

Participant factors associated with transitions to and from Subjective Memory Complaints: Results from NACC UDS (2005-2025)

Ximena A. Oyarzún González^{1,2}, Erin L. Abner^{1,2,3}

1. Sanders-Brown Center on Aging, University of Kentucky; 2. Department of Epidemiology and Environmental Health, College of Public Health, University of Kentucky; 3. Department of Biostatistics, College of Public Health, University of Kentucky;

BACKGROUND

- Subjective Memory Complaint (SMC) is considered a prodromal stage in the pathway to dementia, preceding Mild Cognitive Impairment (MCI). However, its predictive utility as a clinical state remains unclear.
- We aimed to estimate transition probabilities between SMC and other states on the continuum from normal cognition to dementia.

METHODS

- A retrospective cohort of initially dementia-free research participants was created using data from the National Alzheimer’s Coordinating Center (NACC) Uniform Data Set, drawn from visits occurring between September 2005 and March 2025.
- SMC was considered present if the participant was diagnosed with normal cognition in the visit while positively answering the question “Do you feel you have more problems with memory than most?” from the Geriatric Depression Scale or “Does the subject report a decline in memory (relative to previously attained abilities)?” from the Clinician Judgment of Symptoms section.
- Using Markov chain analysis with multinomial logistic regression models, we estimated adjusted probabilities of transition between different cognitive states (Normal, SMC, MCI, Impairment non-MCI, Dementia, and Death without dementia), as well as the factors associated with the transitions.

CONCLUSIONS

- This study provides additional evidence that SMC is a meaningful cognitive state on the pathway to dementia.
- SMC’s predictive utility is still limited by the fact that a higher proportion of individuals with SMC remained stable or returned to normal cognition than declined during the study period
- Transitions to SMC from normal, and from SMC to worse states, were most associated with depression.
- SMC predictive utility is still limited by the fact that a higher proportion of individuals with SMC remained stable or returned to normal cognition than declined during the study period.
- More textured measures of SMC may yield different results with fewer false positives.

RESULTS

Table 1 Cohort characteristics at baseline, stratified by SMC status. Results are n (%) or mean±SD[range].

	No SMC N=14,523	Ever SMC [†] N=9,686	Total N=24,209
Cognitive state at baseline*			
Normal	10,688 (73.6)	4,109 (42.4)	14,797 (61.1)
Impaired not MCI	778 (5.4)	677 (7.0)	1,455 (6.0)
MCI	3,057 (21.1)	4,900 (50.6)	7,957 (32.9)
Age at First Visit (years)	73.6±7.9 [60-109]	72.9±7.4 [60-100]	73.4±7.7 [60-109]
Female sex	9,123 (62.8)	5,192(53.6)	14,315 (59.13)
Years of Education	15.8±3.0 [0-29]	15.6±3.3 [0-31]	15.7±3.1 [0+31]
Diabetes at baseline	1,841 (12.7)	1,317 (13.6)	3,158 (13.1)
Diabetes at anytime	2,497 (17.2)	1,846 (19.1)	4,343 (17.9)
Hypertension at baseline	7,439 (51.2)	4,900 (50.6)	12,339 (51.0)
Hypertension at anytime	9,334 (64.3)	6,286 (64.9)	15,620 (64.5)
Depression at baseline	2,411 (16.6)	3,102 (32.0)	5,513 (19.6)
Depression at anytime	3,964 (27.3)	4,794 (49.5)	8,758 (36.2)
APOE ε2**			
1 Allele	1,739 (14.2)	986 (11.7)	2,725 (13.2)
2 Alleles	73 (0.6)	31 (0.4)	104 (0.5)
APOE ε4**			
1 Allele	3,393 (27.7)	2,872 (34.2)	6,265 (30.4)
2 Alleles	328 (2.7)	573 (6.8)	901 (4.4)
Number of Visits	5.2±3.6 [2-20]	5.2±3.6 [2-20]	5.2±3.6 [2-20]

[†] SMC reported at least once during follow up period. *p-value of <0.05 for comparison between no SMC and SMC. **15% of the data is missing. Depression represents an active depression diagnosis in the last 2 years.

Table 2. Patterns of SMC reporting among participants who reported SMC at least once, stratified by baseline cognitive status. Results are n (%) or mean±SD[range].

	Baseline cognitive status			
	Normal N=4,109	Impaired not MCI N=677	MCI N=4,900	Total N=9,686
Visit of first report	3.1±3.0 [1-19]	2.3±2.0 [1-15]	1.6±1.3 [1-15]	2.3±2.3 [1-19]
Visit 1	1,804 (43.9)	362 (53.5)	3,400 (69.4)	5,566 (57.5)
Visit 2	715 (17.4)	125 (18.5)	888 (18.1)	1,728 (57.5)
Visit ≥3	1,590 (38.7)	190 (28.0)	612 (12.5)	2,392 (24.7)
SMC Pattern				
Reported only once	1,800 (43.8)	259 (38.3)	1,671 (34.1)	3,730 (38.5)
Consecutive	1,188 (28.9)	264 (39.0)	2,448 (50.0)	3,900 (40.3)
Intermittent	1,121 (27.3)	154 (22.8)	781 (15.9)	2,056 (21.2)
Number of SMC reports	2.4±2.0 [1-17]	2.5±2.1 [1-14]	2.3±1.6 [1-17]	2.3±1.9 [1-17]
Age at first report	75.1±8.5 [60-102]	73.9±7.9 [60-98]	74.0±7.6 [60-101]	74.5±8.0 [60-102]
Probability of complaint at a particular visit [†]				
0.01-0.24	1,265 (30.8)	141 (20.8)	354 (7.2)	1,760 (18.2)
0.25-0.49	1,102 (26.8)	151 (22.3)	856 (17.5)	2,109 (21.77)
0.50-0.74	984 (23.9)	203 (30.0)	1,630 (33.3)	2,817 (29.1)
0.75-0.99	291 (7.1)	53 (7.8)	367 (7.5)	711 (7.3)
1.0	467 (11.4)	129 (19.1)	1,693 (34.6)	2,289 (23.6)

*Statistically significant; significant differences for continuous variables based on ANOVA. [†] Rate of # SMC/#visits

Table 3. Observed (unadjusted) one-step transition probability matrix for the Markov Chain. Cells values represent number of transitions and row probabilities. Row probabilities sum to 1.0.

From	Normal	SMC	Impaired not MCI	To MCI	Dementia	Death w/o Dementia
Normal	54,588 (0.85)	2,736 (0.043)	1,431 (0.022)	3,165 (0.049)	413 (0.006)	1,978 (0.031)
SMC	2,870 (0.41)	2,891 (0.41)	229 (0.032)	779 (0.11)	103 (0.015)	218 (0.034)
Impaired not MCI	1,152 (0.19)	242 (0.041)	2,854 (0.482)	1,179 (0.20)	259 (0.044)	236 (0.04)
MCI	1,757 (0.073)	517 (0.022)	976 (0.041)	15,550 (0.65)	4,095 (0.17)	1,203 (0.05)

SMC: Subjective Memory Complaint; MCI: Mild Cognitive Impairment.

Figure 2: State transition probabilities from SMC adjusted by fixed covariates sex, years of education, and dose of APOE ε4 and APOE ε2 alleles, and time-varying covariates age, history of depression, hypertension, and diabetes. Forest plot showing the OR (CI) for variables that were statistically significant for each transition.

