# A Novel Study Paradigm for Long-term Prevention Trials in Alzheimer Disease: The Placebo Group Simulation Approach (PGSA): Application to MCI data from the NACC database

**JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**

**ID** 3183050
**Author(s)** Berres, Manfred; Kukull, Walter A.; Miserez, André R.; Monsch, Andreas Urs; Monsell, Sarah E.; Spiegel, René
**Author(s) at UniBasel** Monsch, Andreas U. ;
**Year** 2014
**Title** A Novel Study Paradigm for Long-term Prevention Trials in Alzheimer Disease: The Placebo Group Simulation Approach (PGSA): Application to MCI data from the NACC database
**Journal** The journal of prevention of Alzheimer's disease
**Volume** 1
**Number** 2
**Pages** / **Article-Number** 99-109

The PGSA (Placebo Group Simulation Approach) aims at avoiding problems of sample representativeness and ethical issues typical of placebo-controlled secondary prevention trials with MCI patients. The PGSA uses mathematical modeling to forecast the distribution of quantified outcomes of MCI patient groups based on their own baseline data established at the outset of clinical trials. These forecasted distributions are then compared with the distribution of actual outcomes observed on candidate treatments, thus substituting for a concomitant placebo group. Here we investigate whether a PGSA algorithm that was developed from the MCI population of ADNI 1*, can reliably simulate the distribution of composite neuropsychological outcomes from a larger, independently selected MCI subject sample.; Data available from the National Alzheimer's Coordinating Center (NACC) were used. We included 1523 patients with single or multiple domain amnestic mild cognitive impairment (aMCI) and at least two follow-ups after baseline. In order to strengthen the analysis and to verify whether there was a drift over time in the neuropsychological outcomes, the NACC subject sample was split into 3 subsamples of similar size. The previously described PGSA algorithm for the trajectory of a composite neuropsychological test battery (NTB) score was adapted to the test battery used in NACC. Nine demographic, clinical, biological and neuropsychological candidate predictors were included in a mixed model; this model and its error terms were used to simulate trajectories of the adapted NTB.; The distributions of empirically observed and simulated data after 1, 2 and 3 years were very similar, with some over-estimation of decline in all 3 subgroups. The by far most important predictor of the NTB trajectories is the baseline NTB score. Other significant predictors are the MMSE baseline score and the interactions of time with ApoE4 and FAQ (functional abilities). These are essentially the same predictors as determined for the original NTB score.; An algorithm comprising a small number of baseline variables, notably cognitive performance at baseline, forecasts the group trajectory of cognitive decline in subsequent years with high accuracy. The current analysis of 3 independent subgroups of aMCI patients from the NACC database supports the validity of the PGSA longitudinal algorithm for a NTB. Use of the PGSA in long-term secondary AD prevention trials deserves consideration.

**Publisher** Serdi
**ISSN/ISBN** 2426-0266
**URL** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4268776/

**Full Text on edoc** No;
**PubMed ID** http://www.ncbi.nlm.nih.gov/pubmed/25530953
**ISI-Number** MEDLINE:25530953
**Document type (ISI)** Journal Article