

Statistical Models for Alzheimer's disease and Aging

<https://neurodegenerationresearch.eu/survey/statistical-models-for-alzheimer%c2%92s-disease-and-aging/>

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France

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Statistical Models for Alzheimer's disease and Aging

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4

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Research Abstract

Currently, about 30 millions of people suffer from Alzheimer's disease (AD) worldwide, and this number is expected to dramatically increase in the coming years with the aging of the population. In this context, a better understanding of the disease and the factors influencing its life-time risk or modifying the course of the disease would be an essential asset when considering interventions to reduce its frequency or its consequences. AD is a complex disease involving multiple processes (cognitive, functional, anatomic...) and different phases of evolution. The study of the natural history and the risk factors or the progression of AD is based on longitudinal analyses of data from observational cohorts of elderly subjects facing several methodological challenges including a high risk of death and complex censoring and truncation

mechanisms (e.g. interval censoring of the age of onset of the disease). Handling these multifactorial aspects and selection processes is the purpose of this project.

Thanks to close collaboration between statisticians, neuropsychologists, epidemiologists and clinicians, this project aims at developing new statistical methods for the study of the lifetime risk of AD and thorough analysis of the natural history of the disease. It is divided in four work packages. The first work package focuses on the comparison of methods for longitudinal analysis when participants' follow-up may be truncated by death in order to make recommendations on the best method according to the purpose of the analysis. The second work package targets the development of regression models for the lifetime risk of AD or the life expectancy without AD, taking into account interval censoring of the age at onset of the disease and the competing risk of death. This will make possible to quantify the association of the factors with these measures of public health impact through a sole parameter. The last two work packages focus on the development of multivariate models for thorough analysis of the progression of the disease before and after diagnosis. In WP3, multi-process models will be proposed to study the simultaneous evolution and interrelationships between the various processes involved in AD and the diagnosis of AD. We will be able, for example, to study the evolution of cognitive processes measured by neuropsychological tests, changes in functional disability levels measured by scales of autonomy, and anatomical processes measured by cerebral imaging. The last WP aims at identifying the different phases of the disease by introducing latent states in these models.

The proposed methods will be applied to data from cohorts managed by teams 2, 3 and 4 (cohorts Paquid, AMI, 3C and sub-cohort COGICARE, cohort MEMENTO). The follow-up times and sample sizes differ between these cohorts but they all include extensive and repeated assessments of cognition and disability and, in some of them, repeated cerebral imaging data are also collected. The data from the ADNI cohort, particularly rich in terms of brain imaging, will also be used.

This project will have two main outcomes:

- Improved methods for the longitudinal statistical analysis of cognitive decline and AD that will also be useful for the study of many chronic diseases.
- A better understanding of pathological processes involved in AD, its main phases of progression and the factors modulating risk and disease progression. This will make possible to identify the factors and key phases for future interventions to reduce the burden of AD. The models for lifetime risk or life expectancy without AD will allow more direct assessment of the possible impact of various scenarios of intervention.

Further information available at:

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France

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