

# The effect of socioeconomic status on mortality among Alzheimer's disease patients

## A nationwide population-based cohort study in Korea

Young Choi<sup>a,b,\*</sup> 

### Abstract

To investigate the effects of household income level on all-cause mortality in patients with Alzheimer's disease (AD). Data was obtained from 7,937 participants in the Korean National Health Insurance cohort who was newly diagnosed with Alzheimer's disease using the anti-dementia medication between 2003 and 2013. All individuals were followed-up until December 2013 or death, whichever came first. Individual income was estimated from the national health insurance premium. Information on mortality was obtained from the Korean National Statistical Office. Cox proportional hazard models were used to compare mortality rates between different income groups after adjusting for possible confounding risk factors. Of 7937 participants, 2292 AD patients (28.9%) died. Those with low, middle-low, middle income level were likely to have more increasing risk of mortality (HR 1.142 [1.022–1.276], HR 1.211 [1.045–1.402], and HR 1.158 [1.009–1.328], respectively), compared to those with high income level. The findings of this study indicate that AD patients with low income level have higher risk for mortality. Promotion of targeted policies and priority support for these groups may help reduce the mortality rate in this vulnerable group.

**Abbreviations:** AD = Alzheimer's disease, ICD-10 = International Classification of Diseases, KNHICD = the Korean National Health Insurance Cohort Data, SES = socioeconomic status.

**Keywords:** all-cause mortality, Alzheimer's disease, socioeconomic status

### 1. Introduction

Alzheimer's disease (AD) is the most common form of dementia, which accounts for 60 to 80 percent of dementia cases.<sup>[1]</sup> It is a general term for memory loss and other intellectual abilities serious enough to interfere with daily life. With increasing ageing population, the prevalence of dementia is increasing rapidly worldwide.<sup>[2]</sup> The number of people worldwide with dementia is estimated to be 44 million in 2014, and this number is expected to almost double in 2030, triple in 2050.<sup>[3]</sup> In South Korea, the prevalence of AD was estimated to be 5.7% in 2008, and is expected to increase rapidly throughout the upcoming decades.<sup>[4]</sup> As the number of AD patients constantly rises, the economic burden of the disease on the society will grow, and increasing families and caregivers will suffer from the economic, enormous emotional and physical burden.<sup>[5]</sup> In particular, caregiver burden among low socioeconomic status (SES) is large such as economic factors including family income and family living with impaired older persons.<sup>[6,7]</sup>

AD is a leading cause of death to reduce the life expectancy.<sup>[8]</sup> People with dementia reportedly have decreased survival compared to those without.<sup>[9–12]</sup> Clinical experience and empirical

study suggest that dementia is a leading cause of death and shortens the lifespan of elderly patients.<sup>[13]</sup> In general, most studies found that increased age, male gender, decreased functional status, and medical comorbidities such as diabetes, cardiovascular disease, and malignancy were associated with a higher mortality rate in dementia patients.<sup>[11]</sup> However, few studies examined that how SES differ in these factors is less known.

The role of SES on health outcome is well documented in various disease.<sup>[14]</sup> Regarding to the AD patients, patients' education level showed mixed results of on survival. Alzheimer's disease patients with low economic status were susceptible to higher all-cause mortality, while more advanced educational and occupational attainment increased the mortality related to AD or dementia (so called 'brain reverse hypotheses').<sup>[15–17]</sup> Recently, socioeconomic inequalities for all-cause, and dementia mortality exists among the nonagenarians.<sup>[18]</sup> Moreover, although disparities in mortality in Asian countries exist, most disparities studies in health are more common in Western society.<sup>[19]</sup> The association between economic status and mortality among dementia patients in Asian country are sparse. In this context, we

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examined whether the household income level was associated with all-cause mortality and mortality caused by Alzheimer's mortality among dementia patients in South Korea via National health insurance cohort data from 2003 to 2013.

## 2. Methods

### 2.1. Data collection and participants

Data was acquired from the Korean National Health Insurance Cohort Data (KNHICD) from 2002 to 2013, which includes the information of approximately one million Korean people starting from 2002. The KNHICD is designed to create nationally representative cohort data on whole Korean population, trace their characteristics over time, reveal the epidemiologic cause of disease, and develop health policies. This cohort data used the 2.5% (n = 1,025,340) stratified random sampling method including age, sex, residences, health insurance type, household income decile (obtained by health insurance premium), and individual total medical costs based on 2002. This cohort data included information such as the unique de-identified number for each patient, age, sex, type of insurance, list of diagnoses according to the International Classification of Diseases (ICD-10), medical costs claimed, prescribed drugs. In addition, the unique de-identified number was linked to information on mortality obtained from the Korean National Statistical Office.

For this study, we conducted a cohort study of newly diagnosed patients with Alzheimer's disease between 2003 and 2013 to investigate the association between household income level and mortality. We adopted three criteria to select the newly diagnosed Alzheimer's disease; (1) patients with AD diagnoses (ICD-10 code: F00, G30) and (2) treated with at least one medication therapy (memantine, rivastigmine, galantamine, and donepezil). In addition, (3) initiation of treatment was defined as no use in the prior a year (i.e., excluded those who use medication in 2002) and, once initiated, continuous use for at least 3 months including the treatment-initiating month. Overall, among 1 025 340 enrollees of KNHIC, we selected 7,937 patients with a diagnosis of Alzheimer's disease (above criteria) from 2003 to 2013. The 12-month look-back period was intended to avoid potential bias in outcome and covariate measures originating from prevalent use of AD.<sup>[20]</sup> The 3-month continuous use criterion was commensurate with the minimum recommended treatment duration for geriatric use in clinical guidelines.<sup>[21,22]</sup>

### 2.2. Follow-up end points

All Individuals were observed from the diagnosis of AD through December 31, 2013 or until death, whichever came first.

### 2.3. SES (Household income)

We used the average monthly insurance premium as a proxy variable for household income. In Korea, the type of health insurance is classified as national health insurance or medical aid. Individuals qualify for medical aid if their household income is less than \$600 per month based on a single household. If the household income is more than \$600 per month, individuals qualify for national health insurance. Individuals who have national health insurance provided by their employer pay a monthly insurance premium according to annual salary, and those who are self-employed pay a premium according to property value. Individuals who qualified for the national health insurance were distributed between the 1st percentile and 100th percentile, and those who had medical aid were classified into the 0 percentile. We classified the household income into the following five groups: (1) low income group (Medical aid and below 20th percentile), (2) middle-low income group (21st–40th percentile), (3) middle income group (41st–60th percentile), (4)

middle-high income group (61st–80th percentile), and (5) high income group (81st–100th percentile).

### 2.4. Covariates

Demographic factors and co-morbidity were included in this study. Demographic factors included sex, type of insurance (health insurance or medical aid), and region (urban or rural). The comorbidities of the AD patients were identified by reviewing their medical history 1 year before the initiation of medication use. The specific ICD codes were as follows: hypertension, I.10–I.15; diabetes, E.10–E.14; hypercholesterolemia, E.78; cerebral infarction, I.63; Mood disorder, F3; and cancer, C.x-D.x.

To adjust the severity of patients, we included the modified barthel index (MBI) and length of stay. The degree of disability was assessed using the Modified Barthel Index. The Barthel score was originally used for assessing the ability of patients to perform activities of daily living after a stroke.<sup>[23]</sup> It has since been widely applied for elderly patients including those with dementia.<sup>[24]</sup> The score ranges from 0 (worst) to 100 (best) and enables patients to be categorized into groups reflecting their degree of disability.<sup>[25]</sup> In this study, those who gained  $\leq 24$  is severe, those who gained  $> 24$  is mild. We calculated the in-patient length of stay rate from the diagnosis of AD to the end of study. The denominator is each individual's follow-up period. The numerator is days of hospitalization during the each individual's follow-up period. We then classified into four categories ( $\leq 24$ , 25–29, 50–74, and  $\geq 75$  %). Additionally, we included the type of hospital at initial diagnosis of dementia (General hospital and hospital /clinic).

### 2.5. Statistical analyses

We calculated the distribution of the general characteristics of patients initiating anti medication therapy. Pearson chi-square test was conducted to compare income groups. Relationships among income level and all-cause mortality were analyzed using time-to-event methods. Kaplan-Meier curves were generated, and a log-rank test was used for comparison of unadjusted kidney transplantation rates. To examine whether income differences existed among those patients with mortality and Alzheimer's mortality (ICD-10 code: F00, G30), multivariable analyses were conducted using Cox proportional hazards models to calculate adjusted hazard ratios (plus 95% confidence limits) as an estimate of the relative rate of mortality. The proportionality assumption was tested by examining curves of log (–log [survivor function]) versus time. A value of  $P < .05$  was taken to indicate statistical significance. All statistical analyses were conducted using the SAS software package (ver. 9.4; SAS Institute, Cary, NC).

### 2.6. Ethical approval

This study adhered to the tenets of the Declaration of Helsinki. The study design was reviewed and approved by the ethical review board at the Graduate School of Public Health in Yonsei University (2–1040939-AB-N-01–2014–239). Since our study used administrative cohort data, the requirement for informed consent was waived as the KNHICD was constructed after anonymization according to strict confidentiality guidelines.

## 3. Results

Overall, Of 7937 participants, 2292 AD patients (28.9%) died during the course of this study. The median survival time is 6.5 years for AD patients. Table 1 presents general characteristics of the patients initiating medication use between 2003 and 2013. Of the 7937 participants, 2032 (25.6%), 719 (9.1%), 942

**Table 1**  
**Socio-demographic characteristics of study participants at diagnosis of AD (2003–2013).**

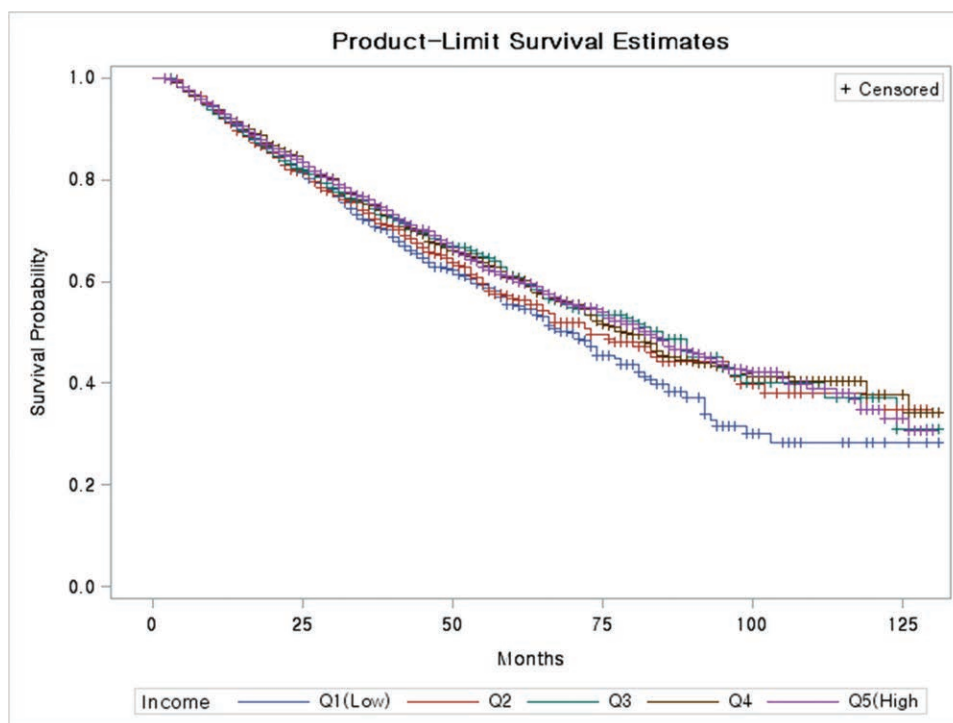
Variable	N	%	Mortality			
			Yes		No	
			N	%	N	%
Total	7937		2292	28.9	5645	71.1
Income						
Q1(Low)	2032	25.6	543	26.7	1489	73.3
Q2(Mid-low)	719	9.1	228	31.7	491	68.3
Q3(Middle)	942	11.9	271	28.8	671	71.2
Q4(Mid-high)	1313	16.5	383	29.2	930	70.8
Q5(High)	2931	36.9	867	29.6	2064	70.4
Sex						
Male	2389	30.1	880	36.8	1509	63.2
Female	5548	69.9	1412	25.5	4136	74.5
Age						
<59	233	2.9	22	9.4	211	90.6
60–69	1049	13.2	187	17.8	862	82.2
70–79	3326	41.9	852	25.6	2474	74.4
80–	3329	41.9	1231	37.0	2098	63.0
City						
Rural	3313	41.7	978	29.5	2335	70.5
Urban	4624	58.3	1314	28.4	3310	71.6
Disability(brain lesions)*						
Normal	7440	93.7	2128	28.6	5312	71.4
Mild (3–6)	206	2.6	53	25.7	153	74.3
Serious (1–2)	291	3.7	111	38.1	180	61.9
Hypertension						
No	2636	33.2	785	29.8	1851	70.2
Yes	5301	66.8	1,507	28.4	3794	71.6
Diabetes mellitus						
No	5056	63.7	1,489	29.5	3567	70.5
Yes	2881	36.3	803	27.9	2078	72.1
Hypercholesterolemia						
No	4764	60.0	1,637	34.4	3127	65.6
Yes	3173	40.0	655	20.6	2518	79.4
Cerebral infarction						
No	5738	72.3	1,615	28.1	4123	71.9
Yes	2199	27.7	677	30.8	1522	69.2
Mood disorder						
No	5132	64.7	1,571	30.6	3561	69.4
Yes	2805	35.3	721	25.7	2084	74.3
Cancer						
No	7068	89.1	2032	28.7	5036	71.3
Yes	869	11.0	260	29.9	609	70.1
Mood disorder						
No	5132	64.7	1571	30.6	3561	69.4
Yes	2805	35.3	721	25.7	2084	74.3
Chronic pulmonary disease						
No	5524	69.6	1613	29.2	3911	70.8
Yes	2413	30.4	679	28.1	1734	71.9
Renal disease						
No	7716	97.2	2198	28.5	5518	71.5
Yes	221	2.8	94	42.5	127	57.5
Length of stay during the follow-up period						
<=24%	6139	77.4	1588	25.9	4551	74.1
25–49%	623	7.9	244	39.2	379	60.8
50–75%	359	4.5	134	37.3	225	62.7
>=75%	816	10.3	326	40.0	490	60.0
Type of hospital at first described						
General hospital	3996	50.4	1006	25.2	2990	74.8
Hospital and clinic	3941	49.7	1286	32.6	2655	67.4

\*The degree of disability is defined as the Modified Barthel Index; those who gained <=24 is severe, those who gained >24 is mild, those who gained >94 is normal.

(11.9%) 1,313 (16.5%), and 2,931(36.9%) were included in the low, mid-low, middle, mid-high, and high-income groups, respectively. Among the 2292 AD patients who died, proportions were higher for male, older, those who lived in rural areas, and those who had longer length of stay during the follow-up period.

Figure 1 displays the Kaplan-Meier survival curves according to the income groups. There were differences in survival rates according to the income levels of the patients with AD (log rank  $P < .0326$ ).

Table 2 lists patients' characteristics according to the income level. Among AD patients, low income groups were more likely



**Figure 1.** Kaplan-Meier survival curves according to the income groups.

to have serious brain disabilities; 4.2% of the low income group had severe kidney disabilities, compared to 3.1% of the highest income group.

Table 3 lists the results of Cox proportional hazards analysis, which assessed the association between income level and mortality among AD patients. Even after adjusting for potential factors for mortality, we found that lower patients were likely to have higher mortality rate. Compared to the high income group, lower income patients had a higher rate of mortality (low, HR = 1.142, CI: 1.022, 1.276; mid-low, HR = 1.211, CI: 1.045, 1.402; middle, HR = 1.158, CI: 1.009, 1.328; and mid-high, HR = 1.094, CI: 0.969, 1.235). Among the AD patients, male, older, and those who had severe disability were more likely to have higher risk of mortality, and those who had longer length of stay were likely to have increasing mortality risk. Regarding comorbidity, those who had diabetes mellitus, cerebral infarction, cancer, renal disease was likely to have higher risk of mortality.

Supplementary Digital Content Table 1, <http://links.lww.com/MD2/B84> shows the results of Cox proportional hazards analysis, which assessed the association between income level and mortality caused by Alzheimer's disease among AD patients. Mortality caused by Alzheimer's disease were likely to be higher in middle and mid-high income groups compared to the high income group, although the findings were not significant (middle, HR = 1.140, CI: 0.820, 1.584; and mid-high, HR = 1.030, CI: 0.969, 1.235).

#### 4. Discussion

This population-based study examined the association between household income and all-cause mortality among Alzheimer's disease patients in Korea using the KNHICD. Based on our results, men, those who are older persons, those who are lived in rural area, those with severe disability are more likely to have higher mortality rate. Regarding to the comorbidity, our result showed that various comorbidities is associated with higher mortality, consistent with other studies,<sup>[26,27]</sup> such as those who had comorbidities including hypertension, diabetes mellitus,

renal disease, and cancer are more likely to have higher mortality rate. We found that lower income level had higher all-cause mortality rate, after adjusting for potential confounding factors.

Previous studies showed the mixed result of the effect of SES on the all-cause mortality. The influence of education is inconsistent, with some reports of increased mortality with lower levels of education,<sup>[10]</sup> while others report no such relation<sup>[28]</sup> or even the reverse.<sup>[29]</sup> One case control study found an association between higher education and increased mortality.<sup>[30]</sup> Other studies found that those dementia patients with lower education had increased mortality,<sup>[29,31]</sup> which is consistent with data demonstrating an association between lower education and increased mortality in non-demented populations.<sup>[32]</sup> Our results supported that the low economic status was associated with a higher mortality rate. The possible explanation of our results included the feature of those with low economic status. When it comes to the socio-economic status, those with low income level had more severity, and longer inpatients days during the follow-up period, while those with high income level had less severity and shorter inpatients days. Given that the higher risk among institutionalized patients reflects that comorbidity and disability have been reported to increase mortality after dementia diagnosis,<sup>[9,33,34]</sup> low economic status patients are vulnerable to higher risk of mortality.

Additionally, those with low economic status are diagnosed from the hospital/clinic the first diagnosis of AD. Our results implicated that low SES patients suffer from early recourse to care, as a proxy of the recourse of care for dementia at the first diagnosis. A French cohort of demented patients recruited in a memory clinic suggested that the shorter the time between first symptoms and first specialized consultation, the longer the patients survived, although the reliability of information about time of first symptoms onset is questionable.<sup>[35]</sup> Recent study suggested that the early recourse to care for dementia play an important role of survival.<sup>[15]</sup> These studies suggested that the worse survival of diagnosed dementia patients could be explained by a delayed access to care that could occur at the time of complications.

**Table 2**  
**General characteristics of study participants according to the income groups.**

Variables	N	Q1(Low)		Q2		Q3		Q4		Q5(High)	
		N	%	N	%	N	%	N	%	N	%
Total	7937	2032		719		942		1313		2931	
Sex											
Male	2389	482	23.7	215	29.9	286	30.4	432	32.9	974	33.2
Female	5548	1550	76.3	504	70.1	656	69.6	881	67.1	1957	66.8
Age											
-59	233	78	3.8	43	6.0	31	3.3	39	3.0	42	1.4
60-69	1049	240	11.8	98	13.6	163	17.3	232	17.7	316	10.8
70-79	3326	767	37.7	282	39.2	383	40.7	536	40.8	1358	46.3
80-	3329	947	46.6	296	41.2	365	38.7	506	38.5	1215	41.5
City											
Rural	3313	1022	50.3	310	43.1	381	40.4	548	41.7	1052	35.9
Urban	4624	1010	49.7	409	56.9	561	59.6	765	58.3	1879	64.1
Disability(brain lesions)*											
Normal	7440	1887	92.9	684	95.1	878	93.2	1220	92.9	2771	94.5
Mild (3-6)	206	59	2.9	19	2.6	24	2.5	36	2.7	68	2.3
Serious (1-2)	291	86	4.2	16	2.2	40	4.2	57	4.3	92	3.1
Hypertension											
No	2636	685	33.7	263	36.6	284	30.1	446	34.0	958	32.7
Yes	5301	1347	66.3	456	63.4	658	69.9	867	66.0	1973	67.3
Diabetes mellitus											
No	5056	1348	66.3	486	67.6	575	61.0	822	62.6	1825	62.3
Yes	2881	684	33.7	233	32.4	367	39.0	491	37.4	1106	37.7
Hyperlipidemia											
No	4764	1299	63.9	462	64.3	548	58.2	765	58.3	1690	57.7
Yes	3173	733	36.1	257	35.7	394	41.8	548	41.7	1241	42.3
Cerebral infarction											
No	5738	1511	74.4	522	72.6	668	70.9	927	70.6	2110	72.0
Yes	2199	521	25.6	197	27.4	274	29.1	386	29.4	821	28.0
Cancer											
No	7068	1853	91.2	649	90.3	844	89.6	1188	90.5	2534	86.5
Yes	869	179	8.8	70	9.7	98	10.4	125	9.5	397	13.5
Mood disorder											
No	5132	1402	69.0	465	64.7	609	64.6	816	62.1	1840	62.8
Yes	2805	630	31.0	254	35.3	333	35.4	497	37.9	1091	37.2
Chronic pulmonary disease											
No	5524	1449	71.3	495	68.8	658	69.9	908	69.2	2014	68.7
Yes	2413	583	28.7	224	31.2	284	30.1	405	30.8	917	31.3
Renal disease											
No	7716	1973	97.1	704	97.9	930	98.7	1272	96.9	2837	96.8
Yes	221	59	2.9	15	2.1	12	1.3	41	3.1	94	3.2
Length of stay during the follow-up period											
<=24%	6139	1442	71.0	569	79.1	763	81.0	1028	78.3	2337	79.7
25-49%	623	178	8.8	60	8.3	61	6.5	116	8.8	208	7.1
50-75%	359	125	6.2	21	2.9	41	4.4	52	4.0	120	4.1
>=75%	816	287	14.1	69	9.6	77	8.2	117	8.9	266	9.1
Type of hospital at first described											
General hospital	3996	812	40.0	372	51.7	491	52.1	699	53.2	1622	55.3
Hospital and clinic	3941	1220	60.0	347	48.3	451	47.9	614	46.8	1309	44.7

\*The degree of disability is defined as the Modified Barthel Index; those who gained <=24 is severe, those who gained >24 is mild, those who gained >94 is normal.

In a broad approach, studies have suggested that there are multiple reasons for socioeconomic inequality in health or mortality: poor health behaviors, material deprivation, psychosocial attributes, early life exposure, biological risk factors, and late recognition of the disease.<sup>[36,37]</sup> Several plausible mechanisms may explain why patients of low SES have high all-cause mortality rates. A Korean study suggested that individuals of low SES have high morbidity rates, low health status, and negative behaviors such as smoking, drinking alcohol, and irregular exercise.<sup>[38]</sup> These findings indicate that individuals of low SES are susceptible to having high mortality rates. In addition, low awareness of AD may contribute to the high mortality rates in individuals of low SES.

The strengths of this study are its population-based design and data collection from the KNHICD, which is nationally representative. Additionally, using the unique personal identity number

of each Korean resident and linking it to the national mortality data, follow-up was completed. Despite these strengths, several limitations should be considered. First, the administrative data are subject to possible coding errors and under- or over-coding problems. However, claims data have low sensitivity and high specificity for dementia diagnoses,<sup>[39]</sup> and we attempted to select the AD patients by using the combined diagnosis (i.e., the newly use of medication and ICD-10 code).<sup>[40]</sup> Therefore, we try to minimize under or overestimation from using single source will underestimate the diagnosis of AD. Second, this study might suffer from certain inherent limitations because of the use of administrative data, which lack information on dementia severity. However, this data include the degree of disability (Brain lesion) measured the Modified bethel index. It has since been widely applied for elderly patients including those with dementia,<sup>[24]</sup> even though it was originally used for assessing the ability

**Table 3**  
**Results of the Cox proportional hazard model, adjusted hazard ratio for survival.**

Variables	HR		95% CI	P-value
Income				
Q1(Low)	1.142	1.022	1.276	.0187
Q2(Mid-low)	1.211	1.045	1.402	.0108
Q3(Middle)	1.158	1.009	1.328	.0366
Q4(Mid-high)	1.094	0.969	1.235	.1447
Q5(High)	1.000			
Sex				
Male	1.938	1.776	2.116	
Female	1.000			
Age				
<59	1.000			
60-69	2.011	1.291	3.132	.002
70-79	3.939	2.573	6.032	
80-	7.725	5.045	11.83	
City				
Rural	1.055	0.969	1.149	.2144
Urban	1.000			
Disability(brain lesions)*				
Normal	1.000			
Mild	1.209	0.916	1.595	.1812
Severe	1.279	1.05	1.557	.0143
Hypertension				
No	1.000			
Yes	1.074	0.979	1.178	.1329
Diabetes mellitus				
No	1.000			
Yes	1.115	1.015	1.224	.0229
Hyperlipidemia				
No	1.000			
Yes	0.719	0.653	0.792	
Cerebral infarction				
No	1.000			
Yes	1.102	1.002	1.212	.0459
Cancer				
No	1.000			
Yes	1.24	1.085	1.416	.0016
Mood disorder				
No	1.000			
Yes	0.907	0.828	0.992	.0331
COPD				
No	1.000			
Yes	1.044	0.952	1.144	.3619
Renal disease				
No	1.000			
Yes	2.106	1.706	2.601	
Length of stay during the follow-up period				
<=24%	1.000			
25-49%	1.164	1.015	1.334	.03
50-75%	1.217	1.018	1.456	.0314
>=75%	1.447	1.281	1.634	
Type of hospital at first described				
General hospital	1.000			
Hospital and clinic	1.457	1.332	1.593	

\*The degree of disability is defined as the Modified Barthel Index; those who gained <=24 is severe, those who gained >24 is mild, those who gained >94 is normal.

of patients to perform activities of daily living after a stroke.<sup>[2,3]</sup> Third, although we used nationally representative data with a long follow-up period, it is necessary to conduct additional research using data including the most recent year since the observation period for this data ended in 2013. Finally, this study used household income estimated from the health insurance premium instead of actual income or education. Thus, we could not fully reflect the various type of SES. However, given that the education attainment is strong associated with income level,<sup>[41]</sup> and the insurance premium is determined by the income, our results may explain inequality of survival among AD patients.

## 5. Conclusion

The findings indicate that AD patients with low incomes have high mortality rates in Korea. Promotion of targeted policies and priority health services for patients with low incomes may help reduce the mortality rate in this vulnerable group.

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## Author contributions

YC designed the study, analyzed the data, and wrote the draft. YC performed the literature review and interpretation for data analysis. All authors read and approved the final manuscript.

Conceptualization: Young Choi.

Data curation: Young Choi.

Investigation: Young Choi.

Methodology: Young Choi.

Writing – original draft: Young Choi.

Writing – review & editing: Young Choi.

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