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Research Article

# Subjective memory impairment in older adults predicts future dementia independent of baseline memory performance: Evidence from the Betula prospective cohort study

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**Abstract**

**Background:** The objective was to examine whether subjective memory impairment (SMI) predicts all-cause dementia or Alzheimer's disease (AD) in a population-based study with long-term follow-up (median = 10 years).

**Methods:** A total of 2043 initially dementia-free participants (≥ 60 years) made three memory ratings ("compared with others", "compared with five years ago", and "complaints from family/friends") at baseline. During follow-up, 372 participants developed dementia (208 with AD).

**Results:** Cox regression revealed that subjective memory impairment ratings predicted all-cause dementia in models adjusting for age and sex (hazard ratio or HR from 2.04 to 3.94), with even higher values for AD (HR from 2.29 to 5.74). The result persisted in models including other covariates, including baseline episodic memory performance, and in analyses restricted to participants with long time to dementia diagnosis (≥ 5 years).

**Conclusions:** The findings underscore the usefulness of subjective memory assessment in combination with other factors in identifying individuals at risk for developing dementia.



*Keywords:* Subjective memory impairment; Objective memory; Dementia; Alzheimer's disease

## 1. Introduction

Given that medical treatments designed to slow down the disease process of dementia disorders such as Alzheimer's disease (AD) are available, early detection of signs of impending disease is crucial. With the advent of more effective treatments, developing methods that aid in identifying preclinical stages of dementia will become even more important.

A potential source of information regarding early signs is the individual's own awareness of and expressed concerns about minor cognitive deficits. Such concerns may, for example, pertain to episodic memory functioning, known to be affected in the preclinical stage of dementia disorders such as AD [1].

The hope that reports of subjective memory impairment (SMI) [2] may help in identifying individuals at risk for future dementia may seem hampered by findings indicating that subjective ratings often show weak, if any, correspondence with concurrent objective test performance, but instead show a consistent relationship with mood state and personality factors, such as neuroticism [3–5].

Despite reports of a poor association between subjective and objective memory measures in cross-sectional studies, SMI tends to be more consistently related to longitudinal

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memory changes [6–8]. Of primary concern at present, a review of clinical and population-based studies provided support for an association between SMI ("memory complaints") and risk of developing dementia [9]. More specifically, four community-based longitudinal studies found that SMI predicted all-cause dementia [10–12] or AD [13]. However, two other studies failed to establish a relationship [14,15], and the association in the former set of studies was sometimes modest [11].

Although the relationship between SMI and future dementia is not fully established, more recent studies seem to confirm it. For example, perceived memory loss during the past year predicted incident dementia over a 5-year period, with an odds ratio of 1.35 after adjusting for age, sex, and depressive symptoms [16]. Another study found that perceived memory change predicted AD conversion over a mean follow-up of 5.2 years [17] and SMI, defined by a single rating made in a primary-care setting, predicted dementia (hazard ratio or HR = 2.27) over a 4-year follow-up, adjusting for other variables, including global cognitive functioning [18]. Thus, despite variability in regard to the strength of the relationship, there is mounting evidence that SMI may predict dementia.

The objective of the present study was to further investigate the relationship between SMI and incident dementia based on data from a population-based study of aging, memory, and health in Sweden [19,20]. Although most prior studies involved relatively short follow-up (1–4 years), the present study involved a follow-up period of up to 17 years. We used three memory ratings to operationalize SMI. The first required an interindividual judgment (one's own memory compared with others), the second a rating of intraindividual change (compared with 5 years ago), and the third concerned feedback from friends/family (how often others complain about one's poor memory). The baseline assessment included major potential confounders (e.g., age, sex, education, depressive symptoms, and *APOE* genotype). A comprehensive objective memory assessment also permitted the examination of the possibility that SMI ratings predict dementia partly independent of the information conveyed by objective tests. Finally, we considered both incident dementia in general and AD [21].

## 2. Methods

### 2.1. Study population

The data were collected in the Betula prospective cohort study, using stratified (age, sex) random sampling from the population register in Umeå municipality, Sweden [19,20]. Data have been collected on five test occasions; 1988–1990 (T1), 1993–1995 (T2), 1998–2000 (T3), 2003–2005 (T4), and 2008–2010 (T5). In the present study, data for participants aged 60 or older were included. T2–T4 served as the baseline, depending on the sample, as questions regarding subjective memory functioning were first included at T2.

Fig. 1 illustrates the study design, including samples, time of baseline assessment, and the follow-up periods for each sample.

As can be seen, the second test occasion, T2 (1993–1995), served as baseline for Sample 1 (S1; that had been assessed on a prior occasion). S1 involved 476 participants (60, 65, 70, 75, 80, 85 years). T2 also served as baseline for S2 (60, 65, 70, 75, 80 years; n = 495) and S3 (60, 65, 70, 75, 80, 85 years; n = 560), which differed in regard to age range. At T3 (1998–2000) S4 (60, 65, 70, 75, 80, 85, 90 years; n = 303) was added. Finally, at T4 (2003–2005) S5 (60, 65, 70, 75, 80, 85, 90, 95 years; n = 306) was added. Each wave (T1–T4) took 2 years to complete and each sample was followed up with regard to dementia diagnoses until 2010. Consequently, maximum follow-up time ranged from 5 years to 17 years across the samples.

### 2.2. Participants

We included participants from samples 1 to 5 (n = 2,140). Excluded were those who died shortly after (<1 year) the baseline assessment (n = 24), and those with incomplete data for the SMI ratings (n = 73). Hence, the final sample comprised 2043 participants. Median follow-up time was 10 years overall (7 years for participants who developed all-cause dementia and AD).

### 2.3. Dementia diagnosis

The diagnosis of dementia was based on the comprehensive analysis of neuropsychological testing, structured interviews conducted by trained nurses, and observations made at each test occasion. Moreover, participants with a low score (≥1.8 SD below age-adjusted norms) on a composite of cognitive/memory test, subjective report of memory impairment, and/or a Mini-Mental State Examination (MMSE) score ≤ 23 were subject to further evaluation. A senior research geropsychiatrist coordinated the diagnostic evaluation and was responsible for the final diagnoses. At test-waves T1–T3, up to four additional geropsychiatricians participated in the evaluation process, establishing a solid

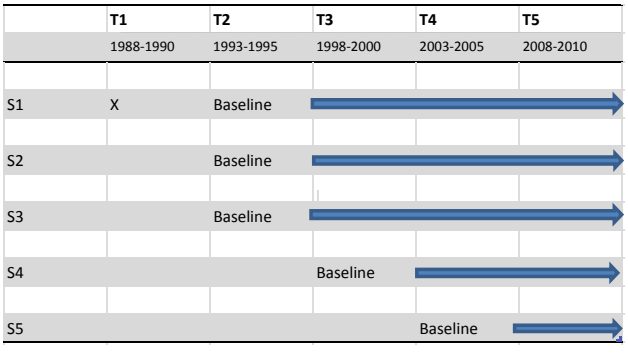


Fig. 1. Overview of the study design.