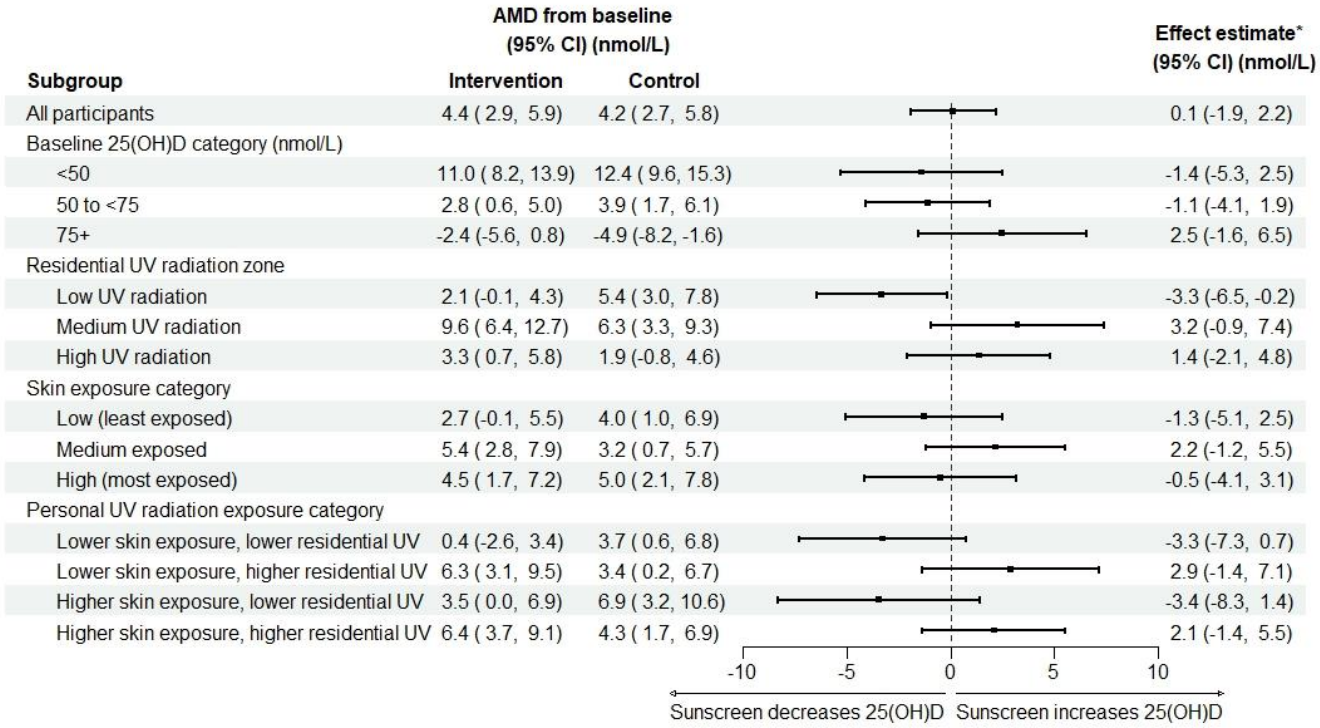


Figure 3. Effect of randomisation to sunscreen on change in 25(OH)D concentration from baseline, in all participants and stratified by selected participant characteristics (NB randomisation group has been simulated for the purposes of the SAP)

*The effect estimate is the difference in the overall change from baseline between the intervention and control groups. The effect estimate and adjusted mean differences were estimated using mixed models for repeated measures. The model included baseline serum 25(OH)D concentration, post-baseline time point (summer, winter (final)), sex, age group, state of residence, and interaction terms between time point and: (i) randomisation group; and (ii) baseline serum 25(OH)D concentration.

Abbreviations: AMD, adjusted mean difference; CI, confidence interval

Appendix B: Planned main tables

Table 1. Participant characteristics by randomisation group **(NB cells for baseline serum 25(OH)D concentration category are empty because the analyst has not been provided with a dataset that contains both real randomisation group and 25(OH)D concentrations)**

Characteristic	N (%)	
	Intervention N = 312	Control N = 316
Median baseline age in years (1st, 3rd quartile)	53 (40, 65)	52 (39, 62)
Sex		
Male	103 (33.0)	107 (33.9)
Female	209 (67.0)	209 (66.1)
Educational attainment		
Highschool or lower	39 (12.6)	41 (13.0)
Certificate/diploma/advanced diploma	98 (31.6)	102 (32.4)
Bachelor degree or higher	173 (55.8)	172 (54.6)
Unknown	2	1
Housing situation		
Home owner	232 (74.4)	231 (73.1)
Renter	57 (18.3)	68 (21.5)
Other	23 (7.4)	17 (5.4)
BMI category		
Underweight/healthy	108 (34.6)	106 (33.5)
Overweight	100 (32.1)	108 (34.2)
Obese	104 (33.3)	102 (32.3)
History of regular smoking		
No	217 (69.8)	227 (71.8)
Yes	94 (30.2)	89 (28.2)
Unknown	1	0
Number of alcoholic drinks per week		
≤1	147 (47.3)	172 (54.4)
2 to 4	58 (18.6)	48 (15.2)
5 to 6	33 (10.6)	37 (11.7)
≥7	73 (23.5)	59 (18.7)
Unknown	1	0
Self-reported overall health		
Excellent	41 (13.1)	35 (11.1)
Very good	127 (40.7)	108 (34.2)
Good	106 (34.0)	134 (42.4)
Fair/poor	38 (12.2)	39 (12.3)
Tendency to sunburn		
Does not burn at all	32 (10.3)	44 (13.9)
Becomes a little bit pink	168 (53.8)	144 (45.6)
Becomes dark pink to red but does not blister or peel	85 (27.2)	105 (33.2)
Becomes dark pink to red and blisters or peels	27 (8.7)	23 (7.3)

Characteristic	N (%)	
	Intervention N = 312	Control N = 316
Skin tanning when outdoors for 30 minutes in summer		
Develops a dark tan	44 (14.1)	44 (13.9)
Develops a medium tan	143 (45.8)	142 (44.9)
Does not tan/develops a pale tan	125 (40.1)	130 (41.1)
Number of sunburns in 12 months before baseline		
None	129 (41.3)	128 (40.5)
1	98 (31.4)	93 (29.4)
≥2	85 (27.2)	95 (30.1)
Lifetime skin cancers excised		
No	235 (75.3)	241 (76.3)
Yes	77 (24.7)	75 (23.7)
Lifetime skin cancers burnt off		
No	217 (69.6)	222 (70.3)
Yes	95 (30.4)	94 (29.7)
Skin cancer/sunspot treatment using ointments		
No	267 (85.6)	271 (85.8)
Yes	45 (14.4)	45 (14.2)
Baseline serum 25(OH)D concentration category (nmol/L)		
<50		
50 to <75		
≥75		
Residential UV radiation zone		
Low UV radiation	132 (42.3)	131 (41.5)
Medium UV radiation	90 (28.8)	91 (28.8)
High UV radiation	90 (28.8)	94 (29.7)
Skin exposure category		
Low (least exposed)	106 (34.0)	104 (32.9)
Medium	99 (31.7)	110 (34.8)
High (most exposed)	107 (34.3)	102 (32.3)
Personal UV radiation exposure category		
Lower skin exposure, lower residential UV	80 (25.6)	69 (21.8)
Lower skin exposure, higher residential UV	79 (25.3)	86 (27.2)
Higher skin exposure, lower residential UV	52 (16.7)	62 (19.6)
Higher skin exposure, higher residential UV	101 (32.4)	99 (31.3)

Abbreviations: BMI, body mass index; UV, Ultraviolet

Table 2. Effect of randomisation to sunscreen on serum 25(OH)D concentration (NB randomisation group has been simulated for the purposes of the SAP)

Statistics	N		Mean 25(OH)D concentration (SD) or change from baseline (95% CI) (nmol/L)		Intervention versus control
	Intervention	Control	Intervention	Control	
Winter (baseline)					
Mean (SD)	314	314	64.0 (22.2)	61.6 (22.4)	
Summer					
Mean (SD)	312	312	78.6 (23.3)	76.8 (21.8)	
AMD from baseline[1]			14.6 (12.8, 16.4)	14.2 (12.3, 16.0)	0.4 (-2, 2.9)
Winter (final)					
Mean (SD)	311	305	58.5 (25.0)	56.6 (21.7)	
AMD from baseline[1]			-5.9 (-7.6,-4.1)	-5.7 (-7.5,-3.8)	-0.2 (-2.6, 2.3)
Overall					
Mean (SD)	314	314	68.6 (26.1)	66.8 (24.0)	
AMD from baseline[1]			4.4 (2.9, 5.9)	4.2 (2.7, 5.8)	0.1 (-1.9, 2.2)

[1]Adjusted mean differences were estimated using mixed models for repeated measures. The model included baseline serum 25(OH)D concentration, post-baseline time point (summer, winter (final)), sex, age group, state of residence, and interaction terms between time point and: (i) randomisation group; and (ii) baseline serum 25(OH)D concentration.
Abbreviations: AMD, adjusted mean difference; CI, confidence interval; SD, standard deviation

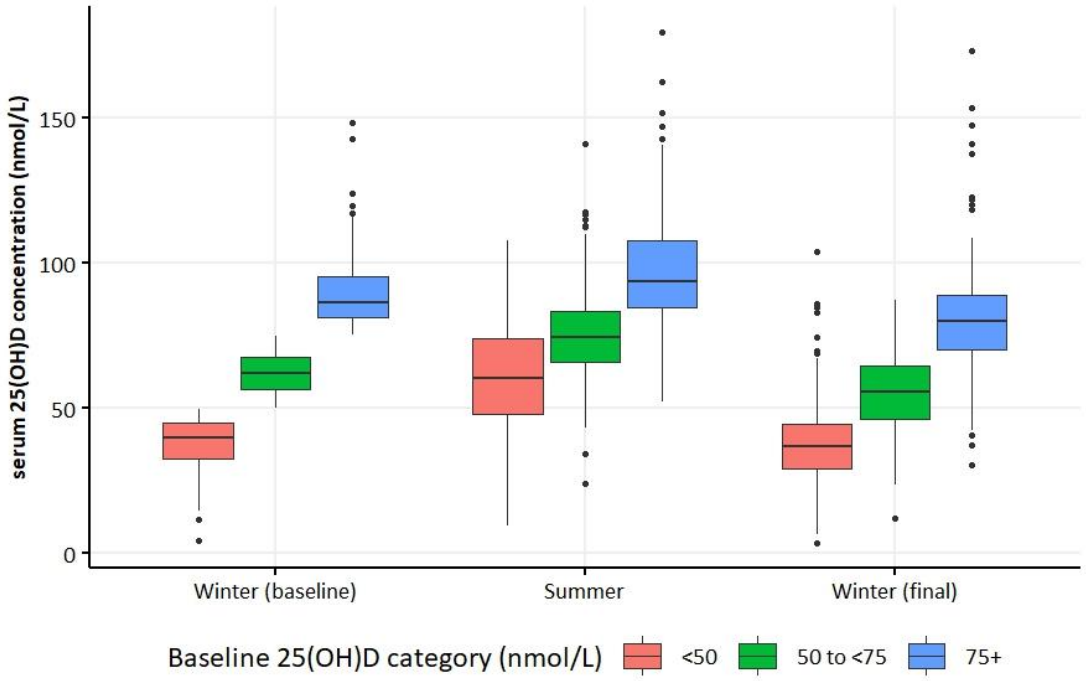
Appendix C: Planned supplementary figures

NOTE: The order of these tables will be determined by the order in which they are referenced in the manuscript.

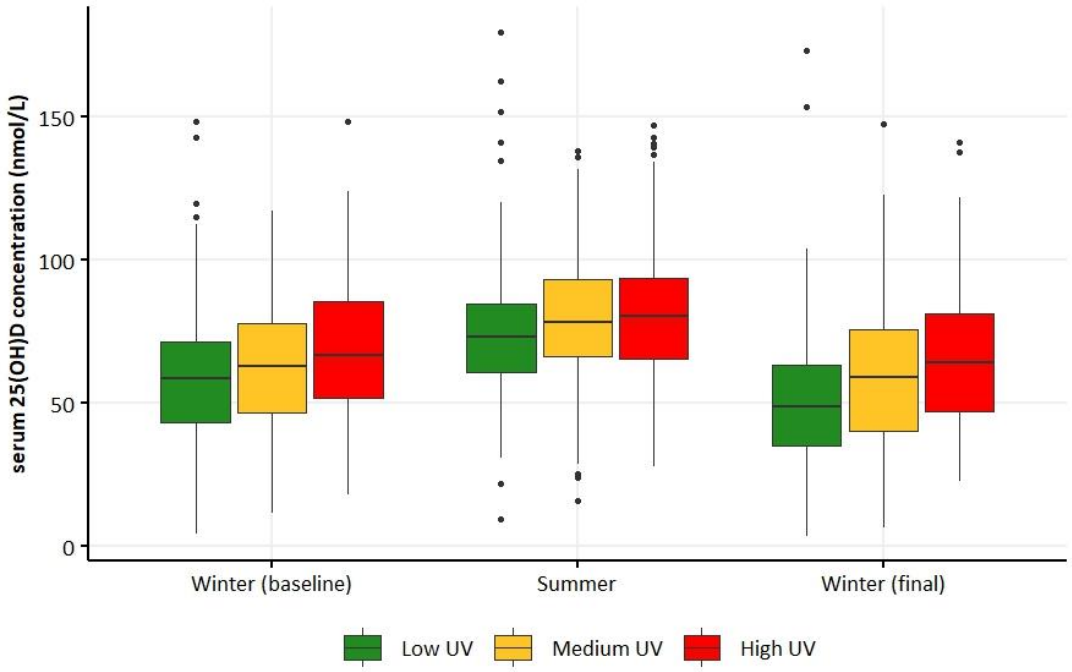
SFigure 1. Love plot of standardised mean differences (intervention minus control) for characteristics of participants included in the per protocol analysis, before and after applying inverse probability weights (NB Weights will be estimated after analyst has been given the final dataset (i.e. dataset that contains true randomisation allocation and 25(OH)D concentrations.)

SFigure 2. Love plot of standardised mean differences (intervention minus control) for characteristics of participants included in the analysis restricted to those who did not use any supplementary vitamin D during the trial

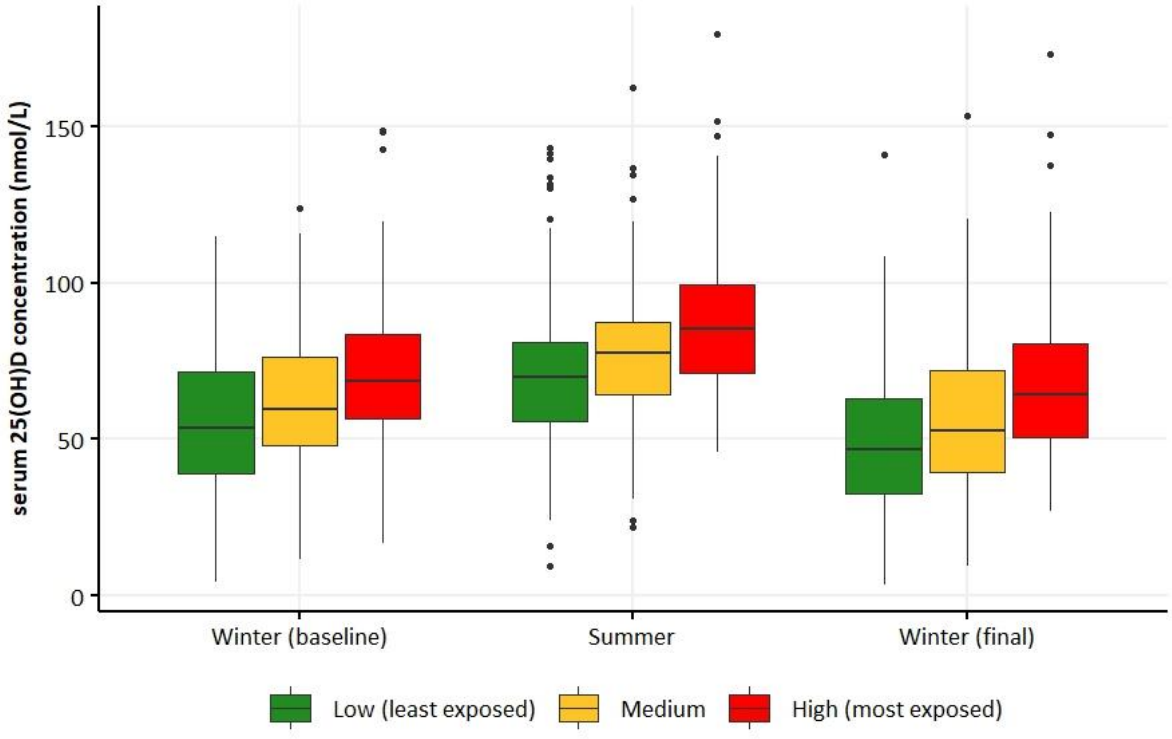
(NB Weights will be estimated after the analyst has been given the final dataset (i.e. dataset that contains true randomisation allocation and 25(OH)D concentrations))



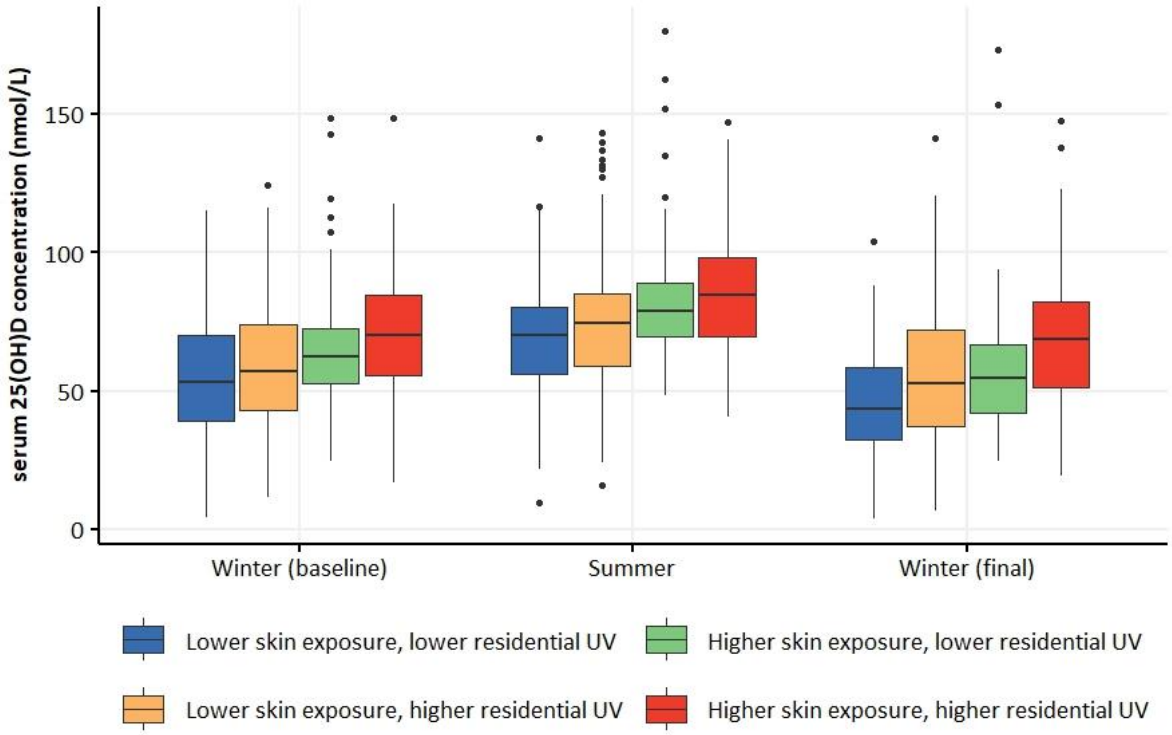
SFigure 3. Outlier box plot of the serum 25-hydroxyvitamin D concentration at each time point within the entire cohort, by baseline serum 25-hydroxyvitamin D concentration category



SFigure 4. Outlier box plot of the serum 25-hydroxyvitamin D concentration at each time point within the entire cohort, by residential UV radiation zone



SFigure 5. Outlier box plot of the serum 25-hydroxyvitamin D concentration at each time point within the entire cohort, by skin exposure category



SFigure 6. Outlier box plot of the serum 25-hydroxyvitamin D concentration at each time point within the entire cohort, by personal UV radiation exposure category

Appendix D: Planned supplementary tables

NOTE: The order of these tables will be determined by the order in which they are referenced in the manuscript.

STable 1. Number of samples returned at each collection by month and randomisation group for all randomised participants.

	Returned samples N (%)	
Sample	Intervention N=319	Control N=320
Baseline (collected in 2022)		
June	30 (9.4)	27 (8.4)
July	46 (14.4)	44 (13.8)
August	85 (26.6)	89 (27.8)
September	91 (28.5)	94 (29.4)
October	59 (18.5)	56 (17.5)
November	8 (2.5)	10 (3.1)
Total baseline samples returned	**319 (100)**	**320 (100)**
Summer (collected in 2023)		
January	16 (5.0)	14 (4.4)
February	266 (83.4)	272 (85.0)
March	28 (8.8)	27 (8.4)
April	1 (0.3)	0 (0)
Not returned	8 (2.5)	7 (2.2)
Total summer samples returned	**311 (97.5)**	**313 (97.8)**
Winter (collected in 2023)		
June	6 (1.9)	0 (0)
July	61 (19.1)	54 (16.9)
August	226 (70.8)	246 (76.9)
September	11 (3.4)	12 (3.8)
Not returned	15 (4.7)	8 (2.5)
Total winter samples returned	**304 (95.3)**	**312 (97.5)**
Returned baseline and at least one other sample*	**312 (97.8)**	**316 (98.8)**
Returned all three samples	**303 (95.0)**	**309 (96.6)**

* Included in analysis

STable 2. Vitamin D status by timepoint and study group[1] **(NB cells are empty because the analyst has not been provided with a dataset that contains both real randomisation group and 25(OH)D concentrations)**

Serum 25(OH)D concentration (nmol/L)	N (%)	
	Intervention	Control
Winter (baseline)		
<50		
50 to <75		
≥75		
Summer		
<50		
50 to <75		
≥75		
Winter (final)		
<50		
50 to <75		
≥75		

[1]Restricted to people included in the analysis. The number at each time varies due to the different number of samples returned.

STable 3. Effect of randomisation to sunscreen on serum 25(OH)D concentration (sensitivity analysis, with additional adjustment for covariates) **(NB randomisation group has been simulated for the purposes of the SAP)**

Statistics	N		Mean 25(OH)D concentration (SD) or change from baseline (95% CI) (nmol/L)		Intervention versus control
	Intervention	Control	Intervention	Control	
Winter (baseline)					
Mean (SD)	314	314	64.0 (22.2)	61.6 (22.4)	
Summer					
Mean (SD)	312	312	78.6 (23.3)	76.8 (21.8)	
AMD from baseline[1]			14.6 (12.7, 16.5)	14.1 (12.2, 16)	0.5 (-2, 2.9)
Winter (final)					
Mean (SD)	311	305	58.5 (25.0)	56.6 (21.7)	
AMD from baseline[1]			-5.9 (-7.8,-4)	-5.7 (-7.6,-3.8)	-0.2 (-2.6, 2.3)
Overall					
Mean (SD)	314	314	68.6 (26.1)	66.8 (24.0)	
AMD from baseline[1]			4.4 (2.7, 6)	4.2 (2.5, 5.9)	0.1 (-1.9, 2.2)

[1]Adjusted mean differences were estimated using mixed models for repeated measures. The model included baseline serum 25(OH)D concentration, post-baseline time point, sex, age group, state, tendency to burn, self-reported overall health, and interaction terms between time point and: (i) randomisation group; and (ii) baseline serum 25(OH)D concentration.
Abbreviations: Abbreviations: AMD, adjusted mean difference; CI, confidence interval; SD, standard deviation

STable 4. Characteristics of participants included in the per-protocol analysis, according to randomisation group; results shown before and after applying inverse probability weights (NB Weights will be estimated after analyst has been provided final dataset (i.e. dataset that contains true randomisation allocation and 25(OH)D concentrations))

Characteristic	N (%)					
	Unweighted			Weighted		
	Intervention N =	Control N =	SMD	Intervention N =	Control N =	SMD
Median baseline age in years (1st, 3rd quartile)						
Sex						
Male						
Female						
Education attainment						
Highschool or lower						
Certificate/diploma/advanced diploma						
Bachelor degree or higher						
Housing situation						
I own my own home						
I pay rent for my home						
Other						
BMI category						
Underweight/healthy						
Overweight						
Obese						
History of regular smoking						
No						
Yes						
Number of alcoholic drinks per week						
≤1						
2 to 4						
5 to 6						
≥7						
Self-reported overall health						
Excellent						
Very good						
Good						
Fair/poor						
Tendency to sunburn						
Does not burn at all						
Becomes a little bit pink						
Becomes dark pink to red but does not blister or peel						
Becomes dark pink to red and blisters or peels						
Skin tanning when outdoors for 30 minutes in summer						
Develops a dark tan						
Develops a medium tan						
Does not tan/develops a pale tan						

Characteristic	N (%)					
	Unweighted			Weighted		
	Intervention N =	Control N =	SMD	Intervention N =	Control N =	SMD
Number of sunburns in the past 12 months						
None						
1						
≥2						
Lifetime skin cancers excised						
No						
Yes						
Lifetime skin cancers burnt off						
No						
Yes						
Skin cancer/sunspot treatment using ointments						
None						
Yes						
Baseline 25(OH)D concentration category (nnmol/L)						
<50						
50 to <75						
≥75						
Residential UV radiation zone						
Low UV radiation						
Medium UV radiation						
High UV radiation						
Skin exposure category						
Low (least exposed)						
Medium						
High (most exposed)						
Personal UV radiation exposure category						
Lower skin exposure, lower residential UV						
Lower skin exposure, higher residential UV						
Higher skin exposure, lower residential UV						
Higher skin exposure, higher residential UV						

SMD = standardised mean difference (intervention minus control); BMI = body mass index; UV = Ultraviolet

STable 5. Effect of randomisation to sunscreen on serum 25(OH)D concentration among participants who adhered to their treatment allocation (i.e., per protocol analysis) (NB Analysis will be performed once the analyst has been provided final dataset (i.e. dataset that contains true randomisation allocation and 25(OH)D concentrations))

Statistics	N		Mean 25(OH)D concentration (SD) or change from baseline (95% CI) (nmol/L)		Intervention versus control
	Intervention	Control	Intervention	Control	
Winter (baseline)					
Mean (SD)					
Summer					
Mean (SD)					
AMD from baseline					
Winter (final)					
Mean (SD)					
AMD from baseline					
Overall					
Mean (SD)					
AMD from baseline					

STable 6. Characteristics of participants included in the analysis restricted to those who did not use any supplementary vitamin D during the trial, according to randomisation group; results shown before and after applying inverse probability weights (NB Weights will be estimated after analyst has been provided final dataset (i.e. dataset that contains true randomisation allocation and 25(OH)D concentrations))

Characteristic	N (%)					
	Unweighted			Weighted		
	Intervention N =	Control N =	SMD	Intervention N =	Control N =	SMD
Median baseline age in years (1st, 3rd quartile)						
Sex						
Male						
Female						
Educational attainment						
Highschool or lower						
Certificate/diploma/advanced diploma						
Bachelor degree or higher						
Housing situation						
Home owner						
Renter						
Other						
BMI category						
Underweight/healthy						
Overweight						
Obese						
History of regular smoking						
No						
Yes						
Number of alcoholic drinks per week						
≤1						
2 to 4						
5 to 6						
≥7						
Self-reported overall health						
Excellent						
Very good						
Good						
Fair/poor						
Tendency to sunburn						
Does not burn at all						
Becomes a little bit pink						
Becomes dark pink to red but does not blister or peel						
Becomes dark pink to red and blisters or peels						
Skin tanning						
Develops a dark tan						
Develops a medium tan						
Does not tan/develops a pale tan						

Characteristic	N (%)					
	Unweighted			Weighted		
	Intervention N =	Control N =	SMD	Intervention N =	Control N =	SMD
Number of sunburns in 12 months before baseline						
None						
1						
≥2						
Lifetime skin cancers excised						
No						
Yes						
Lifetime skin cancers burnt off						
No						
Yes						
Skin cancer/sunspot treatment using ointments						
No						
Yes						
Residential UV radiation zone						
Low UV radiation						
Medium UV radiation						
High UV radiation						
Skin exposure category						
Low (least exposed)						
Medium						
High (most exposed)						
Personal UV radiation exposure category						
Lower skin exposure, lower residential UV						
Lower skin exposure, higher residential UV						
Higher skin exposure, lower residential UV						
Higher skin exposure, higher residential UV						

SMD = Standard mean difference (intervention minus control); BMI = body mass index; UV = Ultraviolet

STable 7. Effect of randomisation to sunscreen on serum 25(OH)D concentration among participants who did not use any supplementary vitamin D during the trial **(NB Analysis will be performed once the analyst has been provided final dataset (i.e. dataset that contains true randomisation allocation and 25(OH)D concentrations))**

Statistics	N		Mean 25(OH)D concentration (SD) or change from baseline (95% CI) (nmol/L)		Intervention versus control
	Intervention	Control	Intervention	Control	
Winter (baseline)					
Mean (SD)					
Summer					
Mean (SD)					
AMD from baseline					
Winter (final)					
Mean (SD)					
AMD from baseline					
Overall					
Mean (SD)					
AMD from baseline					

STable 8. Adherence to sunscreen application in the intervention group

[1] Adherence N (%)[1]		N (%)	Classification
Face, head & neck	Hands & forearms		
≥70	≥70	188 (60.3)	Adherent
≥70	<70	46 (14.7)	Non-adherent
<70	≥70	6 (1.9)	Non-adherent
<70	<70	72 (23.1)	Non-adherent

[1]Adherence is presented as a percentage; the relationship between adherence percentage and days of sunscreen application/week is: ≥70%, approx. 5 or more days/week. A participant in the intervention group was defined as being adherent if their compliance score was 0.7 or higher for both face/head/neck and hands/forearms.

STable 9. Contamination with off-study sunscreen use in the control group

Contamination N (%)[1]		N (%)	Classification
Face, head & neck	Hands & forearms		
<30	<30	252 (79.7)	No contamination
<30	≥30	4 (1.3)	Contamination
≥30	<30	23 (7.3)	Contamination
≥30	≥30	37 (11.7)	Contamination

[1]Contamination is presented as a percentage; the relationship between contamination percentage and days of sunscreen application/week is: <30%, approx. 2 or fewer days/week. Contamination in control group was significant if their contamination score was 30% or higher for either face/head/neck or hands/forearms.

STable 10. Distribution of skin exposure score, by residential UV radiation zone

Skin exposure	N (%)		
	Low UV zone N = 263	Medium UV zone N = 181	High UV zone N = 184
Median skin exposure score (1st, 3rd quartile)	8 (4, 12)	10 (5, 16)	9 (5, 14)
Skin exposure category			
Low (least exposed)	105 (40)	52 (29)	53 (29)
Medium	89 (34)	58 (32)	62 (34)
High (most exposed)	69 (26)	71 (39)	69 (38)

Appendix E: Supplementary methods

1. Residential UV radiation zone

ARPANSA provided ground-based UV index data for Kingston (Hobart), Melbourne, Canberra, Sydney, Newcastle, Gold Coast, Brisbane, Emerald, and Townsville. These datasets included actual and expected daily maximum UV index, and 10-minute average actual UV index for each day and location during the period 01/07/2022 to 30/09/2023.

We converted 10-minute average actual UV index data to a dose of erythemally weighted UV radiation for each 10-minute period (in J/m^2). These were summed and divided by 100 to calculate the number of SEDs per day. The mean daily SED for each site was calculated for the period 01/09/2022 to 31/08/2023.

We created three UV radiation zones based on the similarity of the mean daily SED between the monitoring sites.

- Low UV radiation zone: Kingston (Hobart) and Melbourne;
- Medium UV radiation zone: Canberra, Sydney, and Newcastle;
- High UV radiation zone: Gold Coast, Brisbane, Emerald, and Townsville.

We then assigned participants to the site that was closest to their place of residence at baseline. Table A shows the distribution of total daily SED at each ARPANSA site for the period of interest, and the number of participants assigned to each site.

Supplementary methods Table A. Distribution of total daily SED over September 2022 to August 2023 by ARPANSA monitoring site

ARPANSA Site	Total daily SED				Number of participants	
	Mean	Median	Min	Max		
Kingston (Hobart)	18.78	13.23	1.23	62.74	107	Lower UV
Melbourne	21.29	16.27	2.15	59.45	156	
Canberra	25.45	20.84	1.92	66.36	24	
Sydney	26.89	21.93	3.09	66.89	136	
Newcastle	29.89	23.49	3.04	71.27	21	
Gold Coast	32.19	28.55	5.04	72.12	19	Higher UV
Brisbane	30.57	26.46	5.16	64.25	143	
Emerald	37.90	36.45	5.50	70.00	5	
Townsville	42.43	42.24	8.58	75.31	17	

2. Estimating skin exposure

The skin exposure score integrates the duration of outdoors activity between 8:00 AM and 4:00 PM and the exposed body surface area (BSA) during these activities. For each month, we assigned scores for time spent outdoors and exposed BSA based on self-reported behaviour across all days in a typical week. The overall skin exposure score is the mean of the monthly scores between November 2022 and May 2023, as all participants were actively enrolled in the study throughout this period. Below we provide further details on how we calculated the scores for time outdoors and BSA, and how these were combined to create the skin exposure score.

Time outdoors score

On each monthly survey, participants were asked to select the category (shown in Table B) that represented the amount of time they typically spent outdoors between 8 am and 4 pm on Mondays, Tuesdays, Wednesdays, etc. We assigned a score to the duration reported for each day (Table B).

Supplementary methods Table B. Daily time outdoors score

Time outdoors between 8 am and 4 pm	Score
<15 minutes	0
15 to <30 minutes	1
30 to <60 minutes	2
1 to <2 hours	3
2 to <4 hours	4
≥4 hours	5

Exposed BSA score

The exposed BSA score is determined by the percentage of body area exposed, determined by self-reported clothing worn. We used the Rule of Nines for adults,[1] which divides the BSA into eleven anatomical regions, each representing approximately 9% of the total BSA. These regions include the head, each arm, the chest, abdomen, each thigh, each leg (below the knee), the upper and lower back. We assume:

- Hands are 1% and always exposed.
- Face is 5% and always exposed.
- Feet are 1% and never exposed.

We assigned the exposed BSA for each clothing scenario separately for upper body and lower body as below, not including hands and face.

- Upper body clothing:
    - Top with sleeves below elbow (i.e., long sleeves) – 0%.
    - Top with sleeves elbow length or higher (i.e., exposing forearms and a part of upper arm) – 6% on each arm.
    - Top with no sleeves – 8% on each arm (removed 1% for hands).
    - No upper body clothing – 52% (36% plus 16% for arms).
- Lower body clothing:
    - Clothes to the ankle – 0%.
    - Clothes between the knee and the ankle – 4% each leg (we assume whole leg is 17% - foot 1%, 8% below knee, 9% above knee).
    - Clothes between the hip and the knee – 12% each leg (all of lower leg plus half of upper leg).
    - No leg covering – 17%.

Percentage of exposed BSA for the combination of upper and lower clothing scenario (including 6% exposed BSA from face and hands) is presented in Table C. Finally, we standardised the exposed BSA score by dividing the percentage of exposed BSA by 6 (the lowest value) (Table D).

Supplementary methods Table C. Percent of body area exposed for each combination of upper and lower body clothing

Upper body clothing	Lower body clothing			
	Clothes to the ankle (0%)	Clothes between knee and ankle (8%)	Clothes between hip and knee (24%)	No leg covering (34%)
Top with sleeves below elbow (0%)	6	14	30	40
Top with sleeves elbow length or higher (12%)	18	26	42	52
Top with no sleeves (16%)	24	30	46	56
No upper body clothing (52%)	58	66	82	92

Supplementary methods Table D. Exposed BSA score

Upper body clothing	Lower body clothing			
	Clothes to the ankle	Clothes between knee and ankle	Clothes between hip and knee	No leg covering
Top with sleeves below elbow	1.00	2.33	5.00	6.67
Top with sleeves elbow length or higher	3.00	4.33	7.00	8.67
Top with no sleeves	3.67	5.00	7.67	9.33
No upper body clothing	9.67	11.00	13.67	15.33

Skin exposure score

The skin exposure score on a typical day was calculated by multiplying the time outdoors score by the exposed BSA score on that day. Higher scores indicate greater skin exposure to UV radiation in sunlight. Monthly skin exposure score is the mean of daily scores across all days in a typical week in that month. Finally, the skin exposure score is the mean of monthly scores between November 2022 and May 2023. We then divided individuals into cohort-wide tertiles of skin exposure score.

Monthly data with missing data on either time outdoors score or exposed BSA score was classified as incomplete. Six participants had incomplete data for four or more months within the seven-month period, (i.e., had only two or three months with available skin exposure score (Table E)). After confirming the consistency of their behaviour throughout the study, we included their data in the analysis.

Supplementary methods Table E. Distribution of participants by number of surveys with an available skin exposure score between November 2022 and May 2023 (7 surveys)

Number of surveys with completed skin exposure score	N (%)	
	Intervention	**Control**
≤3	6 (1.9)	0 (0)
4 to 5	19 (6.1)	12 (3.8)
6	79 (25.3)	48 (15.2)
7	208 (66.7)	256 (81)

3. Personal UV radiation exposure category

We reclassified the nine sites with ARPANSA data into two residential UV zones: lower UV radiation (Hobart and Melbourne); and higher UV radiation (Canberra, Sydney, Newcastle, Gold Coast, Brisbane, Emerald, and Townsville). We dichotomised the skin exposure score (based on the cohort-wide

median) into lower skin exposure and higher skin exposure. These two variables were combined to create a four-category variable representing all possible combinations of dichotomised skin exposure and residential UV zone.

4. Estimating adherence and contamination

Monthly adherence in the intervention group

Participants were assigned to one of the nine ARPANSA monitoring sites as described above. We used the expected daily maximum UV index data supplied by ARPANSA to determine how many days of each month the UV index was ≥3 at each of the nine sites (i.e., how many days the participant was expected to wear sunscreen). Self-reported study sunscreen use and additional sunscreen use (from the participant's own supply) was reported separately in each monthly survey as the average number of days per week that they wore sunscreen. Response options included: 0 days, 1 or 2 days, 3 or 4 days, 5 or 6 days, or every day. If a participant selected a response that was expressed as a range (e.g., 1 or 2 days), then we assumed the upper bound of the range was the correct value. Participants were asked to report sunscreen use separately according to five body areas (face/head/neck; hands/forearms; upper arms; legs; and other parts of the body).

When estimating adherence, we did not distinguish between study sunscreen and additional sunscreen provided that additional sunscreen was SPF 50+, and we considered only face/head/neck and hands/forearms. These body areas were selected because they are the most likely to be exposed to UV radiation (i.e., not covered by clothing). Monthly adherence scores were estimated for each of these body areas using Equation A.

Supplementary methods Equation A.

$$\text{Monthly adherence score}_{\text{body area}} = \frac{\text{Estimated no. days SPF 50+ sunscreen applied to body area that month}}{\text{No. days sunscreen required that month}},$$

where the numerator is calculated using

$$min\left(\text{No. days sunscreen required that month}, \frac{\text{No. days in month} \times (\text{reported no. days SPF 50+ sunscreen applied per week})}{7}\right)$$

Monthly contamination in the control group

Monthly contamination from off-study sunscreen with an SPF of 50+ among control group participants was estimated using the same method as above (excluding study sunscreen application which was not relevant).

Defining adherence and contamination

We used all months during the period November 2022 to May 2023 for which data were available to calculate the final adherence/contamination score (calculated as an average, and expressed as a percentage), excluding any months when the UV index did not reach 3 on at least half of the days in that month. This was the case in one month (May 2023) for participants in Hobart, Melbourne and Canberra UV zones. We chose to use data from November 2022 to May 2023 based on the importance of these months in vitamin D production, and because all participants were actively enrolled in the trial at this time.

Table F below shows the percentage of data available to calculate the final adherence/contamination score.

Supplementary methods Table F. Number of surveys available

Percentage of months with data available	N (%)	
	Control	Intervention
<50	-	2 (0.6)
50 – 80	2 (0.6)	7 (2.2)
80- <100	20 (6.3)	17 (5.4)
100	294 (93.0)	286 (91.7)

An individual in the intervention group was defined as being adherent if their compliance score was ≥70% (equivalent to applying sunscreen on 5 or more days per week on average) for both face/head/neck *and* hands/forearms. Contamination from sunscreen application in the control group was considered significant if their contamination score was ≥30% (equivalent to applying sunscreen on 3 or more days per week) for *either* face/head/neck *or* hands/forearms. Hence, an individual in the control group was defined to be non-contaminated if their compliance score was <30% for both face/head/neck *and* hands/forearms.

References

1. Wallace AB. The exposure treatment of burns. *Lancet*. 1951;257(6653):501-504. doi:10.1016/S0140-6736(51)91975-7