# Self- or Physician-reported Diabetes, Glycemia Markers, and Cognitive Functioning in Older Adults in Germany

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**Objectives:** *To assess the association of different diabetes-related variables, including self- and physician-reported information, as well as biomarkers, with cognitive functioning in the elderly general population in Germany.* **Design:** *Cross-sectional observational study.* **Setting and Participants:** *A total of 1,697 subjects with a mean ± standard deviation age of 74 ± 2.8 years were included. These were recruited from among the participants of an ongoing epidemiological study of the elderly general population in Saarland state and had been recruited 5 years earlier on the occasion of a health screening exam by their general practitioners.* **Measurements:** *Cognitive functioning across six subdomains was assessed using the Cognitive Telephone Screening Instrument. Data on prevalent diabetes at baseline were obtained from the study participants and their general practitioners. Baseline fasting glucose was assessed as part of the screening exam, and baseline HbA1c was determined centrally by standardized methods.* **Results:** *The association of cognitive functioning with self-reported diabetes (N = 189) was more pronounced than with physician-reported diabetes (N = 280). HbA1c showed a nonlinear association with cognitive functioning, with a peak of cognitive performance in the central quintile of HbA1c. In the case of fasting glucose, lower cognitive functioning was only observed in the highest quintile. The estimates were robust in confounder-adjusted models, but attentuated when excluding subjects with baseline prevalent or follow-up incident diabetes.* **Conclusions:** *Future studies of diabetes-related biomarkers and cognition should take possible nonlinearity of the relationships into account, as the strength of the associations otherwise might be underestimated.* (Am J Geriatr Psychiatry 2013; ■:■−■)

**Key Words:** Fasting glucose, glycated hemoglobin, mild cognitive impairment

Dementia is a major challenge to global public health in the 21st century. It has been estimated that the number of people living with dementia roughly doubles every 20 years and will reach 80 million by 2040.[1] Detrimental associations of cardiovascular risk factors with cognitive deficits from mild impairment

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to dementia have become widely accepted.[2,3] A better understanding of these associations could help to improve dementia risk stratification as well as preventive measures aimed at risk reduction.

Recent estimates suggest that 350 million adults were living with diabetes mellitus in 2008.[4] Several studies have shown that the risk of developing dementia is roughly doubled in subjects with diabetes, but the relevant physiological pathways are not fully understood.[5] Both chronic hyper- as well as repeated hypoglycemia are among the causal mechanisms that have been hypothesized to be responsible for the patterns described.[6] A recent large study, however, found no association of hyperglycemia (HbA1c) with cognitive functioning and decline in diabetic subjects.[7] Notably, the associations may differ between cognitive domains, which makes it necessary to use detailed cognitive instruments.[8,9]

We have recently described the first application of COGTEL,[10] a cognitive screening instrument, in an epidemiological setting.[11] This instrument covers six cognitive domains, is administered via telephone, and was designed to assess adult cognitive functioning in its entire range. This may render it especially suitable for large epidemiological studies focused on early cognitive changes.

In the present work, we studied cognitive functioning as assessed by COGTEL and its associations with diabetes mellitus−related variables in an elderly community-based cohort. Apart from clarifying whether COGTEL is suitable for future studies of diabetes and cognition, we aimed to compare results based on self-reported versus physician-reported disease information (frequently, only one or the other will be available in epidemiological studies), and also took HbA1c and fasting glucose measurements into consideration. A special focus was on allowing for potentially nonlinear patterns of association, which could account at least for some of the inconsistencies in prior reports based on studies/analyses that did no allow for such nonlinearity.

## METHODS

### Study Design and Participants

Study subjects were recruited from the upper age groups (i.e., aged 65+ years at baseline in 2000−2002) of the ongoing ESTHER prospective cohort study. ESTHER is an epidemiological investigation into distributions, determinants, and prevention potentials of health problems in the German elderly population.[12] The participants of ESTHER were recruited during health screening visits to their general practitioners, with the majority of general practitioners in the state of Saarland participating in recruitment. Comparisons to registry data and epidemiological surveys support a broad representativeness of the ESTHER cohort for the German population of the corresponding age segment.[12] More specifically, the study sample closely resembles the general population in terms of sociodemographic properties, risk factors, and health-related conditions, such as smoking, hypertension, adiposity, and diabetes.[13]

ESTHER study participation was conditional on written informed consent. Subjects with insufficient knowledge of the German language or unwillingness or inability to participate were not eligible for inclusion. In order to maximize generalizability, no further exclusion criteria, including any based on cognitive functioning, were applied. Separate written informed consent was required for participating in the present cognitive substudy. Both the overall ESTHER and the cognitive substudy protocol were approved by the appropriate ethics committees (University of Heidelberg; medical board of the State of Saarland).

### Assessment of Cognitive Functioning

As described previously,[11,14] the cognitive telephone screening instrument COGTEL version A, which covers prospective, verbal short-term, verbal long-term, and working memory, verbal fluency, and inductive reasoning,[10] was administered by trained personnel in the context of the ESTHER year 5 follow-up (2005−2008). The different interview tasks generally originate from well-established neuropsychological instruments, such as the Wechsler Memory Scale-Revised and the Wechsler Adult Intelligence Scale-Revised (see Supplemental Digital Content; available online). The scores in the individual tasks are combined to form a total score of overall cognitive functioning performance by calculating a weighted sum.[10] In each subdomain and in the total score, a higher value is interpreted as better cognitive functioning.

The purpose of this instrument is to provide a global assessment of cognitive functioning that