

Subjective Memory Deficits in People with and without Dementia: Findings from the 10/66 Dementia Research Group Pilot Studies in Low- and Middle-Income Countries

10/66 Dementia Research Group

OBJECTIVES: To compare subjective memory deficit (SMD) in older adults with and without dementia or depression across multiple centers in low- and middle-income countries (LAMICs).

DESIGN: Secondary analysis of data from 23 case control studies.

SETTING: Twenty-three centers in India, Southeast Asia (including China), Latin America and the Caribbean, Nigeria, and Russia.

PARTICIPANTS: Two thousand six hundred ninety-two community-dwelling people aged 60 and older in one of three groups: people with dementia, people with depression, and controls free of dementia and depression.

MEASUREMENTS: SMD was derived from the Geriatric Mental State examination.

RESULTS: Median SMD frequency was lowest in participants without dementia (26.2%) and higher in those with depression (50.0%) and dementia (66.7%). Frequency of SMD varied between centers. Depression and dementia were consistently associated with SMD. Older age and hypochondriasis were associated with SMD only in subjects without dementia. In those with dementia, SMD was associated with better cognitive function, whereas the reverse was the case in controls.

CONCLUSION: Associations with SMD may differ between subjects with and without dementia living in LAMICs. *J Am Geriatr Soc* 57:2118–2124, 2009.

Key words: subjective memory deficit; dementia; depression; elderly

More than 20% of the general population complain of poor memory, a complaint that increases steadily with age.^{1,2} Whereas subjective memory deficit (SMD) refers to a people's feelings that their memory performance has decreased from their former level, objective memory impairment refers to the clinician's observation that a patient's memory capacity has decreased. The frequency of objective memory impairment is approximately half that of SMD, but the gap narrows with increasing age.¹ Factors underlying SMD and its clinical significance are not altogether clear. SMD is commonly reported in depression,^{2,3} dementia,^{1,3,4} and other psychiatric and somatic disorders.^{1,5,6} Investigations of the association between SMD and objective cognitive impairment have led to conflicting findings.^{6–10} Several prospective studies have found that SMD is associated with a small increase in risk of incident dementia.^{3,11} Despite controversy around its meaning, SMD has potential clinical importance, because it represents a frequent reason for help-seeking behavior or secondary care referral and may help identify patients at risk of further cognitive decline.

The association between SMD and personal and contextual factors has been little studied, and this may account for inconsistencies regarding possible associations with SMD. Thus, previous education is not consistently associated with SMD^{1,4,11–14} possibly because of factors that influence a person noticing early cognitive impairment or attributing importance to it. For example, relatives of people with Alzheimer's disease may monitor their own memory performance more diligently.¹⁵ A community survey in South Korea found that the association between SMD and impaired cognitive function was twice as strong in urban as rural residents possibly because of more-strenuous cognitive demands associated with rapidly changing urban environments.¹³

In the 10/66 Dementia Research Program, dementia diagnosis validation studies were conducted in a wide variety of low- and middle-income country (LAMIC) populations, providing a valuable opportunity to investigate SMD across sites in LAMIC. As part of this program, SMD was ascertained using identical procedures in all sites. Based

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Table 1. Characteristics of the Study Participants per Region and Group

Characteristic	Age		Sex		Education		Cognitive Score Derived from the Community Screening Instrument for Dementia	
	n	Mean ± SD	n	Female/Male	n	None/Minimal/ Primary Degree/ Secondary Degree/ College	n	Mean ± SD
India (5)								
Dementia	146	72.9 ± 9.4	148	81/67	145	38/36/31/40/0	149	17.8 ± 8.3
Depression	136	69.6 ± 6.2	135	88/47	134	36/35/30/33/0	136	28.9 ± 4.9
Normal controls	282	69.5 ± 6.7	282	156/126	282	46/86/29/121/0	282	30.8 ± 2.7
China and Southeast Asia (2)								
Dementia	61	76.1 ± 6.2	61	34/27	61	19/8/11/6/17	61	21.7 ± 4.5
Depression	32	71.3 ± 3.8	32	25/7	32	6/4/11/4/7	32	29.3 ± 2.7
Normal controls	124	73.2 ± 6.2	124	82/42	124	37/18/8/25/36	124	31.3 ± 1.6
Brazil (3)								
Dementia	89	78.2 ± 6.6	90	59/31	85	23/25/19/6/12	90	19.3 ± 7.5
Depression	90	73.7 ± 6.7	90	70/20	89	24/26/27/5/7	90	27.7 ± 3.4
Normal controls	180	74.4 ± 6.7	180	115/65	174	45/43/7/32/47	180	29.1 ± 2.7
Hispanic South America (5)								
Dementia	146	75.6 ± 7.8	147	86/61	145	2/21/54/56/12	147	21.2 ± 7.0
Depression	147	72.4 ± 6.7	146	113/33	146	6/44/42/43/11	147	29.1 ± 3.9
Normal controls	293	72.8 ± 6.4	294	192/102	286	12/106/46/88/34	295	30.6 ± 2.9
Middle America (4)								
Dementia	119	77.9 ± 6.8	118	66/52	114	13/23/39/26/13	119	19.6 ± 8.1
Depression	119	72.7 ± 7.3	117	78/39	118	14/17/35/32/20	119	29.3 ± 3.4
Normal controls	243	73.3 ± 7.1	243	142/101	243	27/82/30/64/40	243	31.0 ± 1.8
Caribbean (2)								
Dementia	70	76.9 ± 7.8	70	40/30	61	8/18/20/9/6	70	22.8 ± 5.4
Depression	59	73.6 ± 7.7	58	40/18	57	12/19/13/8/5	59	29.0 ± 3.2
Normal controls	121	73.9 ± 6.6	121	142/101	99	16/40/4/33/6	121	30.5 ± 2.6
Nigeria (1)								
Dementia	20	71.6 ± 7.7	19	7/12	0	Data not available	20	21.7 ± 4.6
Depression	15	67.2 ± 6.4	15	8/7	0	Data not available	16	26.5 ± 3.8
Normal controls	40	61.1 ± 7.0	35	15/20	0	Data not available	40	30.0 ± 2.1
Russia (1)								
Dementia	33	72.9 ± 5.7	33	25/8	30	0/0/3/26/1	33	21.3 ± 5.8
Depression	28	71.1 ± 5.9	28	25/3	28	0/0/1/25/2	28	29.3 ± 2.0
Normal controls	58	73.2 ± 6.2	58	82/42	58	1/7/23/27/0	58	31.3 ± 2.0

SD = standard deviation.

on this valuable data resource, the level of heterogeneity in SMD reporting across sites within the specific groups recruited, that is dementia, depression, and no dementia (selected for high and low levels of education) was investigated. In addition, variation in strength of association between SMD and dementia versus no dementia between these sites in LAMICs was investigated.

METHOD

Participants and Sampling Procedure

Participants were those recruited for the 10/66 dementia diagnosis pilot study described in detail elsewhere.^{16,17} In summary, in each of 26 study centers in India, China and

Southeast Asia, Latin America, Nigeria, and Russia, approximately 30 participants aged 60 and older were recruited in each of four groups: low level of education and no dementia, high level of education and no dementia, mild to moderate dementia, and depression. Characteristics of the study participants per region and group are shown in Table 1.

Local clinicians who recruited known cases for each group made diagnoses of depression and dementia. Depression was ascertained on the basis of a clinical interview using the Montgomery Asberg Depression Rating scale with an entry criterion of 18 or above.¹⁸ Independent clinicians confirmed dementia by conducting assessments blind to diagnosis using *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, dementia criteria and

the Clinical Dementia Rating Scale (CDR),¹⁹ for which preliminary studies show transcultural applicability.²⁰ Key informant reports of normal functioning rather than direct clinical assessment were used to exclude dementia in the groups with depression and high or low education. Trained lay interviewers blind to group status made all further measurements after group attribution. Ethical approval in London and the overseas centers and informed consent or relative agreement were obtained.

Measurements

Subjective Memory Deficits

SMD was ascertained using responses to three questions assessing four relevant symptoms; these questions are part of the Geriatric Mental State Examination (GMS).

- (1) Have you had any difficulty with your memory?
- (2) Have you tended to forget things?
 - (2a) Names of your family or close friends?
 - (2b) Where you have put things?
- (3) Do you have to make more effort to remember things than you used to?

Each of the four symptoms was rated as 0 (normal), 1 (abnormal but mild to moderate intensity or infrequent or fleeting), or 2 (abnormal and severe, frequent or persistent). Item scores were summed to form an ad hoc ordinal scale with a maximum possible score of 8. As with previous research using this scale, SMD was defined as present on the basis of a score of 3 or more.^{13,14}

Mental Health Status

A trained lay interviewer blind to group status administered the GMS—a widely used comprehensive mental health research assessment for older persons.²¹ It is a 25- to 50-minute clinical interview well suited for comparative epidemiological research, given its structured format for eliciting, rating, and recording symptoms and the use of the associated Automated Geriatric Examination for Computer-Assisted Taxonomy (AGECAT) computerized algorithm to generate diagnoses. This algorithm generates nine diagnostic clusters: organicity (dementia and other organic brain syndromes), schizophrenia (and related psychoses), mania, neurotic and psychotic depression, hypochondriasis, phobias, and obsessional and anxiety neuroses. A diagnostic confidence level for each syndrome ranges from 0 (no symptoms) to 5 (very severely affected). Levels 3 and greater represent likely cases and correspond to a degree of severity warranting professional intervention; Levels 1 and 2 are “subcases” that expert clinicians would not consistently diagnose as having the syndrome.

For this study, the depression, anxiety, and hypochondriasis clusters were analyzed. Twelve symptoms of depression (depression, pessimism, wishing death, guilt, sleep, interest, irritability, appetite, fatigue, concentration, enjoyment, tearfulness) are used to generate the depression symptom scale.²² Seven items of the GMS investigate anxiety (type and intensity of worries regarding health, family, or money; general free-floating anxiety; panic attacks). Five GMS items define the diagnosis of hypochondriasis (distressing feeling about one’s physical health, complaints about physicians’ helpfulness to relieve one’s

physical health, attending multiple doctors for the same or similar condition, likeliness that the complaints are due or not to the disease or malfunction claimed). The diagnostic confidence levels for depression, anxiety, and hypochondriasis were analyzed as ordinal scales.

Cognitive Function

The Community Screening Instrument for Dementia (CSI-D) was developed for use in cross-cultural studies. It consists of a 32-item cognitive test administered to the participant (20 minutes) and a 26-item informant interview, inquiring after the participant’s daily functioning and general health (15 minutes).²³ Three summary scores can be generated from the CSI-D, of which the cognitive score (COGSCORE) was used in this study. The COGSCORE is an item-weighted summary score from the participant’s 32-item cognitive test (seven-item object denomination, four-item object definition, two verbal category fluency tasks, word repetition, identification of a famous person, temporal and spatial orientation, three orders, three-word recall, six-chunk story recall, two drawings of intersecting circles and pentagons) incorporating the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) animal-naming verbal fluency task and the modified CERAD 10 word-list learning task with delayed recall.²¹ For the purposes of this study, only the COGSCORE as a measure of cognitive functioning and the CDR as a measure of dementia severity were used.

Analyses

The frequency of SMD (a score of ≥ 3 on the GMS SMD scale), according to center, for the dementia, depression, and control groups is reported. The frequency was calculated for each center, contrasting the frequency of SMD of the groups with dementia and depression with that of controls. The independent effects of site, age, depression, anxiety, hypochondriasis, and cognitive impairment (COGSCORE) on SMD were estimated, separately for those with and those without dementia (i.e., the depression and control groups lumped together) using ordinal regression. Kruskal-Wallis and Fisher exact tests were used to test for intergroup differences. SPSS 15.0 (SPSS, Inc., Chicago, IL) and Stata 9.0 (StataCorp., College Station, TX) were used for statistical analysis.

RESULTS

SMD Frequencies

Only participants who had answered all the SMD questions were included. These data were available from five centers in India (567 participants), two centers in China and Southeast Asia (247 participants), 14 centers in Latin America and the Caribbean (1,682 participants), one center in Nigeria (76 participants), and one center in Russia (120 participants), yielding 2,692 participants from 23 centers, of whom 689 had dementia, 657 had depression, and 1,346 were controls. The internal consistency of the SMD scale was evaluated in the whole sample, yielding a Cronbach alpha of 0.89.

The SMD frequencies are shown graphically according to center in Figure 1.

In general, the frequency of SMD was lowest in control participants, greater in those with depression, and highest

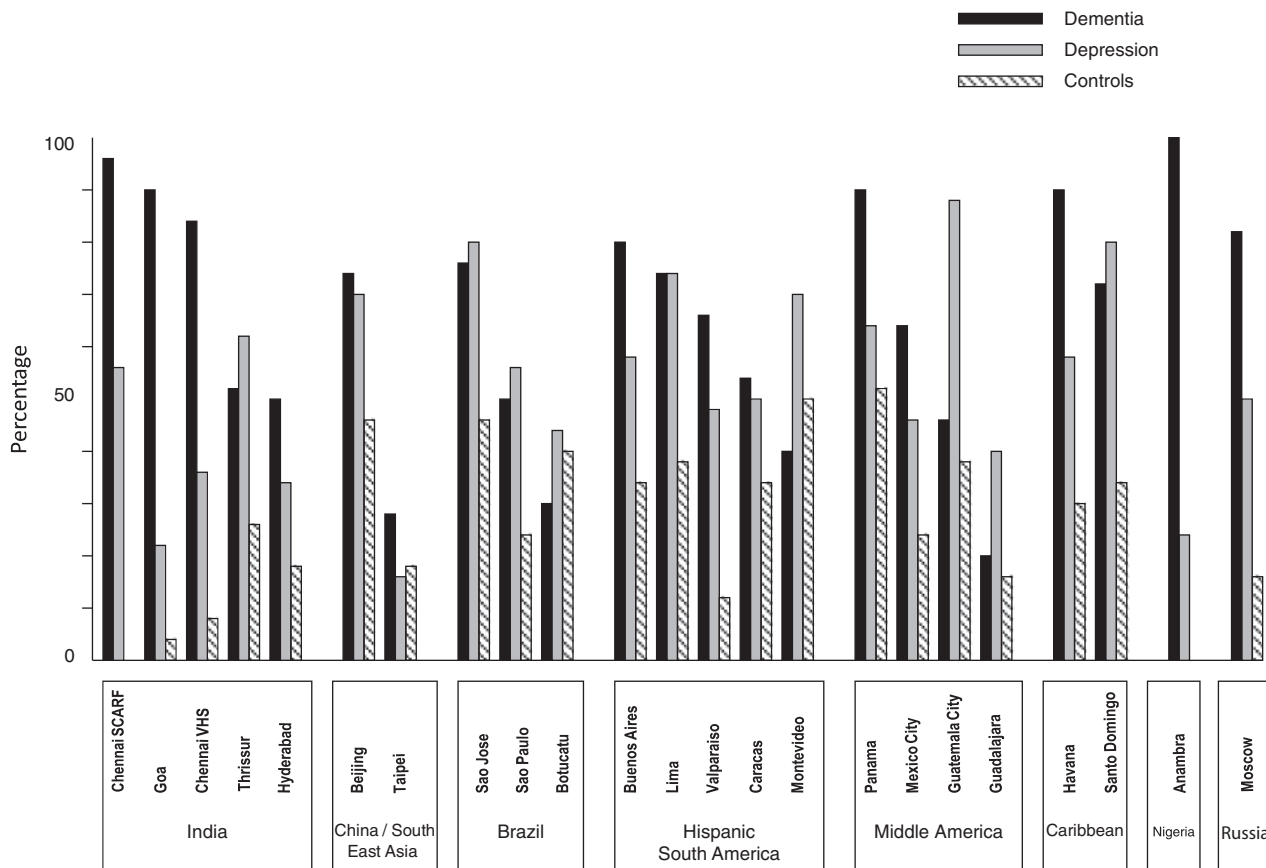


Figure 1. Subjective memory deficit (SMD) prevalence in % according to site arranged according to regions and according to group status (i.e., with dementia (black), depressed (gray), and normal controls (lines); group status is arranged according to decreasing SMD prevalence in subjects with dementia. SCARF = Schizophrenia Research Foundation; VHS = Voluntary Health Service.

in those with dementia, although in Latin American centers, the SMD frequency in the groups with dementia and depression was approximately twice that in the healthy controls, unlike the more gradual increase from the normal controls through the group with depression to those with dementia in the Indian and Southeast Asian sites. The frequency of SMD in those with dementia varied, according to center, from 20.0% to 100.0%, with a median of 66.7% (interquartile range (IQR) = 50.0–81.8%). In those with depression, the frequency varied from 15.6% to 87.1%, with a median of 50.0% (IQR = 40.4–63.3%). In controls, the frequency varied from 0.0% to 55.0%, with a median of 26.2% (IQR = 15.0–38.3%). In most centers, after adjusting for age and sex, dementia and depression were significantly associated with SMD.

Variables Associated with SMD

Site was significantly associated with SMD in the groups with and without dementia ($P < .001$; detailed results per site not shown). Similarly, person-related variables associated with SMD as derived from ordinal regression differed between those with and without dementia (Table 2).

For those with dementia, greater SMD was associated with more-severe depression and better cognitive function. Although dementia severity varied across sites according to CDR score ($n = 572$; Kruskal-Wallis test chi square = 40.9, degrees of freedom = 20; $P = < .001$), there was no asso-

ciation between SMD and CDR score ($n = 572$; Fisher exact test $P = .54$). For those without dementia, greater SMD was associated with older age; more-severe depression, anxiety, and hypochondriasis; and worse cognitive function. For people with dementia and controls, neither sex nor educational level was associated with SMD.

Table 2. Associations with Subjective Memory Deficits (Odds Ratios, with 95% Confidence Intervals) from Ordinal Regression

Predictor	Odds Ratio (95% Confidence Interval)		P-Value
	Without Dementia (Depression Cases and Controls)	With Dementia	
Age (in 5-year bands)	1.22 (1.11–1.34)	0.96 (0.84–1.10)	<.001
Sex (reference is female)	0.94 (0.73–1.20)	1.15 (0.78–1.68)	.11
Educational level	1.05 (0.96–1.16)	1.03 (0.88–1.21)	.64
Depression	1.62 (1.48–1.77)	1.43 (1.24–1.66)	.56
Anxiety	1.30 (1.17–1.44)	1.13 (0.95–1.34)	.63
Hypochondriasis	1.24 (1.04–1.47)	0.99 (0.73–1.35)	.03
Cognitive score derived from the Community Screening Instrument for Dementia	0.94 (0.91–0.98)	1.04 (1.02–1.07)	<.001

The interactions—for effect modification between those with and without dementia—were statistically significant for the effects of age, cognitive function, and hypochondriasis (Table 2).

DISCUSSION

Frequencies

In this data set of elderly people living in LAMICs, SMD frequency was generally higher than the prevalence reported in community-based studies including subjects with depression, those with dementia, and normal controls.^{1,3,4} Among other factors, variable definitions of SMD and, most importantly, the fact that this sample was not community based and cases were likely to be highly selected may explain this difference.

The frequency of SMD varied across the centers of this sample. There was a consistently higher frequency of SMD in people with dementia and depression than in controls. Overall, these results demonstrate a clear association between SMD and dementia and depression and confirm similar trends reported in other studies.^{3,4,6,24} At odds with the traditional view that SMD is associated with depression rather than objective memory impairment,^{5,12} the current study found a higher frequency of SMD with dementia than depression. Similarly, population-based studies have found older adults with dementia to report more SMD than those without, including patients with depression,^{2,4,8} although after adjusting for age and sex, the association between depression and SMD was marginally stronger than that between dementia and SMD.

Associations with SMD

Except for the association between SMD and depression and dementia, correlates of SMD were different for people with and without dementia in this study. In the group with dementia, better cognitive function and more-severe depression each predicted SMD. For those without dementia, significant associations were noted with older age, worse cognitive function, anxiety, and hypochondriasis. These findings suggest that the psychological or physiological mechanisms that underlie SMD may differ in subjects with and without dementia.

Although previous studies have found an association between older age and SMD,¹ only one study has examined the effect of age separately according to dementia status and found no difference in subjects with and without dementia.⁸ In the current study, in people with and without dementia, neither sex nor educational level was associated with SMD. Other studies have produced contradictory findings for sex^{1,7} and education,^{1,4,13} although the only study considering these associations distinguishing between people with and without dementia⁸ found no sex or education effect, similar to the results of the current study.

Although people with dementia with SMD had better cognitive function than those without SMD, people without dementia with SMD had worse cognitive functioning than those without SMD; this corroborates the results of another sample.⁸ Various reports show analogous results for at least one of the two groups.^{1,4,7} The association between SMD

and better cognitive function in people with dementia suggests that these subjects may maintain better insight into their condition. Although this hypothesis was not tested, this finding strengthens the argument that SMD ought to be taken seriously and to be further assessed, especially in the earlier phases of the various dementing disorders.

SMD was only poorly correlated with cognitive test performance in the depressed subjects without dementia, although depression was correlated with SMD in those with and without dementia in the current and other studies.^{6,8} Furthermore, the current study found that anxiety and hypochondriasis might be more relevant people without dementia, although one study reporting on patients with SMD found no difference with regard to hypochondriasis in those with and without dementia.⁶ Although the weak association between SMD and hypochondriasis—with its varying constructs across studies—requires further research for confirmation, these findings are reminiscent of work reporting associations, in people without dementia and mixed groups (without distinguishing those with and without dementia), between SMD and anxiety and neuroticism and a lower feeling of mastery and perceived self-efficacy.^{1,5,25,26}

Variations Between Sites

Site-related parameters including population density, general welfare, or cultural aspects, among others, have seldom been taken into account in previous research into SMD and may be important factors accounting for conflicting results from international studies or even variation within nations. In this study, the frequency of SMD varied notably between sites. The variation in SMD frequency was more marked in people without dementia, although variations in cognitive performance measured using the CSI-D were greater in the people with dementia in this study. These findings have to be considered as preliminary. First, there was no a priori hypotheses about whether specific centers would show a higher or lower frequency. Second, the estimates were based on small and possibly unrepresentative samples of those with and without dementia and hence may have been subject to bias.

Although cultural parameters are likely to influence SMD reporting, this study cannot improve understanding of these influences because no measures of cultural constructs were included in the data. The 10/66 Dementia Research Group's population-based studies from 10 LAMIC centers may provide more-definitive estimates.¹⁷

Further qualitative and quantitative research is warranted because SMD is a common symptom in geriatric practice. SMD is also a component in some definitions of mild cognitive impairment, and any site-related heterogeneity may have important potential implications for the wider application of this concept.

Methodological Considerations

The strengths of the study included the large overall sample size, the wide range of centers in LAMICs situated in five world regions, a clear and quantitative definition of SMD, and good characterization of depression and dementia using standard clinical criteria. SMD was categorized using a standard procedure and assessed (as with other instru-

ments) blind to group status at all sites. Nevertheless, the findings should be treated as preliminary and requiring confirmation because of the nature of the samples drawn. The four samples in each site were chosen primarily to allow cross-cultural validation of a dementia diagnostic instrument that has been reported elsewhere.^{16,17} Although the presence of SMD was unlikely to have influenced sample selection or participation, this cannot be excluded, and this might account for some of the heterogeneity observed. Dementia was specifically excluded for the high and low education groups that constituted the reference category for many analyses and for the depression group, although it should be borne in mind that some of the participants with depression may have had early unrecognized dementia and that depression was not specifically excluded in the two comparison groups. Furthermore, confounding factors examined were limited to few demographic and clinical variables. Although substantial residual confounding is unlikely, this cannot be absolutely excluded.

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