

Per-Protocol Sensitivity Analyses of the Primary Outcome in the BetterBrains Trial to Prevent Cognitive Decline

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Background

Multidomain lifestyle interventions targeting modifiable dementia risk factors (MDRFs) reduce cognitive decline in older adults, but interpretation and generalisation of clinical trial results are limited by low adherence (e.g., ≤50% of sessions in FINGER; 75% in MAPT).

The **BetterBrains Trial** is a person-centred, multidomain intervention delivered via telehealth to support behaviour change through individualised goal setting, motivational interviewing, coaching, and community linkage, tailored to participant’s individual dementia risk profile.

Intention-to-treat analysis indicated the intervention preserved cognitive function over 24 months. Given the potential for adherence to influence outcomes, a per-protocol analysis provides important complementary information about outcomes in intervention participants who adhered to the trial protocol.

This study reports the results of the per-protocol sensitivity analyses of the BetterBrains trial.

Methods

Participants completed assessments of cognition, lifestyle, health and medical characteristics, and self-reported surveys via the BetterBrains online platform (www.betterbrains.org.au) at baseline, 12 & 24 months.

Risk Assessment: At study entry, assessment of 19 self-reported MDRFs across 4 domains (‘**hearts**’, ‘**mind**’, ‘**mood**’, ‘**sleep**’) was conducted and participants with at least 1 MDRF were enrolled.

Methods

Randomisation & Masking: Computer-generated random allocation via permuted blocks of variable sizes (undisclosed) to the BetterBrains program or psychoeducation only (control) in a 1:1 ratio, after baseline assessment completion and identity verification. Randomisation stratified by age (<55 vs. ≥55 years), and rurality (metropolitan vs. regional, rural, remote). All outcomes assessor and investigator blinded.

Intervention: Intervention group received online (telehealth with allied health coach) person-centred goal setting, motivational interviewing, follow-up support, healthcare provider communication and linkage to local healthcare supports for management of identified MDRFs over 12 months.

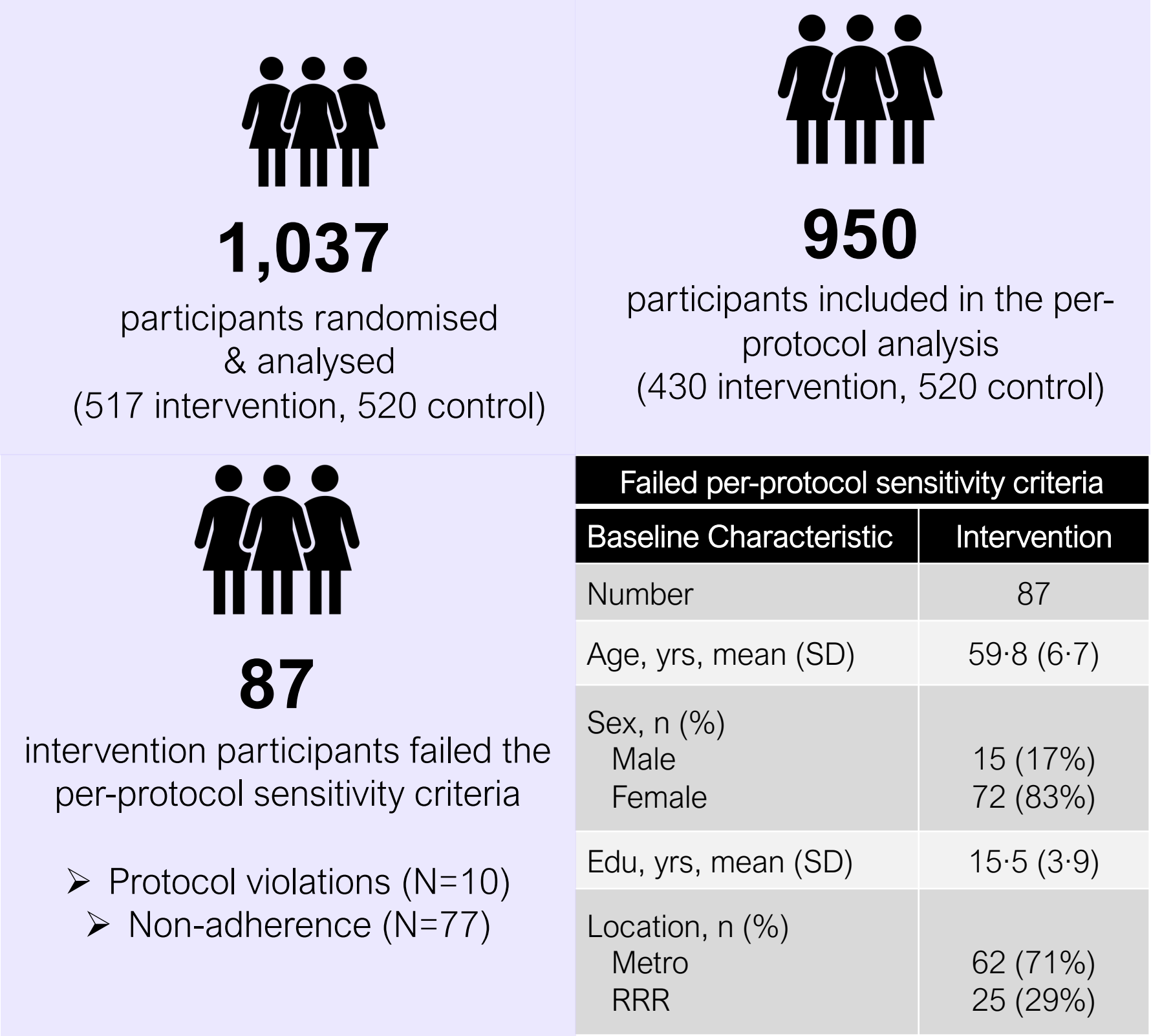
Primary Estimand: Binary indicator of the presence or absence of cognitive decline at 24 months. Cognitive decline: a ≥ 0.5 standard deviation (SD) worsening in performance from baseline to 24 months on any of the following: (1) Cogstate Detection test (speed), (2) Cogstate One Card Learning test (accuracy), (3) Cogstate One Back test (speed), or (4) Cognitive Function Instrument (CFI) total score. Absence of cognitive decline: < 0.5 SD decline on all four measures.

Primary Estimand Analysis: The effect of the intervention on the Primary Estimand was estimated using binary logistic regression, with absence of cognitive decline as the dependent variable, randomisation group as the independent variable, and age and rurality as covariates, reported as an odds ratio (OR) with 95% confidence interval (CI) and two-sided *p* value.

Per-Protocol Sensitivity Criteria & Analysis: A pre-specified per-protocol sensitivity analysis was conducted, using the same individual- and population-level outcome measures as the Primary Estimand but in a restricted population. **The per-protocol population comprised participants who completed at-least six designated coaching calls with no protocol violations.**

Results & Conclusions

Randomised & Per-Protocol Samples.



Primary and Per-Protocol Sensitivity Results.

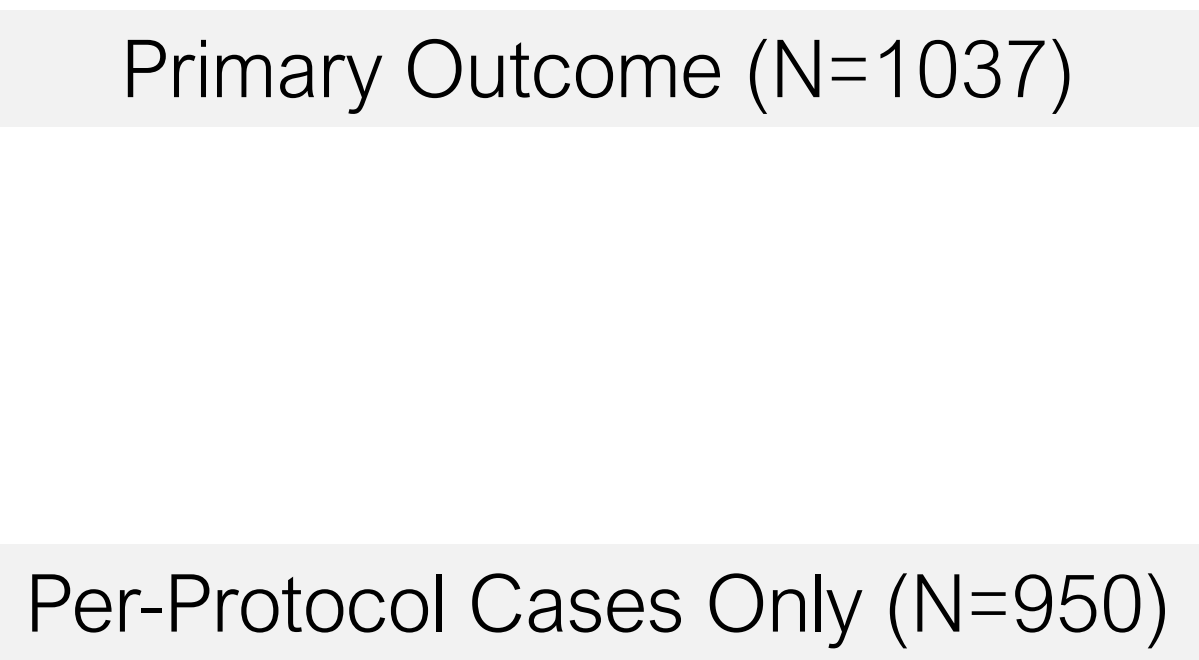
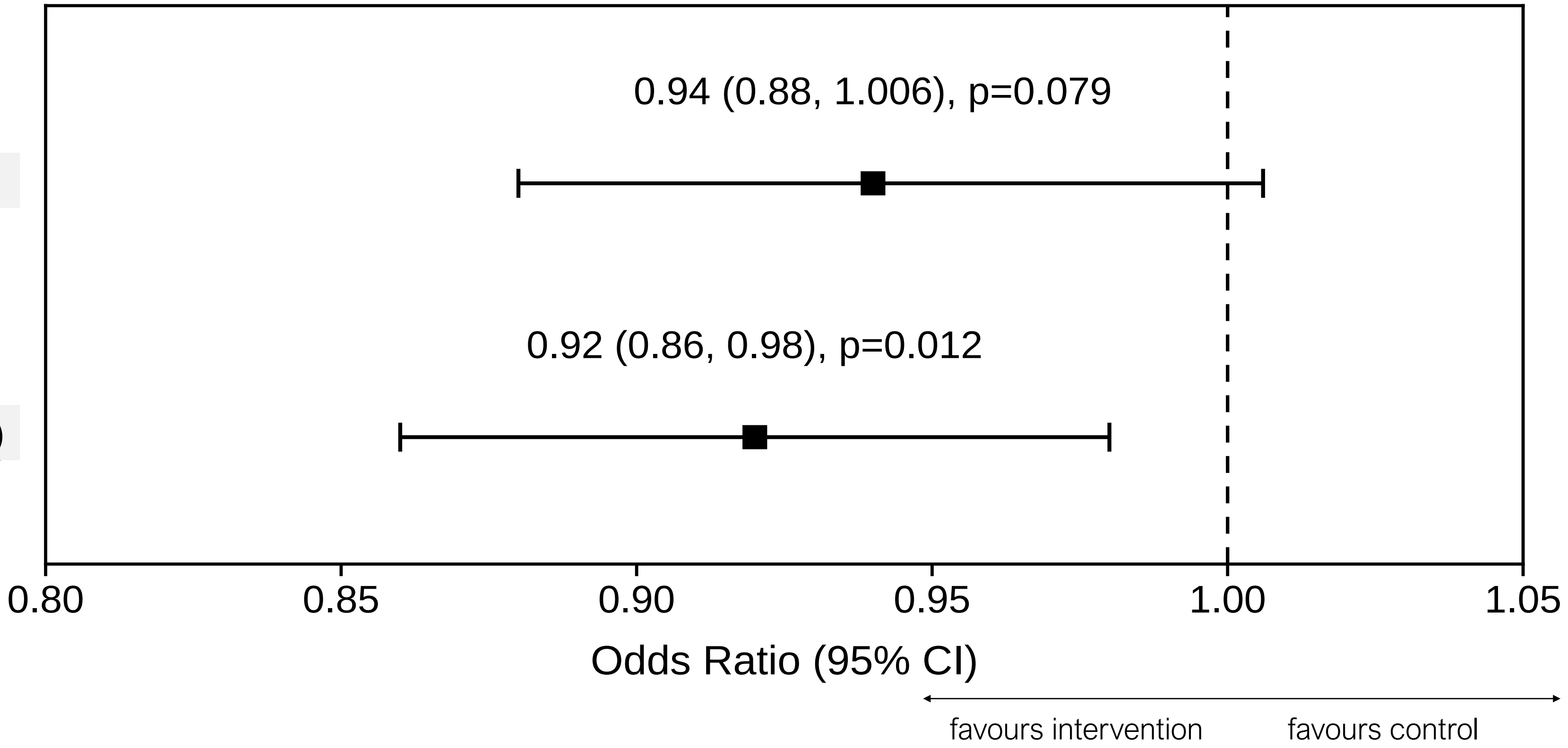


Figure 1. Forest plot of BetterBrains RCT primary outcome & per-protocol sensitivity outcome.



Conclusion: A decentralised, person-centered, multidomain lifestyle intervention program targeting personalised dementia risk factors was effective in preserving cognitive function over 24 months compared with psychoeducation (control), across both primary and per-protocol analyses.