




Dementia Is Associated With Earlier Mortality for Men and Women in the United States

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Abstract

Objectives: Sociodemographic trends in the United States may influence future dementia-associated mortality, yet there is little evidence about their potential impact. Our study objective was to estimate the effect of dementia on survival in adults stratified by sex, education, and marital status. **Methods:** Using survey data from the Health and Retirement Study (HRS) linked to Medicare claims from 1991 to 2012, we identified a retrospective cohort of adults with at least one International Classification of Diseases—ninth revision—Clinical Modification (ICD-9-CM) dementia diagnosis code ($n = 3,714$). For each case, we randomly selected up to five comparators, matching on sex, birth year, education, and HRS entry year ($n = 9,531$), and assigned comparators the diagnosis date of their matched case. Participants were followed for up to 60 months following diagnosis. We estimated a survival function for the entire study population and then within successive strata defined by sex, education, and marital status. **Results:** On average, dementia cases were 80.5 years old at diagnosis. Most were female, had less than college-level education, and approximately 40% were married at diagnosis. In multivariate analyses, dementia diagnosis was associated with earlier mortality for women (predicted median survival of 54.5 months vs. 62.5 months; dementia coefficient = -0.13 ; 95% confidence interval [CI] = $[-0.22, -0.04]$; $p = .003$), but even more so among men (predicted median survival of 35.5 months vs. 54.5 months; dementia coefficient = -0.42 ; 95% CI = $[-0.52, -0.31]$; $p < .001$). We found substantial heterogeneity in the relationship between dementia and survival, associated with both education and marital status. **Conclusion:** Both sex and level of education moderate the relationship between dementia diagnosis and length of survival.

Keywords

dementia, survival, mortality, sociodemographics

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Key Points

Our findings suggest that sex and education are important modifiers of the relationship between dementia diagnosis and length of survival, with a stronger association between diagnosis and earlier mortality observed among men and individuals with higher educational attainment. Our findings highlight the necessity of accounting for dynamic population sociodemographic characteristics when generating predictions about future dementia-associated costs and mortality.

(Trovato & Heyen, 2006). Educational achievement has also increased, with the percent of the adult population with at least a bachelor's degree rising from 20.3% in 1990 to 32.5% in 2015 (Ryan & Bauman, 2016); higher levels of educational attainment have been particularly stark among women (Fry et al., 2018). Adults turning 65 years of age in this decade are also less likely to have ever been married and 3 times more likely to be divorced than prior generations (Stepler, 2017).

Introduction

The sociodemographic profile of the United States has shifted dramatically over the past few decades. Age-adjusted mortality rates decreased from 938 deaths per 100,000 people in 1990 to 733 per 100,000 people in 2015 (Bastian et al., 2019), and the mortality gap that favored females over males has narrowed in recent years

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These sociodemographic trends may have important implications for future dementia-associated mortality, yet there is little evidence about their potential impact. Most prior studies of sociodemographic factors and dementia have focused on how these factors influence a person's lifetime risk of developing dementia, with findings indicating a higher lifetime risk for women, people with lower levels of educational attainment, and people who are widowed or have never married compared with people who are married (Breteler et al., 1998; Mehta & Yeo, 2017; Meng & D'Arcy, 2012; Mielke et al., 2014; Podcasy & Epperson, 2016; Sommerlad et al., 2018). Some prior studies have also focused on how sociodemographic factors influence survival among people diagnosed with dementia. Results from these studies have been inconsistent with respect to level of educational attainment, but have demonstrated an increased risk of mortality among men with dementia compared with women with dementia (Mayeda et al., 2017; Meng & D'Arcy, 2012; Paradise et al., 2009; Podcasy & Epperson, 2016; Todd et al., 2013). To our knowledge, no studies have examined the influence of marital status on survival among people with dementia.

Very few studies, however, have examined the effect of a diagnosis of dementia on length of survival among people with differing sociodemographic characteristics (Ganguli et al., 2005; Langa et al., 2008; Mayeda et al., 2017; Vassilaki et al., 2015). Even fewer studies explore how these sociodemographic factors interact to influence dementia-associated mortality. To address these limitations, we used a large, population-based sample to estimate the effect of a dementia diagnosis on length of survival among older adults stratified by sex, education, and marital status.

Method

Using survey data from the Health and Retirement Study (HRS) linked to Medicare Part A and B claims from 1991 to 2012, we identified a retrospective cohort of adults with at least one International Classification of Diseases—ninth revision—Clinical Modification (ICD-9-CM) dementia diagnosis code ($n = 3,714$) (codes provided in Table 1 of Supplemental Materials). Inclusion criteria were enrollment in Medicare fee-for-service coverage for at least 12 months prior to and 1 month following the date of their first qualifying dementia diagnosis code. For each dementia case, we randomly selected up to five comparators after matching on sex, birth year, education (less than high school, high school graduate, some college, and college and above), and HRS entry year ($n = 9,531$). Comparison group participants met the same Medicare enrollment criteria as dementia cases and had no dementia diagnosis themselves or for their spouse prior to or within 6 years of the diagnosis date of their matched case. Comparison group participants were assigned the diagnosis date of their matched case to allow for an examination of equivalent time periods. Participants were

followed for up to 60 months following diagnosis to assess time to death, as determined from the claims data. 18% of our 13,245 participants were censored prior to 60 months due to survival beyond December 31, 2012, the endpoint of our data. Participants provided verbal informed consent to the survey. Study procedures were approved by the Institutional Review Board at the University of Washington.

To estimate the effect of dementia on length of survival, we use an accelerated failure time model with log-normal time distribution (Orbe et al., 2002). The model was estimated multiple times; first within the entire study population and then within successive strata defined by sex, education, and marital status. To aid interpretation of model coefficients, we used the method of recycled predictions to generate survival estimates with and without dementia (Basu & Meltzer, 2005). Counterfactual predictions for length of survival without dementia were made by “turning off” the dementia indicator among patients with dementia and predicting their survival probabilities over time. Thus, survival estimates were generated using only the predictions made for dementia cases to guarantee the same distributions and types of individual characteristics. Models adjusted for age at diagnosis, sex, self-reported race, education, marital status at diagnosis, quartile of total Medicare part A and B expenditures in the 12 months prior to diagnosis, and separate indicators for all chronic conditions included in the Centers for Medicare and Medicaid Services' chronic condition warehouse. We conducted all analyses in Stata 15 (StataCorp LP, College Station, TX, USA).

Results

Individuals with dementia had a mean age of 80.5 years ($SD 7.6$) at the time of diagnosis (Table 1), 79.1 years ($SD 7.5$), and 81.3 years ($SD 7.6$) among male and female cases, respectively (Table 2 of Supplemental Materials). A smaller proportion of dementia cases were non-Hispanic White (75.5% vs. 78.4%) and were married (39.7% vs. 48.1%) than the matched comparison group. Cases also had a greater number of comorbid chronic medical conditions than the comparison group in the 12 months prior to diagnosis.

In multivariate analyses, dementia diagnosis was associated with earlier mortality among all participants (dementia coefficient = -0.25 ; 95% confidence interval [CI] = $[-0.31, -0.18]$; $p < .001$); median survival among participants with dementia was 46.5 months and predicted median survival without dementia was 59.5 months. Stratified analyses revealed heterogeneity in this relationship, correlated with sex, education, and marital status.

Among men (Table 2), dementia diagnosis was associated with earlier mortality (dementia coefficient = -0.42 ; 95% CI = $[-0.52, -0.31]$; $p < .001$), resulting in a median survival time that was 19 months shorter than predicted without dementia. This association between dementia and earlier mortality persisted when stratified

Table 1. Characteristics of Dementia Cases and Controls.

Characteristics	Dementia cases (n = 3,714)	Controls (n = 9,531)	p value
Sociodemographic characteristics			
Age at diagnosis in years, mean (SD)	80.5 (7.6)	77.3 (7.3)	<.001
Male, no. (%) ^a	1,385 (37.3)	3,905 (41.0)	<.001
Race, no. (%)			<.001
Non-Hispanic White	2,803 (75.5)	7,474 (78.4)	
Non-Hispanic Black	611 (16.5)	1,299 (13.6)	
Hispanic	245 (6.6)	616 (6.5)	
Non-Hispanic other	55 (1.5)	142 (1.5)	
Marital status at diagnosis, no. (%)			<.001
Married	1,474 (39.7)	4,585 (48.1)	
Separated/divorced	271 (7.3)	759 (8.0)	
Widowed	1,663 (44.8)	3,452 (36.2)	
Never married	113 (3.0)	300 (3.2)	
Unknown marital status	193 (5.2)	435 (4.6)	
Educational attainment, no. (%)			.007
Less than high school	1,560 (42.0)	3,714 (39.0)	
High school graduate	1,201 (32.3)	3,231 (33.9)	
Some college	523 (14.1)	1,484 (15.6)	
College and above	430 (11.6)	1,102 (11.6)	
Health characteristics at baseline^b			
Comorbid conditions, no. (%)			
Anemia	1,428 (38.5)	1,806 (19.0)	<.001
Arthritis	1,353 (36.4)	2,396 (25.1)	<.001
Asthma	153 (4.1)	326 (3.4)	.053
Atrial fibrillation	517 (13.9)	741 (7.8)	<.001
Cancer	385 (10.4)	904 (9.5)	.124
Cataracts/glaucoma	1,142 (30.8)	3,107 (32.6)	.040
Chronic kidney disease	622 (16.8)	826 (8.7)	<.001
Chronic obstructive pulmonary disease	740 (19.9)	1,225 (12.9)	<.001
Depression	796 (21.4)	544 (5.7)	<.001
Diabetes	1,144 (30.8)	2,290 (24.0)	<.001
Heart failure	1,242 (33.4)	1,825 (19.2)	<.001
Hip/pelvic fracture	97 (2.6)	66 (0.7)	<.001
Hyperlipidemia	1,166 (31.4)	2,978 (31.3)	.868
Hypertension	2,569 (69.2)	4,910 (51.5)	<.001
Hypothyroidism	536 (14.4)	948 (10.0)	<.001
Ischemic heart disease	1,752 (47.2)	3,242 (34.0)	<.001
Osteoporosis	344 (9.3)	460 (4.8)	<.001
Prostatic hyperplasia	270 (7.3)	508 (5.3)	<.001
Stroke/transient ischemic attack	647 (17.4)	331 (3.5)	<.001
No. of comorbid conditions, mean (SD)	4.6 (2.6)	3.1 (2.3)	<.001
No. of conditions diagnosed during baseline year, mean (SD)	1.0 (1.3)	0.6 (1.0)	<.001
Total expenditures in 2018 (US\$), mean (SD)	17,454 (29,944)	8,871 (19,148)	<.001

Note. SD = standard deviation; no. = number.

^aPercentages may not add up to 100% due to rounding. ^bThe baseline period was defined as the 12 months prior to the diagnosis date.

by education (Figure 1). However, the association was much stronger among men with higher educational attainment; median survival with dementia was 52 months shorter among college-educated men and only 9 months shorter among men with a high school diploma or less. Additional stratification by marital status revealed the association between dementia and earlier mortality was stronger within strata of men who were

married at the time of diagnosis, regardless of level of education. It should be noted, however, that age at diagnosis was higher for males who were not married (80.2 vs. 78.6 years of age).

Among women (Table 2), dementia diagnosis was associated with earlier mortality (dementia coefficient = -0.13; 95% CI = [-0.22, -0.04]; $p = .003$) such that median survival time was only 8 months shorter than

Table 2. Adjusted Associations Between Dementia and Length of Survival.

Strata	Coefficient (95% CI)	p value	Estimated median survival with dementia (months)	Estimated median survival without dementia (months)
Men (n = 5,290)	-0.42 [-0.52, -0.31]	<.001	35.5	54.5
Less than college (n = 3,719)	-0.28 [-0.39, -0.16]	<.001	34.5	45.5
Any college (n = 1,571)	-0.83 [-1.05, -0.61]	<.001	39.5	91.5
Less than college and married (n = 2,425)	-0.38 [-0.53, -0.23]	<.001	39.5	58.5
Less than college and not married (n = 1,108)	-0.04 [-0.24, 0.15]	.673	29.5	30.5
Any college and married (n = 1,175)	-0.94 [-1.19, -0.68]	<.001	41.5	105.5
Any college and not married (n = 315)	-0.66 [-1.15, -0.17]	.008	41.5	80.5
Women (n = 7,955)	-0.13 [-0.22, -0.04]	.003	54.5	62.5
Less than college (n = 5,987)	-0.09 [-0.19, 0.01]	.066	51.5	56.5
Any college (n = 1,968)	-0.27 [-0.44, -0.09]	.003	67.5	88.5
Less than college and married (n = 1,712)	-0.39 [-0.62, -0.16]	.001	68.5	100.5
Less than college and not married (n = 3,992)	-0.01 [-0.12, 0.10]	.852	47.5	47.5
Any college and married (n = 747)	0.06 [-0.27, 0.40]	.712	113.5	106.5
Any college and not married (n = 1,143)	-0.38 [-0.59, -0.16]	.001	52.5	76.5

Note. CI = confidence interval.

predicted without dementia. Similar to the findings among men, stratification by level of education indicated moderation by education in the relationship between dementia diagnosis and length of survival (Figure 1). Among women with a high school diploma or less, dementia diagnosis was not associated with earlier mortality. However, the association between dementia and earlier mortality persisted in women with any college-level education (dementia coefficient = -0.27 ; 95% CI = $[-0.44, -0.09]$; $p = .003$). Additional stratification by marital status revealed inconsistent patterns. Among women with a high school diploma or less, dementia diagnosis was associated with earlier mortality only within the stratum of women who were married at the time of diagnosis. In contrast, among women with any college-level education, dementia diagnosis was associated with earlier mortality only within the stratum of women who were not married at the time of diagnosis. Similar to the finding among men, age at diagnosis was higher for females who were not married (82.4 vs. 78.1 years of age).

Discussion

Overall, our findings suggest that sex is an important modifier of the relationship between dementia diagnosis and length of survival, with a stronger association between diagnosis and earlier mortality observed among men. This result is consistent with Vassilaki et al. (2015) in a study of mild cognitive impairment and mortality, but differs from Ganguli et al. (2005) who found an increased risk of dementia-related mortality only among women. Differences between our study samples and definitions of dementia onset (diagnosis compared with symptomatic onset) could be driving the differences in our findings (Ganguli et al., 2005).

Women have a significantly higher risk of Alzheimer's disease, the most common type of dementia, though

men have a higher risk of vascular dementia, dementia with Lewy bodies, and Parkinson disease dementia (Mielke et al., 2014; Podcasy & Epperson, 2016). Significant differences between the sexes in disease progression have also been demonstrated, with more rapid cognitive decline and shorter survival time in men. These differences in dementia risk and outcomes have been attributed to sex differences in brain development, risk factors for dementia, and health behaviors (Podcasy & Epperson, 2016). It is possible that the association between dementia diagnosis and earlier mortality was less robust among women in our study because of their relatively later age at diagnosis and longer survival duration, such that they faced relatively more competing mortality risks than men. In prior studies, the magnitude of lower survival duration associated with dementia was smaller with advanced age of onset (Larson et al., 2004; Todd et al., 2013).

Our results also suggest that education moderates the relationship between dementia and length of survival. In a study of cognitive impairment and mortality, Langa et al. (2008) demonstrated a similar interaction between cognitive impairment and education, though they did not examine the effect separately by sex.

Higher educational attainment is associated with a decreased risk of dementia (Meng & D'Arcy, 2012). Possible mechanisms include healthier behaviors, increased access to resources and opportunities that are beneficial to health, and improved brain functioning such that clinical manifestations of neurodegenerative processes are delayed (known as the cognitive reserve hypothesis) (Langa et al., 2008). Consistent with the cognitive reserve hypothesis, some studies have also found that cognitive decline occurs more rapidly after a dementia diagnosis among those with higher educational attainment, since neurodegenerative processes are more advanced when clinically detected (Langa et al., 2008; Meng & D'Arcy, 2012; Teri et al., 1995). More

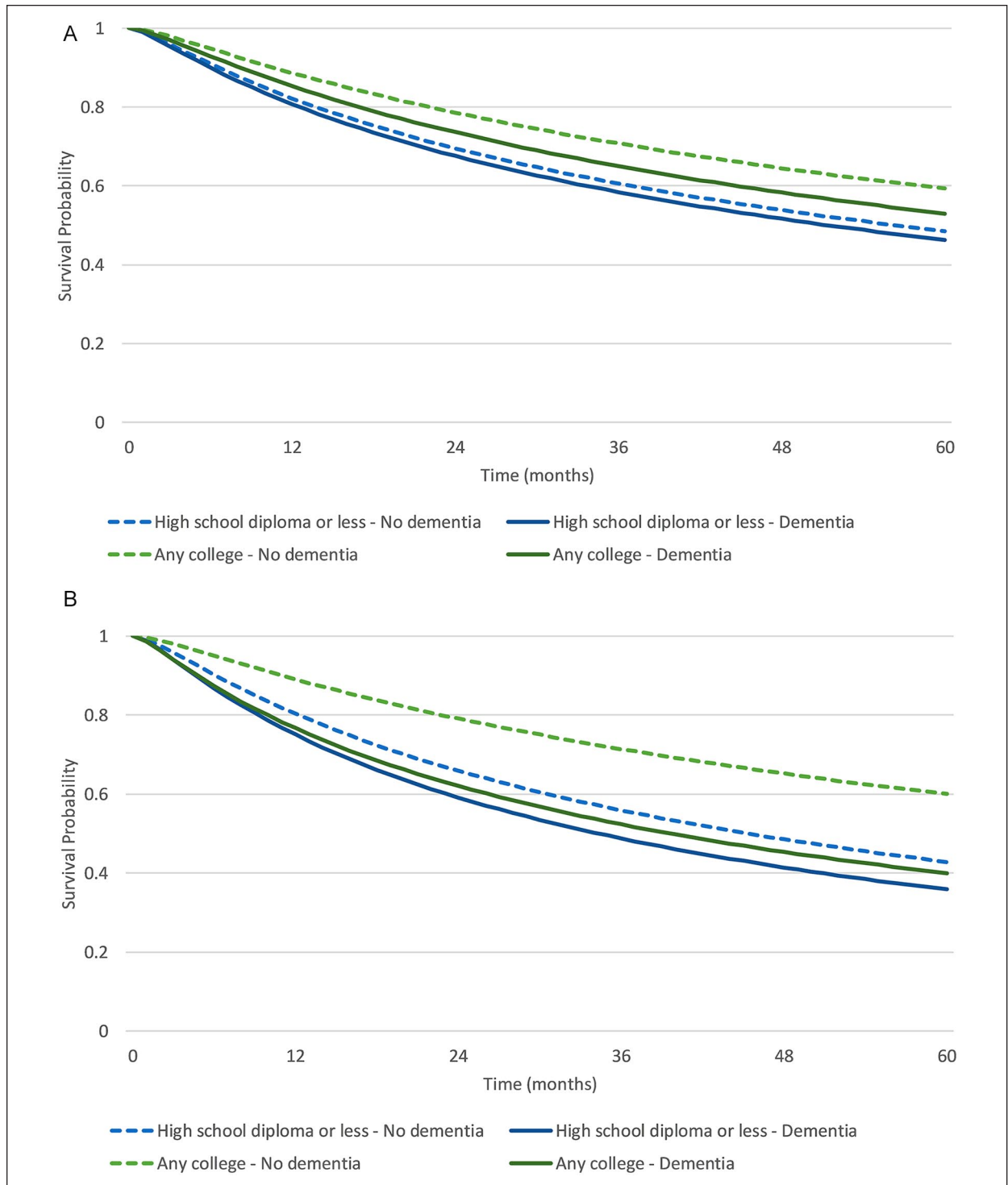


Figure 1. Predicted survival with and without a dementia diagnosis among (A) females and (B) males with and without any college-level education.

rapid cognitive decline may, in turn, result in increased mortality. Our findings are also consistent with the cognitive reserve hypothesis.

Given their inconsistent pattern by gender and education, it is difficult to interpret our findings around marital status. It is particularly challenging given the significant differences in age of diagnosis between those who were married and those who were not married at the

time of onset, which may have confounded our results. A number of studies have shown a lower risk of dementia among married individuals compared with individuals who have never married or who are widowed (Sommerlad et al., 2018; Sundstrom et al., 2016). Although no studies have examined whether marital status influences survival after a dementia diagnosis, one prior study showed a slower rate of cognitive decline in

people with dementia who were cared for by a spouse (Norton et al., 2009).

One possible mechanism for an association between dementia and earlier mortality among married individuals is that the spouse compensates for the cognitive decline experienced by the individual with dementia, leading to a delay in diagnosis and, consequently, a more rapid rate of decline after diagnosis. Other potential mechanisms by which marital status may influence dementia-related mortality include differential health behaviors, social support, and cognitive stimulation between individuals who are married and those who are not, as well as the selection of less healthy individuals into unmarried states. Future studies are needed to tease out the effects of marital status on dementia-associated mortality.

Our study has several limitations. We identified cases using diagnosis codes from claims, which studies have shown to have relatively poor sensitivity for dementia, with sensitivity of 0.85 and a specificity of 0.89 compared with results from a clinical cognitive examination (Taylor et al., 2009). We also lack information on the severity of disease at dementia diagnosis, which is associated with a higher risk of mortality. Finally, household income, an important component of socioeconomic status that may be associated with mortality from dementia, was not included as a covariate in our models.

We found that sex moderates the relationship between dementia diagnosis and length of survival, with a stronger association between dementia and earlier mortality among men. Education also plays a modifying role, with higher educational attainment associated with a greater reduction in length of survival associated with dementia. Our findings have important implications for planning and resource allocation efforts by U.S. health care payment and delivery systems. In particular, they highlight the necessity of accounting for dynamic population sociodemographic characteristics when generating predictions about future dementia-associated needs and mortality.

Author Contributions

All authors played a role in the study concept and design, in analysis and interpretation of results, and in the preparation of the manuscript. L.B. and N.B.C. were responsible for data acquisition.

Sponsor's Role

The funders played no role in the design or conduct of this study.

Disclosures

We certify that we have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript. All authors report no competing interests.

Declaration of Conflicting Interests


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Supplemental Material

Supplemental material for this article is available online.

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