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Role of Co-existence of Multiple Chronic Conditions on the Longitudinal Decline in Cognitive Performance among Older Adults in the US

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Abstract

Background: The primary goal of this study was to examine the influence of the co-existence of multiple chronic conditions on the longitudinal decline in cognitive performance among elderly individuals of the nationally representative Aging Demographic and Memory Study.

Methods: Retrospective longitudinal cohort study of individuals aged 70 years or above. Random effect ordinal logistic regression analysis was performed to assess the impact of co-existing chronic conditions on the longitudinal decline in cognitive function (transitioning from normal functioning to cognitive impairment (no dementia (CIND) to dementia) among older adults. Principal component factor analysis was conducted to identify the clusters of chronic health conditions.

Results: About 35% of respondents had at least one of four cardiovascular risk factors (diabetes, hypertension, high cholesterol or heart problems). The odds of remaining in normal cognitive status (compared to CIND and dementia) were 56% lower for those who experienced an incidence of stroke at baseline compared to those who did not experience a stroke incidence. Cardiovascular risk factors were not associated with cognitive decline.

Conclusions: The lack of significant impact of cardiovascular (CVD) risk factors on cognitive decline may be attributable to indirect but important pathways through which CVD factors are associated with a stroke incidence. The importance of this topic remains as the prevalence of dementia and other cognitive impairments is increasing worldwide, and our limited findings underscore the imperative need for longitudinal studies with a larger group of geriatric patients and wider use of brief assessments of cognitive status. Due to the complexity of managing chronic cardiovascular disease, establishment of a care coordination manager as a bridge between patients and other medical specialists may improve clinical outcomes and prevent cognitive decline.

Keywords: Cognitive retention disorders; Chronic disease; Comorbidity; Dementia; Elderly; Longitudinal study

Introduction

The prevalence of dementia among elderly Americans aged 71 and older was 14% in 2002, comprising about 3.4 million individuals including approximately 10% with Alzheimer's disease (AD) [1]. Based on recent estimates from the 2010 U.S. Census data and Chicago Health and Aging Project, the estimated prevalence of AD for people aged 65 or older in 2010 was 4.7 million and is projected to be 13.8 million in 2050 [2]. However, a milder age-related deficit, cognitive impairment no dementia (CIND), also affects a large proportion of the elderly population in the United States. CIND is the similar clinical state as mild cognitive impairment, which is the most widespread term used to characterize the clinical state between normal cognition and dementia [3]. CIND is defined in Aging Demographic and Memory Study (ADAMS) as mild cognitive or functional impairment reported by either participants or informants, or impaired test performances of neuropsychological tests that did not qualify for dementia [4]. According to Plassman et al. 22% of individuals aged 71 or older in the US had CIND in 2002 [4]. Cognitive decline that does not qualify as a dementia diagnosis is associated with increased risks for progression to dementia, with 10% to 15% progressing per year compared with 1% to 2.5% among age-matched cognitively healthy older adults [4]. Dementia is a disease of particular concern as memory loss and cognitive impairment lead to functional disability and loss of independence that have significant economic and social impacts on families and healthcare systems [5].

As the prevalence of cognitive impairment and dementia increases, the care for impaired individuals incurs substantial direct and indirect costs. Medicare costs for individuals with AD and related dementias are projected to double from $91 billion in 2005 to more than $189 billion in 2015, unless effective treatment or prevention strategies become available to delay the onset or slow the progression of the disease [6]. For AD and other dementias, 15.2 million US citizens provided 17.4 billion hours of care for a family member or close friend in 2011 [7]. The economic value of care provided "informally" by family and friends was estimated to be $210.5 billion in 2011. The incremental annual cost to US businesses from lost productivity associated with family caregiving for persons with dementia was $36.5 billion [8]. Delaying the onset of AD by just 5 years would reduce the prevalent cases by 50%, [9] which would have a huge public health impact. From the costs saving perspective, a 30-day delay in institutionalization for patients with moderate to severe AD would result in savings of $1863 per person per month [10]. One recent estimate indicates that each month's delay in institutionalization may save as much as $2029 in direct healthcare costs and other costs associated with counseling, education and caregiver supports [11]. Apart from heath care costs associated with impaired

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cognitive function, dementia is thought of as one of the leading causes of non-fatal disability in developed countries; by 2030, it will be the third leading cause of years of life lost due to death and disability. The dramatic impact of AD and other forms of dementia suggest the need to explore all possible factors that influence the onset and/or progression of cognitive decline in older adults.

Evidence suggests that chronic diseases and associated risk factors may impact the risk of cognitive decline and dementia. Medical conditions such as heart disease [12], hypertension [13], diabetes [14], and stroke [15] can contribute to cognitive decline. Specifically, Knopman et al. [13] found that hypertension and diabetes mellitus were positively related to cognitive decline, while Ivan et al. [15] documented that a history of stroke was associated with an increased risk of dementia compared with age- and sex-matched controls.

Although a large and growing segment of the elderly population in the US has been diagnosed with multiple chronic conditions, little is known about how clusters of conditions may influence cognitive decline. About 62% of Americans over age 65 have multiple chronic conditions [16]. To date, associations between chronic diseases and cognitive decline have been studied as if these conditions occur in isolation, one at a time. Understanding how combination of conditions impact cognitive decline over time is critical for improving cognitive health of the elderly. However, empirical evidence of the longitudinal impact of comorbid chronic conditions on cognitive trajectories is lacking.

Identifying specific combinations of chronic conditions that may influence the transitions from normal cognition to cognitive impairment to dementia is a major public health priority as this may highlight opportunities for interventions to delay cognitive decline and reduce social and economic burdens of the disease. Particularly, positive gains from prevention strategies such as stroke prevention, or reduction in cardiovascular risk factors (modifying lifestyle behaviors such as lack of exercise, smoking) may delay cognitive decline and lower its prevalence. In this study, we aimed to identify combinations of comorbid conditions associated with the longitudinal decline in cognitive status among the elderly. Our study hypothesis was that individuals with co-occurring conditions were more likely to transition into lower cognitive status over time.

Study Design and Methods

This was a retrospective longitudinal study of persons aged 70 years or above who participated in the ADAMS. ADAMS was a stratified random sample of Health and Retirement Study (HRS) respondents selected for intensive in-home cognitive assessments to provide national estimates of the prevalence of dementia and CIND. The ADAMS subsample of 1770 respondents (drawn from the original HRS sample), aged 70 years and older, both community-dwelling and individuals living in nursing homes, was selected based on cognitive performance in the HRS wave before the ADAMS interview (HRS-2000 or 2002) [17]. A series of neuropsychological and clinical assessment tests assessed cognitive functioning of ADAMS participants (N=856) during the baseline interview, which occurred between July 2001 and December 2003 [18]. This represents participation of 56% of the non-deceased eligible respondents for ADAMS. Reasons for non-response included refusal to participate in ADAMS (26%), deceased before the interview (13%), lost contact (3%), and other reason (7%). No systematic relationship was found between non-response and baseline cognitive status among ADAMS participants [19]. In addition, there was no indication of the mortality-based sample selection bias in the final ADAMS sample, which confirms that the natural mortality of ADAMS sample does not include any sample selection or attrition bias in the final sample.

The ADAMS examination was an in-person structured assessment conducted by a nurse and a neuropsychology technician. The full details of assessments tests and diagnostic procedures are described elsewhere [17]. In summary, the following information about the participant was collected from a knowledgeable informant: medical history, current neuropsychiatric symptoms, chronological history of cognitive symptoms, family history of memory related problems, and severity of cognitive and functional impairment. During the assessment, the participant completed a battery of neuropsychological measures; a self -reported depression measure; a standardized neurologic examination; a blood pressure measurement; collection of buccal DNA samples for apolipoprotein E (APOE) genotyping; and a 7-minute, videotaped segment covering portions of the cognitive status and neurologic examinations. The detailed in-home assessment took 3-4 hours, and the final dementia diagnosis was made by a consensus panel of neuropsychologists, neurologists, geropsychiatrists, and internists who reviewed the in-home assessments and assigned final diagnoses.

Diagnoses were divided into 3 categories: normal cognition, CIND and dementia. The consensus panel used clinical judgment to assign the final diagnosis, based on the following criteria. Dementia diagnosis was based on guidelines from the Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition; [20] the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; [21] diagnoses of Alzheimer disease and other types of dementia were based on currently accepted criteria [22-25]. The definition of CIND and its subtypes was on the basis of the accumulated clinical experience of a group of researchers common to ADAMS and other epidemiologic studies of dementia [4,26,27].

The first follow-up visits among all initial (baseline) participants who were still alive in 2006 and not previously diagnosed with dementia were conducted between July 2006 and May 2008 (82% response rate net of mortality). The reassessment was performed with 315 respondents to document any change in cognitive functioning over time. Second follow-up visits were completed among 217 respondents from January 2008 through December 2009. Linking the ADAMS sample to the expansive HRS data that included chronic conditions, behavioral risk factors, demographics and socioeconomic characteristics provided a unique opportunity to study the impact of combinations of chronic conditions on longitudinal progression of cognitive decline among the HRS cohort. Figure 1 below provides the conceptual model of trajectories of cognitive decline operationalized with HRS-ADAMS data. The upright dotted lines indicate potential points of intervention to prevent transition to CIND or dementia. Our conceptual model shows what individual characteristics can potentially be predictive of dementia and the timing of measurements of those factors in the empirical model.

Study Sample

Figure 2 presents the distribution of respondents transitioning into different cognitive status during the study period. Respondents diagnosed with AD (229) and other dementias (79) at the baseline were excluded. Our sample included respondents (N=315) diagnosed with normal status or CIND at baseline, reassessed during two follow-ups (2006-2008 and 2008-2009, respectively). Seven respondents with a diagnosis of CIND at baseline reverted to normal and were excluded from the analytic sample. This exclusion resulted in a final sample of 308 respondents.

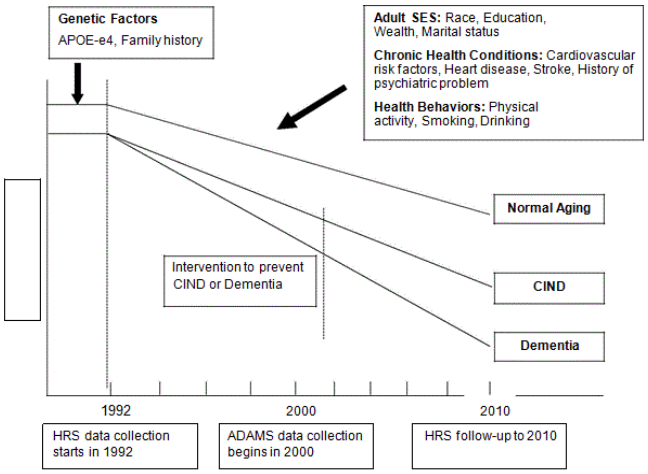

Figure 1: Conceptual model of longitudinal cognitive decline in the HRS-ADAMS.

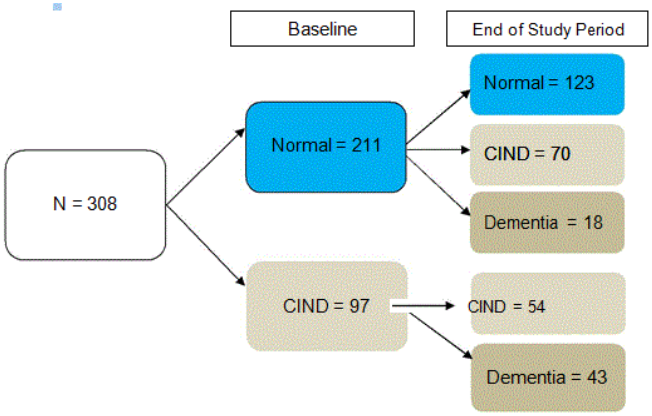

Figure 2: Sample respondents transitioning into different cognitive status during study period (2000-2009).

Variable Measures

Outcome variable

The outcome of interest was the clinical determination of cognitive status. Diagnoses of dementia and CIND are described in the method section. Our outcome variable was an ordered categorical variable with 3 categories: normal, CIND and dementia. The transition in cognitive status during the study period is shown in Figure 2.

Independent variables measured at baseline

Figure 1 describes the timeline of study variables included in analysis. The baseline survey included a list of chronic health conditions related to cardiovascular disease (diabetes, hypertension, heart disease, stroke, cholesterol). For each condition, respondents answered (yes/no) the survey question "has a doctor ever had told you that you had the condition?" Self-reported history of psychiatric disorder was also assessed and included in the analysis. A set of sociodemographic characteristics such as gender, education (number of completed years), and race/ethnicity (White, non-White reference category) were adjusted in the analysis. Behavioral health risk factors included former smoking, current smoking, heavy drinking (more than 1 drink/day for female and more than 2 drinks/day for men), and physical inactivity. Physical inactivity was measured by the participation in regular vigorous physical exercise less than 3 times per week during the 12 months prior to baseline. These indicators were summed to create a summary count of behavioral health risk factors. Because it is well known that the likelihood of dementia increases with age, we did not include age as an independent covariate rather captured time interval between assessments of disease status. We created a continuous variable measuring the time (in years) between the first and second assessments and the second and third assessments for each respondent in the sample. We also constructed a comorbidity score counting presence or absence of the four chronic health conditions that loaded onto the primary factor identified in the factor analysis as described in the next section (range 0-4).

Analytic Strategy

Principal components factor analysis was performed to identify relationships among prevalence of chronic conditions among sample members. Factor analysis is a widely used statistical technique that allows the data to determine how individual characteristics can be grouped together based on their inter-individual correlation coefficients. The factor analysis uses correlation coefficients to create the factor grouping (grouping on chronic conditions) that may coexist in patients (e.g. co-existence of diabetes, hypertension, cholesterol and heart problems). Grouping of conditions was based on factor loadings, which indicate the relative contribution that each individual condition contributes to the factor. Supplementary Figures 3a, 3b, and 3c (shown in the Appendix) showed factor loadings of 3 factors identified from the principal component factor analysis. The factor grouping was based on the value of factor loading for each condition and conditions were grouped into same factor with factor loading of 0.5 or higher. Based on this strategy, hypertension (loading of 0.51), diabetes (loading of 0.60), heart problems (loading of 0.68), and cholesterol (loading of 0.64) were grouped into comorbidity factor 1, while stroke and psychiatric condition remained as separate factors as factor 2 and factor 3 respectively. A factor score was calculated based on the prevalence of each condition in factor 1 as a continuous variable ranges from 0-4 (0 meaning no prevalence of any of 4 conditions, and 4 indicating existence of all four conditions) and this continuous measure was included in the multivariate model.

Random effects ordinal logistic regression models estimated the probability of transitioning between cognitive status from baseline to the successive time points. Models assessed clinical and demographic covariates. Because it is well known that the likelihood of dementia increases with age, our model did not include age as an explanatory

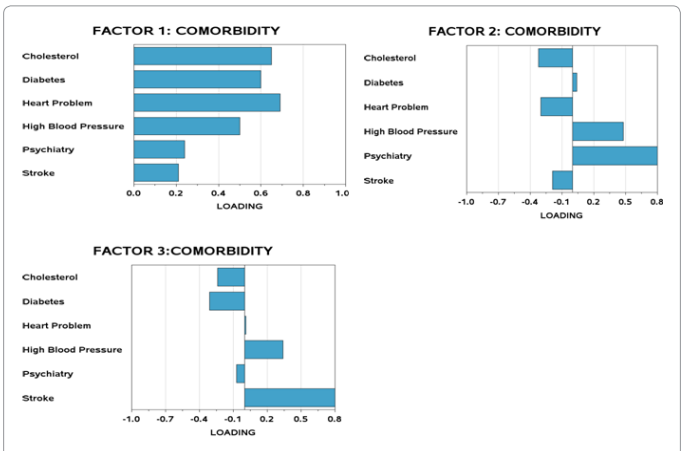

Figure 3: Factor loadings among chronic conditions based on factor analysis.

variable, rather we presumed that assessment time as an indicative of age. Specifically we accounted for longitudinal dependence by including an individual-specific random intercept in the proportional odds model. The model can be written in terms of latent-response formulation by specifying a random intercept model for the latent disease status y_{ij}^{*} as

$$y_{ij}^{*} = \beta_{ij}^{/} x_{ij} + \zeta_{1j} + \dot{o}_{ij}\,; \qquad (1)$$

Where The overall intercept of the cumulative logits is ζ_{1j}, hence varies over individual j. We assume that $\zeta_{1j} | x_{ij} \sim N(0, \psi)$ where Ψ is the random intercept variance-covariance matrix, ζ_{1j} are independent across individuals; and $\dot{o}_{ij} | x_{ij}$, ζ_{1j} have logistic distribution and independent across individuals and occasions. The continuous latent responses y_{ij}^{*} are related to the ordinal severity of cognitive status variable y_{ij} via the threshold relationships

$$y_{ij} = \begin{cases} 1\,if & y_{ij}^{*} \le k_1 \\ 2\,if\ k_1 \le y_{ij}^{*} \le k_2 \\ 3\,if\ k_2 \le y_{ij}^{*} \le k_3 \end{cases}$$

Where k_1, k_2, K_3 are threshold categories to determine the cognitive status. The model was estimated via gllamm procedure using Stata 11 (STATA Corporation, College Station, TX).

There were 62 respondents whose disease statuses were missing at the third measurement period due to the death or lost to follow-up for some other reasons. We performed sensitivity analysis by assuming that these 62 respondents could have three possible disease statuses at the end of the study period: transitioned to dementia, remained in the same cognitive status since the second measurement point, and deteriorated to the next lower category compared to the disease status at the second measurement point. We then compared results with the original sample where data for these 62 sample members who were ignored due to missing value of the outcome variable at the third time point.

Results

Descriptive statistics

Table 1 provides characteristics of our study sample. The majority of sample participants were aged 70-79 years with the average age of 76 years (standard deviation of 5.5). The sample had a range of education levels including 28% with less than a high school education. The ethno/racial composition included 87% non-Hispanic White participants. About 54% of respondents were female. Four health problems loaded significantly onto factor 1 in the factor analysis: diabetes, hypertension, cholesterol, and heart problems. Thirty-five percent of respondents had one chronic health problem of the comorbidity factor 1, 24% had 2 out of 4 conditions that were grouped into factor 1, 12% identified 3 comorbid conditions and 25% of respondents had none of these 4 conditions. About 10% of respondents had stroke and 22% had psychiatric problems at baseline.

Table 2 presents the results from the random intercept model including odds ratios from the three random-intercept ordinal logistic models. The first model included our comorbidity factor score as well as incidence of stroke and psychiatric condition at baseline. Factor score reflecting the co-existence of diabetes, hypertension, cholesterol and heart problems did not appear to be a significant predictor of the transitioning from normal to CIND and to dementia status (OR=0.92, 95% CI: 0.77-1.07); however, an incidence of stroke significantly predicted transition to dementia compared to normal. The odds of remaining in normal cognitive status (compared to CIND and dementia) were 56% lower for those who reported an incidence of stroke at baseline compared to those who did not experience a stroke incidence (OR=0.44). After adjusting for demographic variables in the second model, we observed a significant impact of education on the change on cognitive status (OR=1.10 per point increase in education level, range 1-18). Individuals with higher number of schooling years

Variables	Frequency (%)
Demographic	
Age (mean=76, SD=5.5)	
70-79 yrs	70
80-89 yrs	27
90 and above	3
Gender	
Female	55
Male	45
Education	
0-11 yrs	28
12 yrs	30
Above 12 yrs # of years (mean=11.6, SD=3.6)	42
Race/Ethnicity	
White	87
Non-White	13
Health Behavior	
Smoking	
Current	9
Ever	53
Drinking	25
Physical Exercise	44
Chronic health Conditions	
Hypertension	59
Diabetes	18
Cholesterol	42
Heart problems	34
Stroke	10
Psychiatric problems	22
Chronic conditions	
Chronic conditions Clusters[a]	
0-1 conditions	24
2 conditions	16
3-4 conditions	24
[a]The cluster includes: diabetes, hypertension, cholesterol and heart problems.	

Table 1: Descriptive of Study Sample at Baseline (N=308).

Variables	Model 1	Model 2	Model 3
Comorbidity cluster[a]	0.92 (0.93)	0.96 (0.41)	0.97(0.29)
Stroke	0.44 (2.31)*	0.44 (2.35)*	0.49(2.26)*
Psychiatric problem	0.97 (0.08)	0.88 (0.44)	0.92(0.30)
Time	0.54 (5.91)*	0.52 (6.16)*	0.51(6.29)*
Female	-	0.67 (1.95)*	0.73(1.51)
White	-	1.23 (0.79)	1.16(0.58)
Education	-	1.10 (3.00)*	1.10(3.08)*
Health risk behaviors	-	-	0.79(1.96)*
Constant 1	-4.4(13.28)*	-3.4(7.52)*	-2.34(6.02)*
Constant 2	-1.8(6.85)*	-0.81(1.94)	0.11(0.31)
Notes: [a]It is a interval measure indicating # of conditions present out of 4 clustered conditions (diabetes, hypertension, heart problems, and cholesterol), Absolute value of Z-statistics are shown in parentheses. *p ≤ 0.05.			

Table 2: Odds Ratios from the Random Effects Ordered Logistic Model (Dependent Variable=Disease status: 1=dementia; 2=CIND and 3=Normal).

completed were more likely to remain in the normal cognitive status. Result indicated that an increase in each year of schooling increases the likelihood of being in normal cognitive status by 10%. In the full model, which accounted for behavioral health risk factors, we found a significant association between the prevalence of higher number of health risk behaviors and lower odds of maintaining normal cognitive status (OR=0.79). We did not observe any significant impact of the co-existence of multiple chronic conditions (such as diabetes, hypertension, cholesterol and heart problems; OR=0.97, n.s.) on the deterioration of cognitive status over time.

Finally, recognizing the important potential role of CVD risk factors, we conducted a sub-analysis looking at the association with stroke. Based on one-way analysis of variance, the mean number of co-occurring cardiovascular risk factors is higher among persons with stroke relative to those without (F-value=11.50; $p<0.001$). This association may in part explain the lack of an independent effect of CVD in our primary model.

Discussion

The current study investigated the impact of co-existence of chronic health conditions on the longitudinal transition of cognitive status among older adults. We did not find evidence to support our hypothesis that co-existence of multiple chronic conditions (diabetes, hypertension, cholesterol and heart problems) influence the deterioration of cognitive function over time. The longitudinal association between stroke incident and cognitive decline, however, further confirmed the importance of primary prevention of stroke in prevention of cognitive decline over time. Although post-stroke dementia has been extensively examined, the decline in cognitive function among normal elderly and individuals with CIND has received less attention. We confirmed that incidence of stroke not only increases the risk of dementia, but also increases the risk of cognitive decline in the elderly.

The lack of significant finding regarding our primary hypothesis may reflect a lack of power, as our sample was small. If diabetes and cardiovascular conditions affect cognitive change through ischemic event, stroke incidence may explain much of the effect of these prevalent diseases on longitudinal decline in cognitive functioning [28]. Few studies have assessed the needed baseline data and longitudinal outcomes of cognitive status over a sufficient period of time. Evidence suggests that increased use of preventive treatments and reducing cardiovascular risk factors including hypertension, cholesterol and diabetes leads to decline in stroke incidence [29,30]. Ciccone et al. review suggests the mechanisms that may underlie the connection between prediabetes, cardiovascular disease, and stroke [31]. It has been well documented that diabetes is associated with increased risk of stroke [32]. According to the World Heart Federation, hypertension alone accounts for 50% of ischemic stroke incidence [33]. Furthermore, co-existence of diabetes and hypertension increases the risk of stroke twice compared to only hypertension. Protecting against cardiovascular risk factors leads to decline in stroke incidence significantly [4]. We found that mean number of co-existent cardiovascular risk factors is significantly higher for individuals with a history of stroke compared with those without. This observation implies that cardiovascular risk factors are likely to be responsible for the underlying mechanism or indirect pathway that increases the risk of cognitive decline attributed to stroke in this population.

The current study finds that strokes as well as risky lifestyle factors (smoking; drinking; sedentary habits) are significant predictors of cognitive decline over time. Since cardiovascular risk factors (such as diabetes, hypertension or high cholesterol) are likely to be associated with a stroke incident and also smoking and low physical activity level, the need for better management of cardiovascular risk factors may reduce the likelihood of stroke and hence prevent cognitive decline due to stroke incidence. Due to complexity of management of chronic cardiovascular disease, establishment of the care manager, as a bridge between patients and other medical specialists may improve clinical outcomes and prevent adverse health consequences [34]. For example, project Leonardo indicated that the presence of a care manager for patients with cardiovascular disease can offer positive impact on patient health and self-management. In this project care managers acted as key healthcare collaborators between patients and primary care physicians and hence offered opportunities for better clinical and health related outcomes [35]. Future research may consider these potentially important factors in preventing cognitive decline over time.

The main limitation of our study was the small sample size with measures of cognitive status in all three time points. Clearly, lack of disease status information of our 62 sample members decreased the likelihood of detecting effect of our 'comorbidity cluster' variable on the longitudinal decline in cognitive functioning. We did find, however, that this limitation was outweighed by an extensive assessment of cognitive performance measures by an expert team in conjunction with medical record history and clinical diagnosis mechanisms; these all increase the likelihood of accurate diagnosis of cognitive status in a national sample over the period of ten years. Another limitation is that due to retrospective nature of the study, causal inferences about cognitive decline cannot be established. Also, it is not possible to ascertain that clinical manifestation of cognitive decline occurred after the diagnosis of chronic disease and therefore comorbid conditions are indeed precursor of cognitive decline. This information would require having data on timing of clinical diagnosis of chronic conditions in this population, a goal for future researchers to target. However, The importance of this topic remains, and our limited findings underscore the imperative need for larger studies and wider use of brief assessments of cognitive status among geriatric patients, repeatedly over the many years of old age. With the rapidly increasing number of large health care systems using electronic medical record systems that can incorporate patient-reported outcomes and status measures such as cognitive functional status, we strongly advocate for identification of the most efficient yet accurate measures and for their inclusion in routine care visits.

In conclusion, we found no evidence of the influence of co-existence of multiple chronic conditions (especially cardiovascular risk factors) on longitudinal decline in cognitive status. However, incidence of stroke contributes independently to the longitudinal decline in cognitive status. Therefore we believe that prevention, early detection and appropriate management of cerebrovascular disease may ameliorate cognitive functioning among older adults.

Conflicts of Interest

The authors declare that there is no conflict of interest.

References

1. Plassman BL, Langa KM, Fisher GG (2007) Prevalence of dementia in the United States: the aging, demographics, and memory study. Neuroepidemiology 29: 125-132.

2. Hebert LE, Weuve J, Scherr PA, Evans DA (2013) Alzheimer disease in the United States (2010-2050) estimated using the 2010 Census. Neurology 80: 1778-1783.

3. Chertkow H, Massoud F, Nasreddine Z (2008) Diagnosis and treatment of dementia: 3. Mild cognitive impairment and cognitive impairment without dementia. CMAJ 178: 1273-1285.

4. Plassman BL, Langa KM, Fisher GG (2008) Prevalence of cognitive impairment without dementia in the United States. Ann Intern Med 148: 427-434.
5. Langa KM, Chernew ME, Kabeto MU (2001) National estimates of the quantity and cost of informal caregiving for the elderly with dementia. J Gen Intern Med 16: 770-778.
6. Lewin Group (2004) Saving Lives, Saving Money: Dividends for Americans for Investing in Alzheimer Research. A report commissioned by the Alzheimer's Association. Washington D.C.: Alzheimer's Association.
7. Alzheimer's Association (2012) Alzheimer's disease facts and figures. Alzheimers Dement 8: 131-168.
8. Koppel R (2014) Alzheimer's Disease: The Cost to U.S. Business in 2002.
9. Brookmeyer R, Gray S, Kawas C (1998) Projections of Alzheimer's Disease in the United States and the public health impact of delaying disease onset. Am J Public Health 88: 1337-1342.
10. Leon J, Cheng CK, Neuman PJ (1998) Alzheimer's disease care: cost and potential savings. Health Aff (Millwood) 17: 206-216.
11. Stefanacci RG (2011) The cost of Alzheimer's disease and the value of effective therapies. Am J Manag Care 13: S356-362.
12. Lopez OL, Jagust WJ, Dulberg C (2003) Risk factors for mild cognitive impairment in the Cardiovascular Health Study Cognition Study; part 2. Arch Neurol 60: 1394-1399.
13. Knopman D, Boland LL, Mosley T (2001) Cardiovascular risk factors and cognitive decline among middle-aged adults. Neurology 56: 42-48.
14. Kodl CT, Seaquist ER (2008) Cognitive dysfunction and diabetes millitus. Endoc Rev 29: 494-511.
15. Ivan CS, Seshardi S, Beiser A (2004) Dementia after stroke: the Framingham Study. Stroke 35: 1264-1268.
16. Vogeli C, Shield AE, Lee TA (2007) Multiple chronic conditions: prevalence, health consequences, and implications for quality, care management, and costs. J Gen Intern Med 3: 391-395.
17. Langa KM, Plassman BL, Wallace RL (2005) The Aging, Demographics, and Memory Study: study design and methods. Neuroepidemiology 25: 181-191.
18. Heeringa SG, Fisher GG, Hurd M (2007) Aging, Demographics and Memory Study(ADAMS): sample design, weighting, and analysis for ADAMS.
19. Crimmins EM, Kim JK, Langa KM, Weir DR (2011) Assessment of cognition using surveys and Neuropsychological Assessment: The Health and Retirement Study and the Aging, Demographics and Memory Study. J Gerontol B Psychol Sci Soc Sci 66: i162-i171.
20. American Psychiatric Association (1987) Diagnostic and Statistical Manual of Mental Disorders. Washington, DC: American Psychiatric Assoc.
21. American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders. Washington, DC: American Psychiatric Assoc.
22. McKhann G, Drachman D, Folstein M, Katzman R, Price D, et al. (1984) Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 34: 939-944.
23. Román GC, Tatemichi TK, Erkinjuntti T (1993) Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology 43: 250-260.
24. (1994) Clinical and neuropathological criteria for frontotemporal dementia. J Neurol Neurosurg Psychiatry 57: 416-418.
25. McKeith IG, Galasko D, Kosaka K (1996) Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology 47: 1113-1124.
26. Plassman BL, Havlik RJ, Steffens DC (2000) Documented head injury in early adulthood and risk of Alzheimer's disease and other dementias. Neurology 55: 1158-1166.
27. Breitner JC, Wyse BW, Anthony JC (1999) APOE-epsilon4 count predicts age when prevalence of AD increases, then declines: the Cache County Study. Neurology 53: 321-331.
28. Chodosh J, Miller-Martinez D, Aneshensel CS, Wight RG, Karlamangla AS (2010) Depressive symptoms, chronic diseases, and physical disabilities as predictors of cognitive functioning trajectories in older Americans. J Am Geriatr Soc 58: 2350-2357.
29. Lee S, Shafe AC, Cowie MR (2011) UK stroke incidence, mortality and cardiovascular risk management 1999-2008: time-trend analysis from the General Practice Research Database. BMJ Open 1: e000269.
30. Arboix A (2015) Cardiovascular risk factors for acute stroke: Risk profiles in the different subtypes of ischemic stroke. World J Clin Cases 3: 418-29.
31. Ciccone M, Scicchitano P, Cameli M (2014) Endothelial Function in Pre-diabetes, Diabetes and Diabetic Cardiomyopathy. J Diabetes 5: 364.
32. Air EL, Kissela BM (2007) Diabetes, the metabolic syndrome, and ischemic stroke: epidemiology and possible mechanisms. Diabetes Care 30: 3131-40.
33. (2015) World Heart Federation, Cardiovascular Disease Risk Factors.
34. Cecere A, Scicchitano P, Zito A (2014) Role of Care Manager in Chronic Cardiovascular Diseases. Ann Gerontol Geriatr Res 1.
35. Ciccone MM, Aquilino A, Cortese F (2010) Feasibility and effectiveness of a disease and care management model in the primary health care system for patients with heart failure and diabetes (Project Leonardo). Vasc Health Risk Manag 6: 297-305.

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