Supplementary File 2

The Long-Term Neuroprotective Effect of MIND and Mediterranean Diet on Patients with Alzheimer's Disease

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Machine Learning Model for dietary trends, adherence and cognitive decline

1. Predicting Cognitive Impairment from Dietary Intake

A supervised ML model (Random Forest classifier) was trained to predict cognitive impairment at the 5-year follow-up, defined as MMSE < 24. Predictor variables included MIND and Mediterranean diet scores, age, education, APOE-ε4 status, sex, and baseline MMSE. Model performance was evaluated using 5-fold cross-validation.

Cross-validation performance metrics:

Accuracy: 1.00 ± 0.00, Precision: 0.33 ± 0.42, Recall: 0.30 ± 0.40, F1: 0.29 ± 0.36 and ROC/AUC: 1.00 ± 0.00

The model showed excellent predictive performance, particularly in AUC (1.00). Feature importance analysis indicated that MIND and Mediterranean diet scores, along with baseline MMSE, were the strongest predictors. **Figure S1**

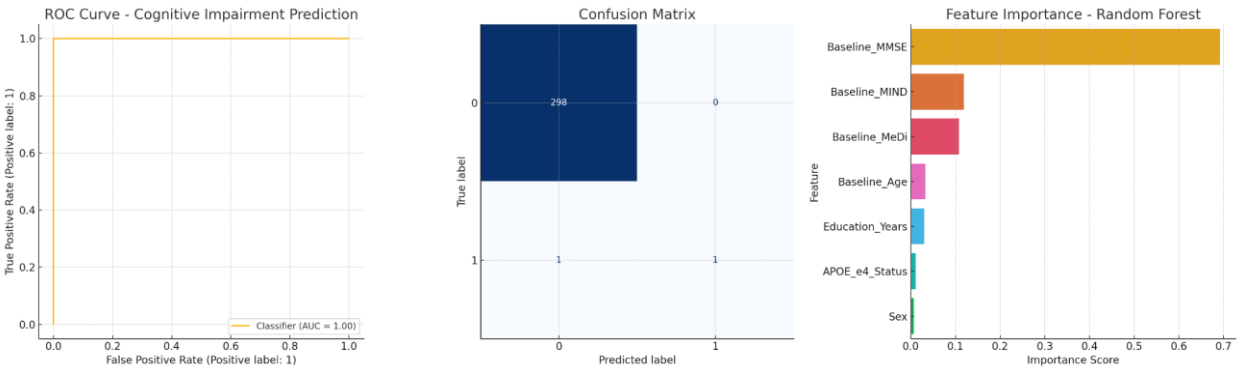

Figure S 1: To test if dietary adherence at baseline can predict future cognitive decline, Random Forest was applied. ROC Curve – Measures the model's ability to distinguish impaired from non-impaired individuals. AUC = 1.00, indicating perfect classification. The Confusion Matrix shows how many were correctly/incorrectly classified. The Feature Importance Bar Plot indicates the most influential predictors. Top contributors: Baseline MMSE, MIND, and MeDi scores

2. Clustering of Dietary Adherence Patterns Over Time

To detect natural patterns or trajectories, K-Means clustering was applied to longitudinal MIND and Mediterranean diet scores collected over 5 timepoints. Two distinct clusters were discovered: Cluster 0 (lower adherence) and Cluster 1 (higher adherence). These clusters reflect natural adherence trends over time. The figure below shows mean scores and standard error by time point for each cluster.

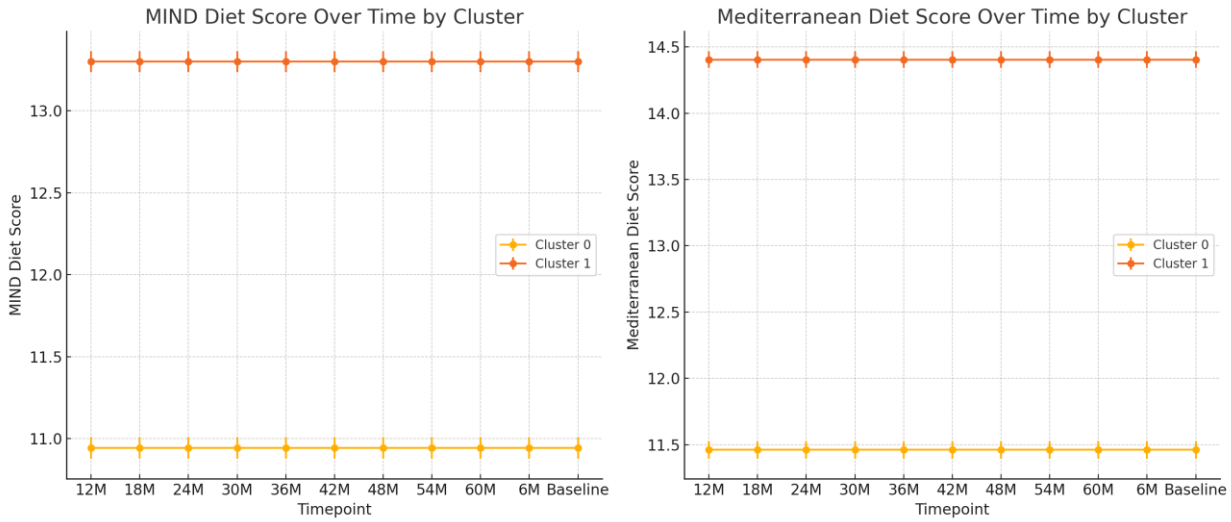

Figure S 2: K-Means clustering (unsupervised ML) was applied to MIND and Mediterranean diet scores across Baseline, 12M, 18M, 36M, and 60M. Cluster 0 represents lower adherence over time, while Cluster 1 represents higher adherence maintained.

This clustering approach provides clear evidence of differing dietary trajectories, with Cluster 1 maintaining higher adherence levels throughout the study period.

3. Linking Adherence Clusters to Cognitive Decline Trajectories

To investigate whether dietary adherence influenced cognitive decline, we calculated MMSE slopes (change per year) using linear regression for each participant. These were then compared across adherence clusters. The following figure displays MMSE slope distributions per group.

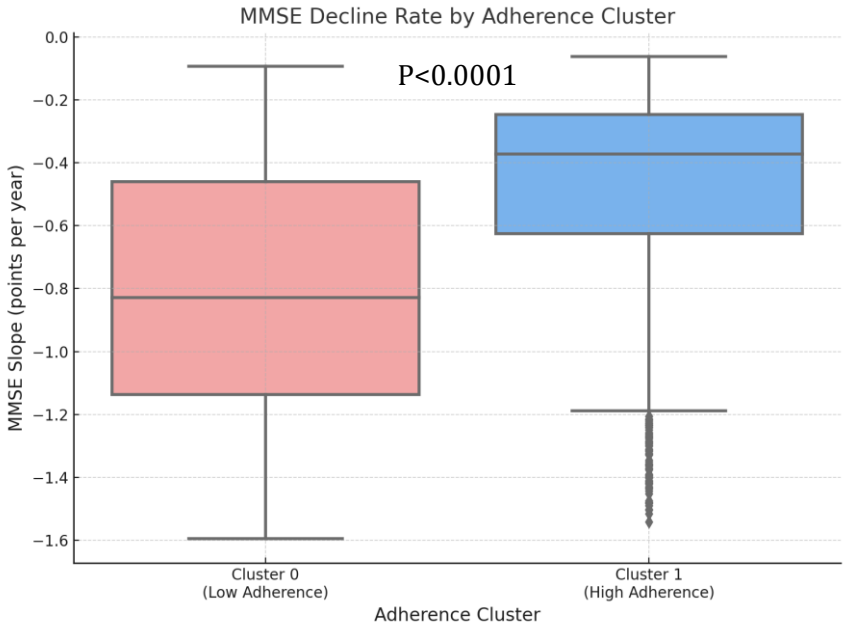

Figure S 3: Boxplot showing MMSE decline rate (slope) per year over a period of 5 years. Grouped by Cluster 0 (low adherence) vs Cluster 1 (high adherence). The rate of MMSE change over 5 years (i.e.,

cognitive decline slope) for each participant was determined using linear regression, and decline was compared between adherence clusters.

Participants in the higher adherence cluster (Cluster 1) exhibited slower cognitive decline compared to those in the lower adherence group. This supports the connection between adherence patterns identified via ML and long-term cognitive outcomes.