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Mild Cognitive Impairment in General Practice: Age-Specific Prevalence and Correlate Results from the German Study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe)

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Key Words
Mild cognitive impairment · Apolipoprotein E ε4 · Comorbidity · Primary care

Abstract
Background: Although mild cognitive impairment (MCI) represents a high-risk factor for developing dementia, little is known about the prevalence of MCI among patients of general practitioners (GPs). ***Aims:*** Estimation of age-specific prevalence for original and modified concepts of MCI and their association with sociodemographic, medical and genetic (apoE ε4 genotype) factors among patients of GPs. ***Methods:*** A GP practice sample of 3,327 individuals aged 75+ was assessed by structured clinical interviews. ***Results:*** Prevalence was 15.4% (95% CI = 14.1–16.6) for original and 25.2% (95% CI = 23.7–26.7) for modified MCI. Rates increased significantly with older age. Positive associations were found for apoE ε4 allele, vascular diseases and depressive symptoms. ***Conclusion:*** MCI is frequent in elderly patients of GPs. GPs have a key position in secondary prevention and care of incipient cognitive deterioration up to the diagnosis of dementia.

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Introduction

Several studies have shown that elderly individuals with mild cognitive impairment (MCI) are more likely to develop dementia [1, 2]. General practitioners (GPs) could play a decisive role in early detection of incipient cognitive deterioration up to the diagnosis of dementia, since they have regular and long-term contact with elderly people [3] enabling them to identify possible risk factors. In addition, the general ability of GPs to detect MCI after

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previous training is proved [4]. In order to assess the need of secondary prevention of incipient cognitive deterioration and developing dementia in general practices, the provision of information on prevalence of MCI among GPs' patients is required. Whereas several population-based studies have shown prevalence rates of MCI [5, 6], little is known about the special prevalence of MCI among patients of GPs. Thus, the main objective of the present study is to provide age-specific prevalence rates of four subtypes of MCI among elderly patients (75+ years) of GPs. Furthermore, the association between MCI and sociodemographic, medical and genetic (apoE $\varepsilon 4$ genotype) factors will be analyzed. Although the International Working Group on Mild Cognitive Impairment [7] has provided a broadly applied definition of MCI, the required diagnostic criterion of cognitive complaints is still controversial [8]. Original and modified concepts of MCI, which omit the criterion of cognitive complaints, were therefore applied in the present study.

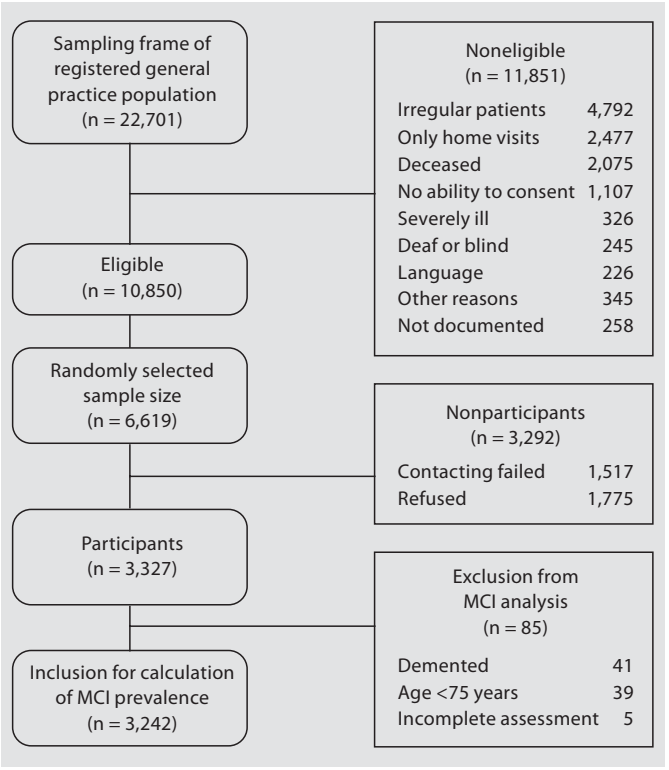

Fig. 1. Sampling frame and sample.

Materials and Methods

Sample

The study cohort consisted of all subjects participating in the baseline assessment of a prospective longitudinal study on early detection of MCI and dementia in primary care that is funded by the German Competence Network Dementia. The subjects were recruited in six study centers (Hamburg, Bonn, Düsseldorf, Leipzig, Mannheim and Munich) between January 1, 2003 and November 30, 2004. In each center, 19–29 GPs participated in the recruitment process – 138 GPs altogether. Inclusion criteria for patients were age 75 years and over, absence of dementia in the GP's view and at least one contact with the GP within the last 12 months. Exclusion criteria were consultations only by home visits, residence in a nursing home, severe illness the GP would deem fatal within 3 months, insufficient facility in German, deafness or blindness, lacking ability to consent and not being a regular patient of the participating practice. On average, each practice comprised 24 patients.

Information on sampling frame, eligible subjects and respondents is provided in figure 1. Of the 6,619 patients invited to participate in the study, 1,517 (22.9%) could not be contacted and 1,775 (26.8%) refused participation. Finally, 3,327 (50.3%) selected GP patients were assessed by structured clinical interviews. 85 (2.6%) of the 3,327 interviewed subjects were excluded from the following MCI analyses: 41 (48.2%) were classified as having dementia, 39 (45.9%) fell short of the age limit of 75 years, and 5 (5.9%) had incomplete neuropsychological test data. The calculation of the prevalence of MCI is based on the remaining 3,242 subjects.

In order to analyze possible nonresponse bias, data on age and gender could be collected for 1,770 (99.7%) of the 1,775 subjects refusing participation. Participants were significantly younger and included more males than subjects refusing participation. The mean age of the included participants was 80.1 years (SD = 3.6) vs. 80.8 years (SD = 3.8) for those refusing participation ($t = -6.104$, $p = 0.000$). Of study participants, 2,126 (65.6%) were female and 1,116 (34.4%) were male; among subjects refusing participation, 1,219 (68.9%) were female and 551 (31.1%) were male ($\chi^2 = 5.594$, d.f. = 1, $p = 0.018$).

Assessment Procedures

Structured clinical interviews were conducted by trained physicians and psychologists during visits to the participants' homes. Sociodemographic, clinical and psychometric baseline data were collected.

Neuropsychological assessment was based on the Structured Interview for Diagnosis of Dementia of Alzheimer type, Multi-infarct Dementia and Dementia of other Etiology according to DSM-III-R, DSM-IV and ICD-10 (SIDAM) [9]. The SIDAM consists of (1) a neuropsychological test battery and (2) a section for clinical evaluation and diagnosis, including data on sociodemographic characteristics, potential risk factors for cognitive impairment and dementia and a scale for the assessment of activities of daily living with 14 items (SIDAM-ADL Scale). The neuropsychological test battery consists of 55 items, including the 30 items of the Mini-Mental State Examination [10]. The items cover several areas of cognitive functioning grouped into 4 subscales: orientation, memory, intellectual abilities and higher cortical functioning (verbal abilities, calculation, constructional abilities and language). In order to evaluate impairment in cognitive function-

ing, age- and education-specific norms for the cognitive domains were applied [11].

As an agreement has not yet been reached as to how subjective cognitive complaints should be generally operationalized, subjective complaints were measured before cognitive testing by asking a common question, which may be similarly used by GPs: 'Do you feel like your memory has gotten worse?' (Answer: yes/no/I don't know). Depressive symptoms were assessed by the short version of the Geriatric Depression Scale with 15 items (GDS) [12]. A GDS score of 6 and higher corresponds to depressive symptoms [13]. For each study participant, the attending GP took a blood sample for genetic analysis and filled out a questionnaire about comorbidity. Possible clinical diagnoses of interest were predetermined by the questionnaire (answer: yes/no/I don't know); additional relevant diagnoses could be given by the GP.

Definition of Cases

MCI was diagnosed according to new consensus criteria proposed by the International Working Group on Mild Cognitive Impairment [7]. The criteria include: (1) absence of dementia according to DSM-IV or ICD-10, (2) evidence of cognitive decline: self-rating or informant report and impairment on objective cognitive tasks and/or evidence of decline over time on objective cognitive tasks, and (3) preserved baseline activities of daily living or only minimal impairment in complex instrumental functions.

Dementia according to DSM-IV was excluded with the SIDAM. The criterion of subjective cognitive complaints was fulfilled when the question on subjective memory impairment was positively answered. The objective cognitive decline was derived from the SIDAM neuropsychological test battery. Impairment in all four cognitive domains was defined as test performance of more than 1 SD below the main value for age- and education-specific norms. The functional activities were surveyed with the SIDAM-ADL-Scale. Subjects with only one impairment or with no impairments in the 14 items of the SIDAM-ADL Scale were regarded as functionally unimpaired.

According to Winblad et al. [7], four subtypes for MCI were examined based solely on differences in the criterion of objective cognitive decline. Subjects having an objective deficit in memory but not in any other area of cognitive functioning received a diagnosis of 'amnestic MCI'. Because the term 'amnestic MCI' is used in different ways in the literature, the more precise term 'single-domain amnestic MCI' is used throughout the paper in order to avoid confusion. 'Single nonmemory MCI' was diagnosed only if a single domain other than memory was impaired. If at least two cognitive domains other than memory showed an objective impairment, subjects received a diagnosis of 'multi-domain MCI nonamnestic'. Finally, 'multi-domain MCI amnestic' was diagnosed if memory and at least one other cognitive domain were impaired.

In addition to the subtypes described above, modified versions of the MCI concept were also evaluated. Each of these modifications was defined by the same criteria as the original subtypes, except for subjective cognitive complaints. The exclusion results in a diagnostic overlap, since all subjects diagnosed with the original criteria of MCI will meet the modified criteria as well.

Apolipoprotein E ε4 Genotyping

For DNA analysis, leukocyte DNA was isolated with the Qiagen blood isolation kit according to the instructions of the manufacturer (Qiagen, Hilden, Germany). The apoE ε4 genotype was studied as described elsewhere [14]. In analyses, subjects were divided into those with at least one copy of the ε4 allele and those without an ε4 allele.

Table 1. Demographic characteristics of subjects included in calculation of prevalence of MCI

Demographic variables	Study sample (n = 3,242)
Age	
75–79 years	1,725 (53.2)
80–84 years	1,209 (37.3)
85–98 years	308 (9.5)
Mean ± SD (range)	80.2 ± 3.6 (75–98)
Gender	
Female	2,126 (65.6)
Male	1,116 (34.4)
Level of education[a]	
Low	2,011 (62.0)
Middle	886 (27.3)
High	345 (10.6)
Marital status	
Married	1,379 (42.5)
Widowed	1,469 (45.3)
Divorced	193 (6.0)
Single	201 (6.2)

Figures in parentheses represent percentages, unless otherwise indicated.

[a] Based on the revised version of the international CASMIN educational classification [16].

Data Collection and Statistical Analysis

The data were collected in the centers via an internet-based remote data entry system into a central ORACLE version 9 database.

The statistical analyses were performed with SPSS for Windows, version 14.0 and Statistical Analysis System version 9.1. Prevalence rates of original and modified MCI concepts were estimated as the percentage of the completely assessed nondemented subjects aged 75 years and over. In addition to prevalence, 95% confidence intervals (95% CI) were calculated. Associations between categorical variables were analyzed with the χ^2 test. In order to analyze the relationships between MCI and explanatory variables, multivariate logistic regression models were applied and the adjusted odds ratios (ORs) with 95% CIs were stated. The method of multivariate logistic regression modeling has been described in detail elsewhere [15]. Age, gender, apoE ε4 genotype, subjective cognitive complaints (only for MCI-modified) and comorbid diseases which were significantly associated with MCI in univariate analyses were included in the regression models as explanatory variables. A p value less than 0.05 was considered statistically significant. If necessary, the Bonferroni-Holm procedure for adjustments for multiple testing was applied.

Table 2. Age-specific prevalence rates according to the original and modified subtypes of MCI

Diagnostic criteria	Age 75–79 years (n = 1,725)			Age 80–84 years (n = 1,209)			Age 85–98 years (n = 308)			Age 75+ years (n = 3,242)		
	cases	prevalence		cases	prevalence		cases	prevalence		cases	prevalence	
		%	95% CI		%	95% CI		%	95% CI		%	95% CI
MCI-original												
Single-domain amnestic MCI	43	2.5	1.8–3.2	15	1.2	0.6–1.9	6	1.9	0.4–3.5	64	2.0	1.5–2.5
Single nonmemory MCI	138	8.0	6.7–9.3	108	8.9	7.3–10.5	37	12.0	8.4–15.6	283	8.7	7.8–9.7
Multi-domain MCI amnestic	48	2.8	2.0–3.6	30	2.5	1.6–3.4	14	4.5	2.2–6.9	92	2.8	2.3–3.4
Multi-domain MCI nonamnestic	27	1.6	1.0–2.2	23	1.9	1.1–2.7	10	3.2	1.3–5.2	60	1.9	1.4–2.3
Total MCI	256	14.8	13.2–16.5	176	14.6	12.6–16.5	67	21.8	17.1–26.4	499	15.4	14.1–16.6
MCI-modified												
Single-domain amnestic MCI-modified	62	3.6	2.7–4.5	27	2.2	1.4–3.1	8	2.6	0.8– 4.4	97	3.0	2.4–3.6
Single nonmemory MCI-modified	247	14.3	12.7–16.0	182	15.1	13.0–17.1	57	18.5	14.2–22.8	486	15.0	13.8–16.2
Multi-domain MCI amnestic-modified	71	4.1	3.2–5.1	43	3.6	2.5–4.6	20	6.5	3.7–9.2	134	4.1	3.4–4.8
Multi-domain MCI nonamnestic-modified	45	2.6	1.9–3.4	40	3.3	2.3–4.3	16	5.2	2.7–7.7	101	3.1	2.5–3.7
Total MCI-modified	425	24.6	22.6–26.7	292	24.2	21.7–26.6	101	32.8	27.5–38.0	818	25.2	23.7–26.7

Original subtypes of MCI according to Winblad et al. [7]; modified ones exclude the criterion of a subjective cognitive complaint.

Results

Prevalence of MCI

Sociodemographic characteristics of the sample investigated are presented in table 1. Original criteria of all four MCI subtypes were fulfilled in 15.4% (95% CI = 14.1–16.6) of all subjects (table 2). Regarding subtypes, prevalence was lowest for multi-domain MCI nonamnestic (1.9%; 95% CI = 1.4–2.3) and highest for single nonmemory MCI (8.7%; 95% CI = 7.8–9.7).

All subtypes of MCI-modified without the criterion of subjective cognitive complaints were diagnosed in 25.2% (95% CI = 23.7–26.7) of subjects. Regarding modified subtypes separately, prevalence was lowest for 'single-domain amnestic MCI-modified' (3.0%; 95% CI = 2.4–3.6) and highest for 'single nonmemory MCI-modified' (15.0%; 95% CI = 13.8–16.2).

Correlates of MCI

Age and Gender

The impact of age and gender as well as comorbidity, apoE ε4 genotype and subjective cognitive complaints (only in MCI-modified) on prevalence of MCI was analyzed by multivariate logistic regression models (table 3).

Both the prevalence rates of the original and the modified MCI concepts only slightly decreased from age group 75–79 years to age group 80–84 years (MCI-original: OR = 0.99; MCI-modified: OR = 0.95). By contrast, prevalence rates increased with older age. Age group 85–98 years versus age group 75–79 years yielded an OR = 1.59 for MCI-original and an OR = 1.50 for MCI-modified.

Whereas no significant gender differences in prevalence rates for MCI-original were found, MCI-modified was significantly more prevalent in females (26.8%; 95% CI = 24.9–28.6) than in males (22.3%; 95% CI = 19.9–24.8). Thus, gender yielded an OR = 1.36 on prevalence of MCI-modified (table 3).

Subjective Cognitive Complaints

A total of 1,895 subjects (58.5%) of the study sample had subjective cognitive complaints. Subjective complaints were significantly more frequent in males than in females (61.6 vs. 56.8%; $\chi^2 = 7.163$, d.f. = 1, p = 0.007) and more frequent in age group 85–98 years than in age group 75–79 years and 80–84 years (64.9 vs. 57.3 vs. 58.5%; $\chi^2 = 6.314$, d.f. = 2, p = 0.043). By contrast, significant differences in the frequency of subjective cognitive complaints between subjects with and without objectively reduced

Table 3. Relationship between MCI and covariates

Covariates	d.f.	Wald's χ^2	p values	OR	95% CI
MCI-original					
Age					
80–84 years (vs. 75–79 years)	1	4.35	0.037*	0.99	0.80–1.23
85–98 years (vs. 75–79 years)	1	9.16	0.003**	1.59	1.16–2.17
Gender (female vs. male)	1	1.35	0.245	1.14	0.92–1.41
Comorbidity					
Peripheral arterial obstructive disease	1	2.26	0.133	1.26	0.93–1.72
Transient ischemic attack	1	2.59	0.108	1.34	0.94–1.91
Stroke	1	4.11	0.043*	1.57	1.02–2.43
Parkinson's disease	1	2.29	0.130	1.65	0.86–3.17
Depressive symptoms	1	13.77	<0.001***	1.74	1.30–2.33
ApoE ε4 genotype	1	8.41	0.004**	1.40	1.12–1.76
MCI-modified					
Age					
80–84 years (vs. 75–79 years)	1	6.47	0.011*	0.95	0.80–1.14
85–98 years (vs. 75–79 years)	1	10.26	0.001**	1.50	1.14–1.97
Gender (female vs. male)	1	11.43	<0.001***	1.36	1.14–1.63
Comorbidity					
Peripheral arterial obstructive disease	1	10.54	0.001**	1.53	1.18–1.97
Transient ischemic attack	1	0.37	0.542	1.10	0.81–1.51
Stroke	1	13.41	<0.001***	2.04	1.39–2.98
Parkinson's disease	1	0.98	0.322	1.36	0.74–2.47
Depressive symptoms	1	5.31	0.021*	1.36	1.05–1.78
ApoE ε4 genotype	1	2.65	0.104	1.18	0.97–1.43
Subjective cognitive complaints	1	1.61	0.204	1.12	0.94–1.32

Original subtypes of MCI according to Winblad et al. [7]; modified subtypes exclude the criterion of a subjective cognitive complaint; relationship between MCI and covariates was analyzed by multivariate logistic regression models using maximum likelihood values. Adjusted ORs with 95% CIs were calculated.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

cognitive performance could not be found ($\chi^2 = 2.931$, d.f. = 1, p = 0.087). Additionally, significant differences in the frequency of subjective complaints between subjects with and without MCI-modified could not be found by multivariate logistic regression (table 3). Regarding the 818 subjects with objectively reduced cognitive performance, 319 (39.0%) did not fulfill the criterion of subjective cognitive complaints: 233 (40.9%) of 569 females, and 86 (34.5%) of 249 males. Thus, they were classified as not having MCI according to the original criteria of Winblad et al. [7].

Comorbidity

Significant differences in comorbidity were found between subjects with and without MCI (table 4). With regard to all independent variables of the multivariate logistic regression models (table 3), stroke (OR = 1.58) and depressive symptoms (OR = 1.74) were diagnosed more frequently among subjects with MCI-original. Stroke (OR = 2.04) and depressive symptoms (OR = 1.36) were also more prevalent among subjects with MCI-modified. In addition, the prevalence of MCI-modified was also affected by the diagnosis of peripheral arterial obstructive disease, which yielded an OR = 1.53.

ApoE ε4 Genotype

Data on apoE ε4 genotype were collected for 3,119 (96.2%) of the 3,242 subjects of the study sample. 123 (3.8%) subjects had no analyzable blood sample. No differences in age ($\chi^2 = 3.496$, d.f. = 2, p = 0.174), gender ($\chi^2 = 2.604$, d.f. = 1, p = 0.107), prevalence of MCI-original ($\chi^2 = 0.000$, d.f. = 1, p = 0.986) and MCI-modified ($\chi^2 = 0.000$, d.f. = 1, p = 0.994) were found between subjects with and without available data on apoE ε4 genotype.

Table 4. Comorbidity of subjects with and without MCI (n = 3,223)

Diagnoses	MCI-original			MCI-modified		
	diagnostic criteria met (n = 497), %	diagnostic criteria not met (n = 2,726), %	p value	diagnostic criteria met (n = 815), %	diagnostic criteria not met (n = 2,408), %	p value
Hypertonia	72.4	71.0	0.522	72.8	70.7	0.267
Cardiac arrhythmia	30.2	30.3	0.957	30.7	30.1	0.778
Coronary heart disease	36.8	34.2	0.257	37.2	33.7	0.073
Myocardial infarction	9.3	10.1	0.585	9.6	10.0	0.692
Peripheral arterial obstructive disease	12.9	9.9	0.049	13.4	9.4	0.001*
Carotic artery stenosis (>80%)	3.4	2.5	0.258	2.9	2.6	0.571
Transient ischemic attack	11.5	7.3	0.002*	10.4	7.1	0.002*
Stroke	7.4	4.0	0.001*	7.4	3.6	<0.001*
Diabetes mellitus	22.7	22.5	0.917	24.5	21.9	0.117
Hyperlipidemia	39.8	39.9	0.976	39.6	40.0	0.856
Hypercholesterolemia	55.9	53.2	0.253	55.0	53.1	0.359
Epilepsy	1.2	0.8	0.377	1.2	0.7	0.202
Parkinson's disease	2.8	1.5	0.038	2.2	1.5	0.200
Alcohol abuse	0.4	0.9	0.247	0.4	1.0	0.089
Depressive symptoms (GDS >5)[a]	15.1	8.6	<0.001*	12.5	8.6	0.001*

Original subtypes of MCI according to Winblad et al. [7]; modified subtypes exclude the criterion of a subjective cognitive complaint. There were missing data on comorbidity from GPs for 19 subjects of the study sample. Significance of differences between proportions was calculated by two-sided χ^2 test. Adjustment for multiple testing was effected by the Bonferroni-Holm procedure. p values shown to be significant after adjustment for multiple testing by the Bonferroni-Holm procedure are marked by an asterisk.

[a] Missing data for 4 subjects of the study sample.

Table 5. MCI and apoE ε4 status (n = 3,119)

Diagnostic criteria	ApoE ε4 status			
	noncarriers		carriers	
	n	%	n	%
MCI-original				
Single-domain amnestic MCI	41	68.3	19	31.7
Single nonmemory MCI	213	78.3	59	21.7
Multi-domain MCI amnestic	58	65.2	31	34.8
Multi-domain MCI nonamnestic	44	74.6	15	25.4
Total MCI-original	356	74.2	124	25.8
Unimpaired	2,108	79.9	531	20.1
MCI-modified				
Single-domain amnestic MCI-modified	66	71.7	26	28.3
Single nonmemory MCI-modified	379	81.2	88	18.8
Multi-domain MCI amnestic-modified	87	67.4	42	32.6
Multi-domain MCI nonamnestic-modified	74	74.7	25	25.3
Total MCI-modified	606	77.0	181	23.0
Unimpaired	1,858	79.7	474	20.3
Total	2,464	71.7	655	21.0

Original subtypes of MCI according to Winblad et al. [7]; modified subtypes exclude the criterion of a subjective cognitive complaint. 123 of the 3,242 subjects declined submitting blood samples, or their blood samples could not be analyzed.

655 subjects (21.0%) of the study sample with an analyzable blood sample were identified as carriers of at least one apoE ε4 allele (96.5% heterozygote, 3.5% homozygote). Whereas no significant impact of apoE ε4 allele on prevalence of MCI-modified was found by multivariate logistic regression, the apoE ε4 allele yielded an OR = 1.40 on prevalence of MCI-original (table 3).

Table 5 demonstrates the presence of the apoE ε4 allele subject to the different MCI-subtypes. Significant differences between subtypes were found for MCI-original ($\chi^2 = 16.380$, d.f. = 4, p = 0.003) and MCI-modified as well ($\chi^2 = 16.338$, d.f. = 4, p = 0.003). In particular, apoE ε4 was identified more frequently in original MCI subtypes with required memory impairment (single-domain amnestic MCI, multi-domain MCI amnestic) than in those without ($\chi^2 = 6.728$, d.f. = 1, p = 0.009). Findings for MCI-modified are similar ($\chi^2 = 10.477$, d.f. = 1, p = 0.001).

Discussion

Prevalence of MCI

To our knowledge, the study is the first to investigate the particular prevalence rates of all MCI subtypes among elderly patients of GPs. Prevalence rates of 15.4% for MCI-original and 25.2% for MCI-modified were found among patients aged 75 years and older.

Artero et al. [17] have reported a prevalence rate of 16.6% for all MCI subtypes in GP patients aged 60 years and over, which corresponds approximately to our findings for total MCI-original (15.4%). Ritchie et al. [18] have examined exclusively the prevalence of single-domain amnestic MCI in a sample of GP patients aged 60 years and over. A rate of 3.2% was stated, which is slightly higher than our finding for single-domain amnestic MCI (2.0%). Prior studies [3, 19] have also reported prevalence rates for cognitive impairment without dementia in primary care or in particular in GP practice samples. For example, Cooper et al. [3] stated a rate of 17% for 'milder, non-disabling degrees of cognitive impairment' for GP patients aged 65 years and over. However, the comparability between these and our findings is limited, since cognitive impairment was assessed by rating scales or cognitive screening tests rather than by diagnosis according to MCI criteria.

For the diagnosis of MCI-original in population-based studies of subjects 75 years and older, Busse et al. [5] reported a prevalence rate of 15.0% and Lopez et al. [6] a rate of 18.8%. Although the prevalence rates were also affected by slightly different diagnostic criteria and assessment procedures, the results indicate that elderly patients of GPs are not at much less risk for MCI than the general elderly population. Hessel et al. [20] have shown that the majority of older people in Germany are registered at a GP. Thus, the results of the present paper may also indicate that the population of elderly patients of GPs corresponds to the general elderly population.

The real prevalence rate of MCI in GP practices might be rather underestimated; patients who were only visited at home as well as residents of nursing homes were excluded a priori, even though an increasing number of individuals cared for in institutions develop dementia [21]. Furthermore, 1,517 (22.9%) of 6,619 patients invited to participate in the study could not be contacted and 1,775 (26.8%) refused participation. Particularly with regard to older age, patients refusing participation might have been more cognitively impaired than the participants. Whether the rate of 22.9% of subjects who could not be contacted caused a systematic bias is difficult to assess, since no sociodemographic data could be collected. It is possible that many of these patients should not have been on the GPs' databases, since they may have either moved or died. However, a nonresponse bias cannot be excluded. As a result of the high nonresponse rate, a severe underestimation of prevalence of mild cognitively impaired patients of GPs is rather unlikely taking the findings on prevalence of MCI in population-based samples [5, 6] under consideration.

Correlates of MCI

Panza et al. [22] pointed out that the impact of age and gender on prevalence rates of predementia syndromes like MCI is not yet completely clarified. An increase in prevalence of MCI with age was found in some studies [6, 23]. In the present study, prevalence rates only differ slightly between the age group 75–79 years and the age group 80–84 years but clearly increase with older age (85–98 years). Because the criterion of cognitive impairment is corrected for age by using age- and education-specific norms [11], the prevalence of the cognitive criterion should normally remain stable across ages. Thus, the effect of age on prevalence of MCI might be due to possible differences between the sample of the present study and the normative dataset (e.g. cognition-related health factors; characteristics of subjects who refused participation) and to age differences in other MCI criteria such as the observed increase in subjective cognitive complaints with age (for MCI-original).

With regard to the impact of gender, higher prevalence rates of MCI-modified were found in females, whereas

the prevalence of MCI-original was not affected by gender. However, these discrepancies probably result from the fact that fewer females than males with objectively reduced cognitive performance and diagnosis of MCI-modified, respectively, had subjective cognitive complaints, and were therefore classified as not having MCI according to the original criteria of Winblad et al. [7].

Corresponding to the majority of cross-sectional studies of selective samples [24, 25], no association between subjective cognitive complaints and reduced cognitive performance was found. Whether the subjective complaints should be a mandatory criterion of MCI or not, however, creates a controversial issue. On the one hand, the criterion could be disadvantageous for studies not based on small selective samples of memory clinics, since a high percentage of objectively memory impaired individuals do not complain about their memory [24]. Thus, they would be excluded a priori from a risk population for progression to dementia. With regard to the present study, almost 40% of the cognitively impaired subjects did not fulfill the criterion of a subjective cognitive complaint and were therefore classified as not having MCI according to the original criteria of Winblad et al. [7].

On the other hand, the lack of association between subjective complaints and cognitive performance in the present study and other cross-sectional studies, as well, might be caused by variations in definition and assessment of subjective complaints. Compared to findings from cross-sectional studies, a predictive value of subjective memory complaints to objective memory decline and developing dementia, respectively, was demonstrated in some longitudinal studies [26, 27]. Additionally, subjective complaints are often the only indication of incipient cognitive deterioration in highly educated persons who show no noticeable problems in a sole measurement of cognitive performance [28]. Thus, information on cognitive performance over time is essential for definition of MCI. If only one measurement of cognitive performance at a single point of time is available, subjective cognitive complaints should not be excluded from a definition of MCI. With regard to the controversial findings for the subjective complaints, cognitive decline should be measured by deficits on objective cognitive tasks over time rather than by a subjective complaint in conjunction with deficits on objective cognitive tasks at a single point of time. Furthermore, structured clinical interviews (e.g. Clinical Dementia Rating [29]) can be used complementarily to substantiate the assessment of a cognitive decline.

Vascular diseases were identified as risk factors for MCI in some studies [30, 31], but not in all [32]. Bickel et al. [28] have shown that patients particularly in general hospitals represent a high-risk group for MCI, since risk factors like cardiovascular diseases are quite common. Present findings emphasize the impact of vascular diseases on MCI as well, since MCI-original was positively associated with stroke and MCI-modified with stroke and peripheral arterial obstructive disease.

According to other studies [30, 33], MCI was positively associated with depressive symptoms. The association is not unexpected, since depression oftentimes causes cognitive deficits such as decreased working memory or processing speed in elderly persons [34]. However, depression has not been consistently related to conversion to dementia in individuals with MCI [35, 36]. Further data on prospective studies are therefore required.

Association between MCI and apoE $\varepsilon 4$ status largely depends on MCI subtype. In accordance with other findings [30], the allele was identified more frequently in MCI subtypes with memory impairment than in those without. In addition, several studies have already demonstrated an increasing risk of developing Alzheimer's disease in individuals with an apoE $\varepsilon 4$ allele in association with memory impairment generally [37] and with an amnestic type of MCI in particular [38]. Nevertheless, further studies are required to determine the impact of apoE $\varepsilon 4$ genotype in association with the specific subtypes of MCI on prediction of the risk of developing dementia.

In summary, elderly patients of GPs are at risk for MCI. With regard to the importance of GPs in primary health care and long-standing health monitoring [3] and their proved ability in detecting MCI after previous training [4], GPs have a key position in secondary prevention and care of incipient cognitive deterioration up to the diagnosis of dementia. In order to assess the need of secondary prevention and care, the present article provides information on the prevalence of MCI in GPs' patients.

Our findings indicate that individuals with vascular diseases and depressive symptoms are more likely to develop MCI. An association between MCI and apoE $\varepsilon 4$ status was found especially for MCI subtypes with required memory impairment. Findings on subjective cognitive complaints serving as reliable information on cognitive performance over time are controversial. Therefore, cognitive decline should preferably be measured by deficits on objective cognitive tasks over time. However, in order to substantiate influencing factors on MCI and clinical outcome of MCI, further data from prospective studies are required.

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