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## **Determinants of cognitive impairment in older adults**

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Cognitive impairment is common in older adults. Cognitive impairment interferes with autonomous living in old age and puts older adults at increased risk of disability and premature death. Moreover, cognitive impairment could represent a high-risk state for the development of dementia. Due to the aging of societies, cognitive impairment and dementia are expected to increase dramatically in the coming years with profound social and economic consequences for individuals and societies. Given the urgent need to prevent dementia as early as possible, research has focused on the identification of determinants of cognitive impairment. The primary aim of this thesis was to examine potential determinants of cognitive impairment that are changeable, under-researched and highly prevalent in older adults. Factors selected for evaluation were smoking (primary aim I), sleep abnormalities (primary aim II) and variables related to the social environment (primary aim III). A secondary aim was to evaluate the reproducibility of the telephone interview used for data collection and to examine whether these cognitive tools were able to reproduce expected associations with established determinants of cognitive impairment (secondary aim I). Another secondary aim was to describe the changes in cognitive function according to different cognitive tests, and to estimate the prevalence and incidence of cognitive impairment in a population-based study of older adults living in Germany (secondary aim II).

I addressed these research aims in two different epidemiological studies. For primary aim I, II and for both secondary aims, I drew on data from a population-based study on cognitive function of older adults (aged  $\geq 70$ ) from Heidelberg and surroundings (the HeiDE DenkMal! study). In this study, data was gathered by means of telephone interviews, which included nine different cognitive tests. I coordinated all aspects of the collection of cognitive data in this study between 2005 and 2007 and conducted all 747 interviews myself. For primary aim

III, data from one site of a large prospective US study (the EPESE study) could be analyzed, which offered cognitive data (based on two tests) for more than 3,000 adults. In the HeiDE DenkMal! study, the following exposure information was available for primary aims I and II: smoking status, pack-years exposure, self-reported lack of sleep, self-reported hours of nocturnal sleep. The EPESE study offered data on marital status, living arrangements and the number and frequency of social contacts with relatives, friends and children (primary aim III). Associations between these exposures and cognitive impairment (according to individual cognitive tests or summary scores) were estimated by prevalence ratios (PRs) (in HeiDE DenkMal!) or risk ratios (EPESE) based on log-linear regression models. In addition, in HeiDE DenkMal!, linear regression was used to calculate mean test score differences between exposure groups. All estimates were adjusted for major confounders using advanced multivariable models. The 4-week test-retest reliability of the HeiDE DenkMal telephone interview was evaluated in a sample of 60 study participants by means of correlation measures. Established determinants of cognitive impairment that were investigated by multivariable PRs included, e.g., age, stroke, and education (secondary aim I). I assessed the change in cognitive function scores on different cognitive tests over a 3.3-year follow-up and estimated the prevalence and incidence of cognitive impairment (based only on a test-based cut-off) (secondary aim II).

Among those alive, high response rates were reached in the baseline and follow-up assessment of cognitive function (66% and 83%, respectively) and in the reproducibility study (97%). Primary aim I: overall, neither smoking status nor pack-years smoked were related to cognitive impairment or cognitive test scores. Sensitivity analyses revealed that this lack of association might partly be due to selective survival, particularly in current and heavy smokers. Primary aim II: neither a self-reported lack of sleep nor short sleep durations were associated with cognitive measures. A prolonged nocturnal sleep duration might be a marker of a reduced cognitive function or cognitive impairment in older adults. One might speculate that a potential causal relation involves arteriosclerosis. However, an exact plausible biological explanation is currently lacking and methodological explanations are also possible. Primary aim III: marital status/living arrangements were not related to cognitive decline. Having one or more friends or relatives (versus having none) was inversely related to cognitive decline with a more pronounced association in women over 3 years of follow-up, but not over 6 years. One explanation for this gender-specific association involves gender-differences in social support. Secondary aim I: the reproducibility study revealed that the individual cognitive tests had fair to substantial stability. The test-retest reliability was

excellent when tests were collapsed into summary scores. Expected associations with major determinants of cognitive impairment could be detected. Secondary aim II: the test scores of HeiDE DenkMal! study participants declined in the domains of verbal memory, verbal fluency and in global cognitive functioning over 3.3 years. On the other tests, no decline or improvements were observed. A substantial prevalence and incidence of cognitive impairment was observed, even when hypothetical cases of dementia were excluded.