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## Classification of evolutionary trajectories of cognitive functions

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### Introduction

While demographic aging is inevitable, preventive approaches may prove effective against the cognitive functions decline and Alzheimer's disease. Prevention trials implemented to slow down the decline in cognitive functions with age have yielded unconvincing results. The aim of our work was to cluster cognitive evolution profiles in the context of Alzheimer's disease prevention trials.

### Material and Methods

The Multidomain Alzheimer Preventive Trial has been presented in [1]. The primary endpoint of this trial was a composite Z-score combining 4 cognitive tests. Data were collected longitudinally.

We used k-means for longitudinal data (kml), a method of partitioning without distribution hypothesis. An extension allows clustering trajectories according to the shape of them [2]. The aim is to divide the population into k homogeneous subgroups in terms of trajectories shape regardless of time, so this should lead to unstationary and similar profiles.

We also used the hierarchical cluster analysis (HCA) [3] which is unsupervised and not required specifying the number of groups. We calculated rates of change between each visit for the composite Z-score to apply the HCA. The aim is to create homogeneous subgroups with the most similar individuals (intra-class homogeneity) and well-defined groups (inter-class heterogeneity).

The seriation was the last method which consisted in transforming and optimally reordering a data matrix in order to bring to light, via shades of colors [4], a structure of the data. Only lines were swapped to keep the measurements' chronology and we restricted us to three colors to caricaturize information. The objective is to have even more homogeneous groups than with the previous methods.

### Results

All the methods described were tested on the MAPT data set, on complete follow-up (1143 subjects). We identified stationary profiles: with HCA in the first group (containing 93% of subjects, see Fig.1), with seriation in 12-36 months (Fig.2). We also observed evaluative profiles (seriation in 0-12 months - Fig.2) and all other groups with HCA (Fig.1).

Groups' characteristics for each method were not statistically different, except for two baseline cognitive tests with seriation: Trail Making Test ( $p < 0.01$ ) and Mini Mental Status Examination ( $p = 0.03$ ) in the sense that constant group had the best average score (28.33 points).

### Discussion/Conclusion

Exploratory methods, not widely mobilized in the biomedical field, were applied to cluster cognitive evolution profiles. The results led to observations that were difficult to interpret clinically. We conclude that, in prevention trial, population remains cognitively constant during the first three years. Secondly, information provided is complex and another approach must be considered for future.

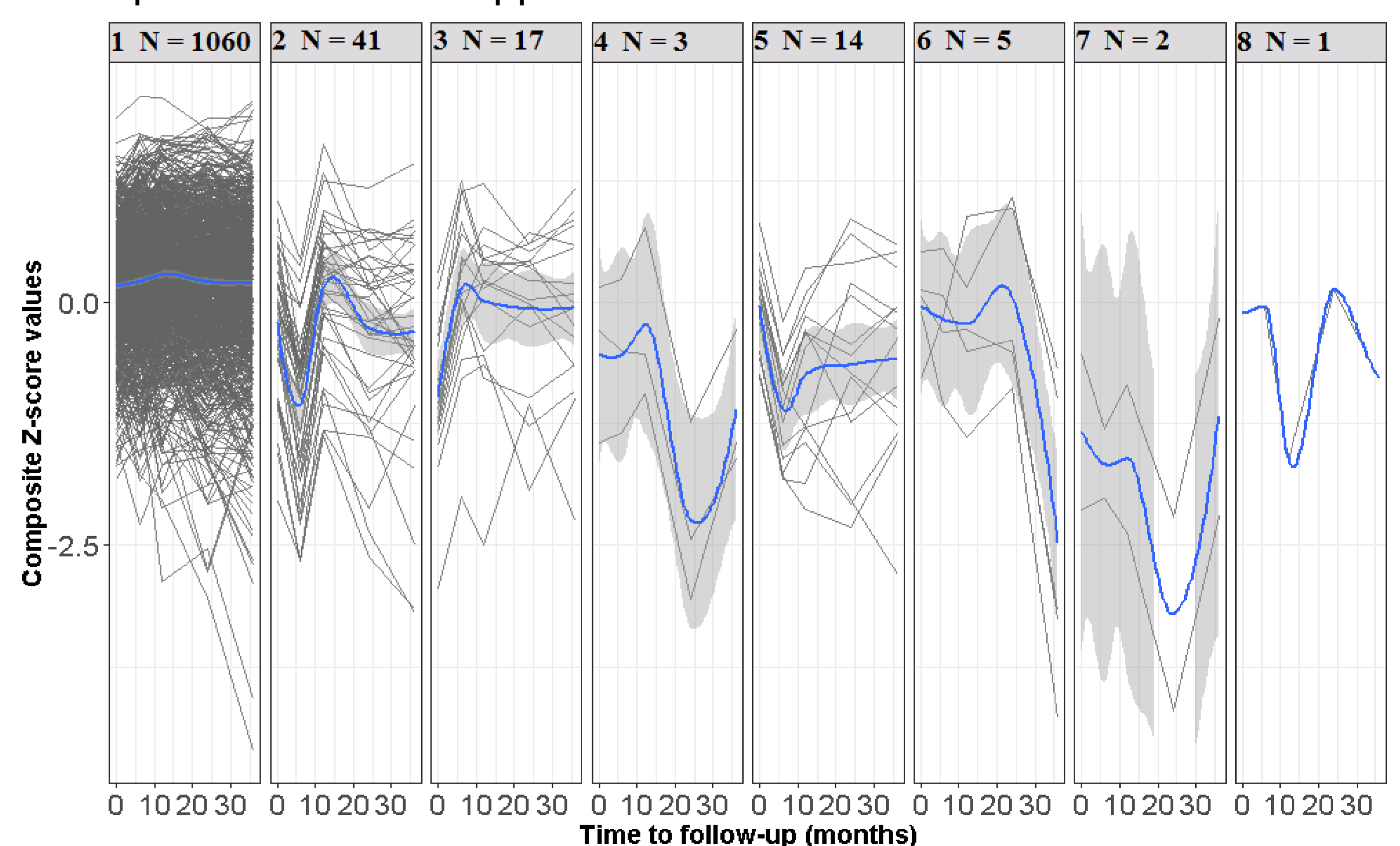


Figure 1- Representation of individual trajectories of the composite Z-score for the subgroups identified by the HCA method, MAPT data (N = 1143 subjects)

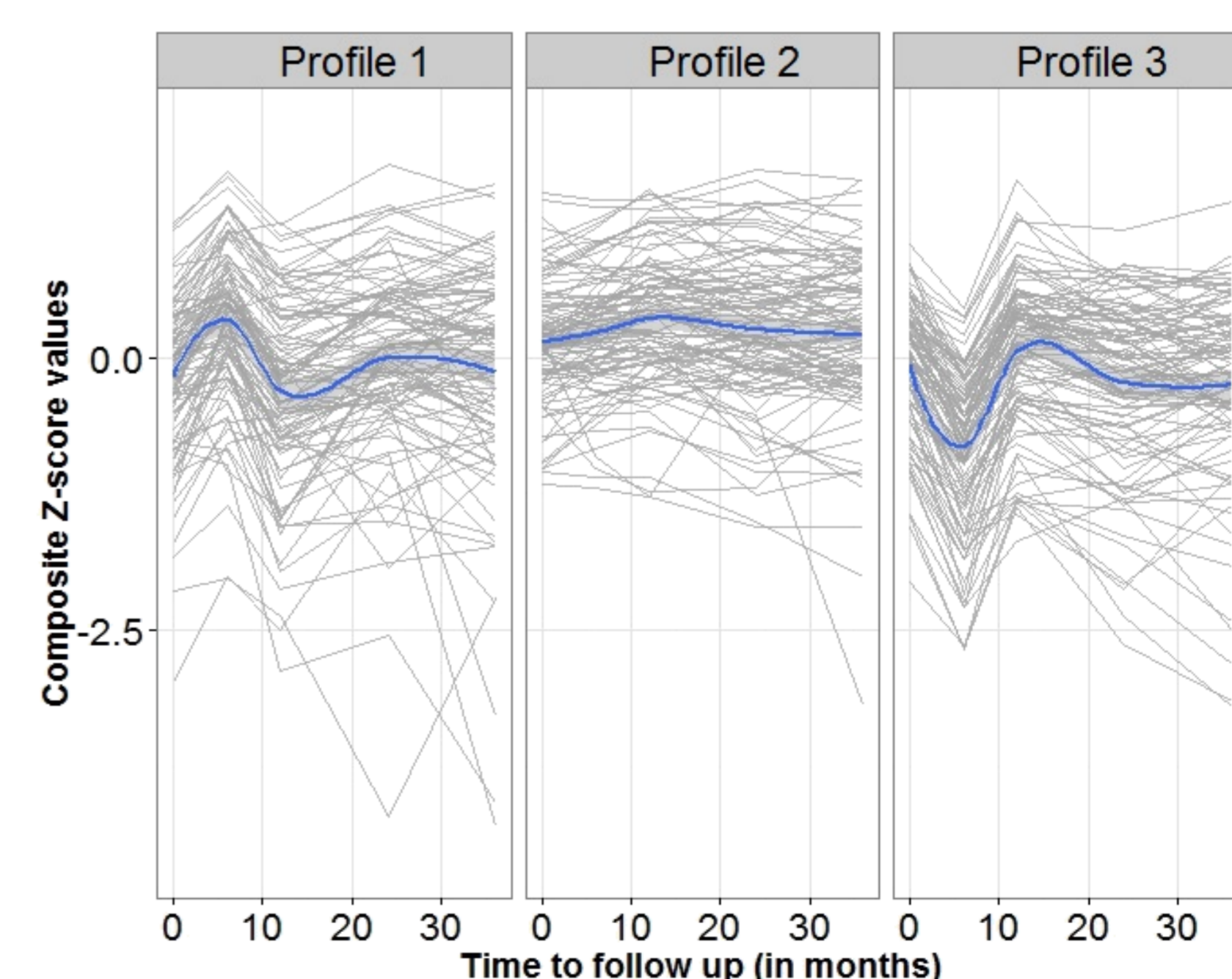


Figure 2- Representation of individual trajectories of the composite Z-score for the 3 seriation subgroups, MAPT data (N = 3x 100 subjects)

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