SOCIO-SPATIAL DISPARITIES IN DEMENTIA MORTALITY IN THE UNITED STATES

by

Wei Xu

A Dissertation Submitted in

Partial Fulfillment of the

Requirements for the Degree of

Doctor of Philosophy

in Geography

at

The University of Wisconsin-Milwaukee

May 2019

ABSTRACT

SOCIO-SPATIAL DISPARITIES IN DEMENTIA MORTALITY IN THE UNITED STATES

by

Wei Xu

The University of Wisconsin-Milwaukee, 2019
Under the Supervision of Professor Changshan Wu

Mainly due to the expansion of the geriatric population, the number of deaths attributable to dementia in the United States is likely to increase rapidly in the coming decades. In the hope of offering some valuable insights into discovering disease risk factors linked to geography, advocating place-based prevention and intervention strategies and supporting equitable access to end-of-life care, this study examines three aspects of socio-spatial disparities in dementia mortality in the U.S.: (i) small area spatial and temporal variations in dementia mortality risk; (ii) "place effects" on the differentials in individual dementia mortality risk; and (iii) disparities in place of death of decedents from dementia across populations and places.

Results from the study indicate that, first, there are substantial spatial and temporal variations in dementia mortality risk in the U.S. Specifically, regions including Pacific Northwest, Ohio River Valley and the Carolinas were found to be the most likely high-risk clusters; while counties in the Northeast and Florida were the most likely low-risk clusters. Temporal information of clusters suggested a reduction in the relative risk of Alzheimer's disease and all-cause dementia mortality in most of the highly likely clusters. The results may provide etiologic clues linked to geography and time and propel public health agencies to evaluate the capacity of local health and social care to meet dementia patients' needs before death, especially in those high-risk cluster areas.

Second, differences in individual dementia mortality risk were in part due to the "place effects." Among the three environmental variables examined, area socioeconomic deprivation and $PM_{2.5}$ concentration were significantly associated with dementia mortality risk; area social integration did not have a significant relationship in models adjusted for individual-level factors. Although the relationship between area socioeconomic deprivation was nonlinear, the association between $PM_{2.5}$ concentration and individual dementia mortality risk revealed a dose-response relationship. The relationship between the three environmental factors and dementia mortality risk also differed by age group. The results suggested that environmental interventions, especially improving local air quality, might be an effective measure to reduce dementia mortality risk.

Third, results showed a persistent shift from deaths at institutional settings (hospitals and nursing home/long-term care facilities) to deaths at home and other places among decedents from dementia during 2000 and 2014. There were wide interstate variations in place of death of decedents from dementia. In addition to socio-demographic characteristics of the decedents, state-level factors including access to care facility resources and Medicare and Medicaid expenditure on long-term care might have contributed to the changing landscape.

Although biomedical approaches still dominate in our efforts to understand the diseases, this dissertation research examined the effects of factors "outside the body" on socio-spatial disparities in dementia mortality. The findings provide new insights to inform future epidemiological and health services research related to dementia.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGEMENTS

I would like to express my deepest gratitude to my advisor Dr. Changshan Wu, who has provided the greatest support system a graduate student could ever ask for. I am also greatly indebted to other members of my committee, Dr. Kirsten Beyer from the Medical College of Wisconsin, Dr. Woonsup Choi, Dr. Alison Donnelly, and Dr. Kevin Matthews from the Centers for Disease Control and Prevention, for all the guidance and support they have provided through every stage of my PhD program. Their pursuit of academic excellence has been inspirational.

I am grateful to the Graduate School at the University of Wisconsin-Milwaukee for awarding me the Distinguished Dissertation Fellowship. It enabled me to focus on my dissertation research without distractions in the last year of my program. I owe many thanks to the Mary Jo Read Foundation for all the travel awards I received throughout my graduate student career. It helped my professional development immensely.

I would like to thank other faculty members and staff in the Geography department at the University of Wisconsin-Milwaukee. Your insightful comments and words of encouragement enabled me to carry on through this whole process, especially when I was at my lowest points. Thank you also to other fellow graduate students in the department for their emotional support and friendships. I will miss talking with you over beer and dinners. I would also like to extend my deepest gratitude to the whole Hofhine family (especially Eric, Jo Ann, Duane) for their everlasting support. You have taken me in as a member of the family, and I am extremely grateful for all of your presence. And finally, I would like to thank my dad, mom and brother for their support of me pursuing a PhD overseas. You are my rock.

CHAPTER 1: INTRODUCTION

1.1 Background

Dementia is a major public health crisis in the United States today. It has been estimated that in 2010 approximately 4.7 million American older adults (individuals aged 65 years and older) were afflicted with Alzheimer's disease (AD), the most common form of dementia (Hebert et al., 2013). Most recent projection of dementia prevalence estimated that by 2060, nearly 13.9 million U.S. older adults will be living with AD and related dementias (Matthews et al., 2019). Dementia risk increases exponentially with age. The prevalence of dementia increases from 5.0% in persons aged 71-79 years to 37.4% in those aged 90 years and older (Plassman et al., 2007). According to the U.S. Census Bureau, the number of older adults is expected to double from 49 million in 2016 to 95 million in 2060, among which 19 million will be 85 years and older (U.S. Census Bureau, 2017). The greater number of older adults, combined with improvements in life expectancy and declining fertility, will increase the proportion of the overall population affected by dementia drastically in the near future (James and Bennett, 2019).

Due to the fact that there are no effective curative treatments so far, an increase in dementia related mortality will accompany the increasing prevalence of dementia. According to the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC), AD was the underlying cause of 110,561 deaths in 2015, making it the 6th leading cause of death among all and the 5th leading cause of death among older adults in the U.S. (Murphy et al., 2017). Another study estimated that 503,400 deaths in Americans aged 75 years and older were attributable to AD in 2010 (James et al., 2014). When other types of dementias are accounted for, dementia is the 2nd largest contributor to mortality among U.S. older adults, contributing to 13.6% of all deaths among U.S. older adults (Tinetti et al., 2012). In

contrast to the declining mortality rates of other major causes of death (e.g. heart disease, cancer) in recent years, the U.S. annual age-standardized AD mortality rate increased by 63.3% from 18.0 per 100,000 people in 2000 to 29.4 in 2015 (Miniño et al., 2002; Murphy et al., 2017).

Although dementia poses a significant challenge to the U.S. as a whole, the disease burden is not shared evenly across populations and places. To date, the extent of such disparities and their contributing factors remain poorly understood. However, due to the availability of routinely collected nation-wide mortality records and recent advances in computation software, it is feasible to examine disparities in dementia mortality using large-volume data over a long period of time. Using national death certificate data, this dissertation examines the disparities in dementia mortality in the U.S. from a socio-spatial perspective. Specifically, it engages with three aspects of dementia mortality disparities: (i) small area spatial and temporal variations in dementia mortality risk; (ii) "place effects" on the differentials in individual dementia mortality risk; (iii) disparities in place of death of decedents from dementia across populations and places.

1.2 Overview of the dissertation

This dissertation is organized into 6 chapters. *Chapter 1* introduces background information, structure and significance of the dissertation research. The introduction chapter is followed by *Chapter 2*, which reviews the current literature on disparities in dementia mortality in the U.S.

The main body of the dissertation is composed of three papers. In *Chapter 3*, I employ the retrospective space-time scan statistic to detect the spatiotemporal clusters of dementia mortality between 2000 and 2010 in the U.S. This study falls into one of the major branches of inquiry in health/medical geography: disease mapping/cluster detection. Putting disease risks on

a map is important in medical/health geography research, especially in spatial epidemiology, because it helps to identify areas/people with excess risks, to generate hypotheses of possible associations between place characteristics and health behaviors and outcomes, and to encourage community engagement in improving public health (Beyer et al., 2010; Waller and Carlin, 2010). Currently, disease maps of dementia mortality risk are still rare. This study aims to create a set of disease maps that demonstrate concentrated dementia mortality risk at a fine geography (county) in the U.S. over a long period of time, and then examine these patterns for evidence of statistically significant clustering. By carrying out the analysis, I intend to answer following questions: (i) were there any significant spatiotemporal clusters of dementia mortality in the U.S. during the study period? (ii) if so, where and when did they occur? What were the differential relative risks associated with those clusters? (iii) given the vast body of research on sex difference in dementia, was there any difference in the spatiotemporal clusters in populations stratified by sex? (iv) what etiological hypotheses might be generated from the cluster results? In this chapter, I aim to demonstrate that the risk of dementia mortality was shared unevenly across space and time in the U.S.

In *Chapter 4*, I build upon the findings of dementia mortality risk clusters in the previous chapter, as well as other evidence of spatial variations in dementia mortality risk in the U.S. (Figueroa et al., 2008; Gillum and Obisesan, 2011; Gillum et al., 2011). The chapter examines whether characteristics of the place of residence at death is associated with one's risk of dementia death. Health/medical geographers are keen to understand the sources of area variations in disease risk. Specifically, whether those area variations are attributable to the characteristics of the people who live in certain locales (compositional effects) or the environments in which they live, work or play (contextual/place effects) is of primary interest

(Macintyre et al., 2002). Drawn on the multilevel *ecosocial theory* of health (Krieger, 1994, 2000, 2001) and an extensive body of literature on *social determinants of health* (Blane, 1995; Braveman, Egerter, & Williams, 2011; Cockerham, Hamby, & Oates, 2017; Marmot & Wilkinson, 2007; Marmot, 2005; Regidor, 2006; Scribner, Simonsen, & Leonardi, 2017), this chapter looks at the combined effects of three socio-physical environmental factors-area socioeconomic deprivation, area social integration and $PM_{2.5}$ concentration-on individual dementia mortality risk. I intend to answer following questions: (i) What are the differences in dementia mortality risk associated with individual attributes and county socio-physical environmental indicators, before and after adjusting for potential confounders? (ii) Are there any interaction effects between individual and contextual attributes on dementia mortality? If so, which variables are involved? (iii) What are the implications for dementia prevention and intervention?

Using national death certificates data between 2000 and 2014, *Chapter 5* assesses the changing landscape of place of death of U.S. older adults for whom a dementia-related disease as the underlying cause of death. This chapter aims to quantify the extent to which the place of death of decedents from a dementia-related disease has changed in the nation and across states. Additionally, this study attempts to relate those changes to state factors that might have influenced dementia patients' decision on where to die. Those state factors include the socio-demographic structure of decedents, the availability of care facility resources and the public care investment. In this chapter, following questions are asked: (i) How do the distributions of place of death for dementia decedents differ between the years 2000 and 2014? (ii) How do the distributions of place of death for dementia decedents differ among population groups and across states? (iii) Is a dementia decedent's place of death associated with state-level factors,

particularly availability of care facility resources and public care investments? (iv) What are the implications of study findings for public health policies aiming at supporting dementia patients to age and die in place?

The last chapter summarizes the findings of the studies and identifies directions for future research.

1.3 Significance of study

The contributions of this dissertation research to our understanding of socio-spatial disparities in dementia mortality are multi-fold. First, although a number of studies have examined geographical variations in dementia mortality in the U.S., their usefulness is limited due to small geographical coverage, coarse spatial unit, and short time period. The first paper, by using nation-wide death certificate data (geocoded to county) for a ten-year period and the space-time scan statistic, will provide evidence of the small area variations in dementia mortality risk in both space and time. The findings may be helpful for generating etiological hypotheses of dementia and for federal and state public health agencies to allocate end-of-life care resources for dementia patients more efficiently.

Second, a considerable number of studies have examined the influence of environmental factors on incident dementia; however, the investigation of the synergistic effects of multiple environmental (both social and physical) factors and how those factors may interact with individual-level characteristics to impact one's dementia mortality risk is limited. Using a large, multi-racial/ethnic sample and a multilevel framework, the second paper investigates the extent to which three environmental factors may contribute to the area variations in individual dementia mortality risk. The study also assesses whether the associations between those three

environmental factors and individual dementia mortality risk vary by age. The results provide further cross-sectional evidence that differentials in individual dementia mortality risk are in part due to environmental constraints and that public health policies aiming at reducing dementia mortality risk may need to incorporate environmental interventions.

Third, the last paper examines the extent to which the place of death of decedents from dementia has changed in the U.S., through a comparison of the years 2000 and 2014, both nationally and across states. The results will help identify the gaps between preferred and actual place of death among local dementia patients. Different from cross-sectional research, this study uses panel/time-series data analysis to relate the changes in place of death to state policies over time. It will provide new insights into the structural drivers of the changing landscape of place of death of dementia decedents and inform federal and state health agencies on how to efficiently organize end-of-life care for dementia patients across settings.

CHAPTER 2: LITERATURE REVIEW

2.1 Geographical disparities in dementia mortality

Studies of the geographical disparities in dementia mortality risk may help generate some important etiological hypotheses on the socio-environmental contributions to dementia. In addition, they may inform public health entities to better delineate preventive and therapeutic resources. Russ and colleagues (2012) provided a systematic review of studies examining the geographical variations in dementia risk, with a few articles focusing on mortality in the U.S.

Disparities among administrative units. Using National Center for Health Statistics (NCHS) death certificate data between 1999 and 2004, Steenland et al. (2009) found that age-standardized mortality rates of AD as the underlying cause were notably higher in the northwestern and southeastern states. The state with the highest rate (Washington, 33.7 per 100,000) was more than 4 times that of the lowest rate (New York, 8.2 per 100,000). In a study of racial disparities in dementia mortality in the U.S. at the census region level, Gillum and Obisesan (2011) reported that, between 1999-2004, dementia mortality rates for Blacks were highest in the South Atlantic and West North Central census divisions, whereas rates for Whites were highest in the East South Central division and lowest in New England, Middle Atlantic and East North Central divisions. Gillum, Yorrick, and Obisesan (2011) reported that in 2005 and 2006 combined, the age-adjusted mortality rate of dementia as the underlying or contributing cause of death among persons aged 65 years and over varied substantially by state, with Oregon having the highest (921 per 100,000) and New York the lowest (458 per 100,000). Rates for Alzheimer's disease varied by more than 3-fold from 133 per 100,000 in New York to 419 in Washington.

Small area comparisons of dementia risk have been carried out in other developed countries such as Canada (Frecker, 1991; Perron et al., 1993; Jean et al., 1996) and Switzerland (Huss et al., 2009), while only one study reported such data for the U.S. Gillum, Yorrick, and Obisesan (2011) calculated mortality rates of AD and other dementia-related illnesses for persons aged 65 years and over at the county level. They found high rates in most Oregon counties, western Washington, some counties in Mountain states, Ohio, northern New England, the Appalachian region and the Carolinas, and low rates in most New York counties and south and central Florida. Although they provided a more nuanced picture of the spatial disparities in dementia mortality that was previously available, the study period was rather short (two periods: 1999-2000 and 2005-2006) and many counties were impacted by suppressed or unreliable values due to small numbers of dementia deaths. In general, small area comparisons of dementia mortality remain scarce, despite its high relevance in identifying risk factors and allocating health care resources. Among those studies that attempted to examine temporal trends, the usual approach was to compare area mortality rates between two or more pre-defined time periods (Schrijvers et al., 2012).

Disparities between rural and urban settings. A number of *prevalence* and *incidence* studies have attempted to examine urban/rural disparities in AD/dementia risk. Rural living was associated with elevated risk in some studies (Jean et al., 1996; Yip et al., 1997; Zhang et al., 2006; Arslantaş et al., 2009; Jia et al., 2013) but not others (Prince et al., 1994; Azzimondi et al., 1998; Matthews et al., 2005; Bermejo-Pareja et al., 2008; Llibre Rodriguez et al., 2008). One meta-analysis of the geographical variation in dementia concluded that there was some evidence of rural living, especially in early life, being associated with elevated AD prevalence and incidence, although this association was much weaker for vascular and non-specific dementia

(Russ et al., 2012). Among studies that focused on the U.S., one study, by incorporating a life course approach in measuring risk exposure, emphasized the detrimental effects of rural living in early life on late-life AD risk (Ogunniyi et al., 2000). In another study that identified risk factors for incident AD between African Americans and Yoruba, rural living in childhood was found to be associated with higher AD incidence for African Americans (Ogunniyi et al., 2006). It is interesting that urban/rural disparities in AD/dementia prevalence and incidence vary in other parts of the world but remain consistent in the U.S. It is worth noting that the definition of urbanicity/rurality in dementia studies has shown substantial heterogeneity, making a comparison of results challenging. These measures include population size and density, economic structure, whether the area contains villages or cities, and urban influence code. Other studies did not provide explicit definitions (Russ et al., 2012). The studies of the associations between rural living and dementia risk were descriptive at best. The aspects of rural living that may be associated with dementia risk remain understudied.

To my knowledge, very little research has related urbanicity/rurality to dementia *mortality* directly. Law and Morris (1998) found that metropolitan areas had a lower mortality risk for senile dementia compared to rural areas in England and Wales (relative risk = 0.89, 95% CI (confidence interval) = 0.89-0.95). Wen et al. (2011) discovered that in China, mortality risk of dementia and its major subtypes (AD and vascular dementia) was significantly lower in urban areas as compared to rural ones. Prince et al. (2012) reported that the absolute and relative dementia mortality risk was much higher in urban areas in Latin American countries such as Peru and Mexico; however, a reverse relationship was found in China. The measures of rurality in these studies were dominated by the urban-rural dichotomy and the directions of the

rural/urban-dementia risk relationship was inconsistent. Studies focusing on urban/rural disparities in dementia mortality in the U.S., however, are very scarce.

Overall, the study of geographical variations in dementia mortality in the U.S. has been mostly restricted to large study units such as the census region and state, even though small area comparisons may provide more valuable insights for disease etiology and health services research. For those studies at sub-state levels, the temporal range was usually short, and risk measures were missing for areas with few events. A more complete but nuanced picture of the geographical patterning of dementia mortality in the U.S., based on finer scales and longer study periods, is needed.

2.2 Social disparities in dementia mortality

Age

The risk of dementia mortality increases substantially with age. Fratiglioni et al. (1999) reported that in males, the mortality rate of dementia per 100 person-years was 1.8 (95% CI = 0.8-3.5) in persons aged 85 years and older, compared to 1.3 (95% CI = 0.4, 2.9) in persons aged between 77 and 84; in females, the rates were 3.8 (95% CI = 2.9-4.8) compared to 0.9(95% CI = 0.4-1.7), respectively. Using U.S. death certificate data from 1999 to 2004, Steenland et al. (2009) reported that the age-adjusted AD mortality rate per 100,000 persons aged 85 years and older was 1098.6, compared to 0.3 in persons younger than 45 years old and 32.1 in persons aged between 65 and 69. The exponential increase in AD/dementia mortality rate with age was present across gender and race categories. According to U.S. annual deaths data, AD mortality rates were 18.7 per 100,000 in the 65-74 age group and 667.7 in people aged 85 years and older in 2000; in 2013, the rates were 18.1 and 929.5, respectively (Murphy et al., 2016). The disparity in

AD/dementia mortality risk between the oldest (>85 years old) and younger has widened over time.

Sex

In the same two studies mentioned above, the authors also compared the AD/dementia mortality risk by sex. Fratiglioni et al. (1999) reported that the mortality rate of dementia per 100 person-years was 2.7 (95% CI = 2.1-3.4) in females compared to 1.5 (95% CI = 0.8-2.6) in males; the mortality rate of AD was 2.2 (95% CI = 1.6-2.8) in females versus 0.9 (95% CI = 0.4-1.8) in males. In Steenland and colleagues' study, the age-adjusted mortality rate of AD as the underlying cause of death was consistently higher in females than males aged 75 and over. This disparity by sex was found in whites, non-whites and all races combined (Steenland et al., 2009).

Race/ethnicity

Steenland et al. (2009) reported that the age-adjusted AD mortality rate was higher in Whites (19.7 per 100,000 persons) than in non-Whites (12.6 per 100,000 persons) and this disparity was found across all age cohorts. Using the same dataset, Gillum and Obisesan (2011) reported that in the U.S. the overall age-adjusted dementia mortality rates were similar between Whites and Blacks (628 per 100,000 in Blacks, 647 in Whites). However, the racial disparity in dementia mortality rate varied greatly by region. In another mortality study of nursing home residents with AD, Blacks had shorter lives, among men (RR=0.80, 95% CI = 0.65-0.99) and women (RR=0.89, 95% CI = 0.76-1.06), compared to Whites. Men in other racial/ethnic minority groups showed similar longevity (RR=1.0, 95% CI = 0.70-1.44) compared to Whites but women lived much shorter lives (RR=0.82, 95% CI = 0.65-1.05) (Lapane et al., 2001). However, another study concluded that Black (mortality hazard ratio [HR]=0.85, 95% CI = 0.74-0.96) and Latino AD patients (HR=0.57, 95% CI = 0.46-0.69) may have longer survival

compared to White patients (Mehta et al., 2008). It appears that Whites have higher AD/dementia mortality rates than other racial/ethnic groups but the difference in the length of time they live after diagnosis remains inconclusive.

Socioeconomic status

In epidemiological studies, Socioeconomic status (SES) is traditionally measured by education, income and occupation (Winkleby et al., 1992; Braveman et al., 2005). In studies using education as the sole indicator of SES, the relationship between SES and AD/dementia mortality risk has been inconsistent. An inverse relationship between SES and AD/dementia mortality risk was found in some studies (Agüero-Torres et al., 1998) but not in others (Stern et al., 1995; Geerlings et al., 1997; Helmer et al., 2001; Qiu et al., 2001; Pavlik et al., 2006; Bruandet et al., 2008). In a study of gender-specific effects of education on dementia death, Russ et al. (2013) reported that women who left school aged 14 or younger had a 76% increased risk of dementia death compared to those who left school aged 16 or older. However, the protective effect of higher education was not found in men. In contrast, a number of studies have reported an association between a higher education level and increased AD mortality risk (Stern et al., 1995; Geerlings et al., 1999; Freels et al., 2002). Moreover, Brehaut, Raina, and Lindsay (2004) reported that higher education reduced mortality risk among people without cognitive impairment, while it does not affect mortality among those with cognitive impairment. A systematic review on the effects of education on the survival of AD patients concluded that higher education may delay dementia manifestations of AD but it does not affect survival after diagnosis (Paradise et al., 2009). To my knowledge, a systematic review or meta-analyses that focus on education-based SES and other types of dementia mortality risk has yet to be

conducted. As suggested above, more research is needed to explain the relationship between education-based SES and AD/dementia mortality risk.

Some studies used income as opposed to education as the sole indicator of SES. For example, Lower SES, measured by disposable household income, is associated with a higher 5-year mortality rate and shortened survival time among people diagnosed with dementia in both sexes and different care settings (van de Vorst et al., 2016). When SES was based on occupational social class, it was not significantly related to dementia death risk in both sexes (Russ et al., 2013). One study used a compositional measure of SES (generated from education level, income, occupational class, and rural/urban living) and found that lower SES is associated with significantly higher mortality risk among people with dementia (Chen et al., 2014). Most of the research above was based on cohort studies and focused on the relationship between *individual* SES and dementia risk (survival rate or survival time). Nonetheless, how living in an economically deprived area (*area* SES) may affect individual dementia mortality risk remains understudied.

Social networks

Social relationships have been widely recognized as exerting a significant influence on physical and mental health. Different aspects/measures of social relationships have been examined, including social network, social integration, social capital, and social ties. Berkman et al. (2000) asserted that social network structures and characteristics of social ties can influence health through five mechanisms: social support, social influence, social engagement, person-to-person contact, and access to resources and material goods. Recent studies have demonstrated that people reporting stronger social ties and engagement were much less likely to develop dementia during follow-up (Bassuk et al., 1999a; Fratiglioni et al., 2000; Wang et al., 2002;

Crooks et al., 2008). Moreover, Amieva et al. (2010) emphasized the importance of the quality of social networks in protecting against subsequent dementia. A recent review article concluded that the negative influence of social isolation on incident dementia is comparable to low education, physical inactivity and depression (Kuiper et al., 2015). Using marital status as a measure for social relationships, other dementia studies have also shown a consistent relationship between being non-married and increased AD and dementia risk (Bickel and Cooper, 1994; Helmer et al., 1999; Sundström et al., 2016). Helmer et al. (1999) found that the relative risks of dementia and AD incidence were higher among individuals who were never married compared with individuals who were married or cohabitants. Adjusting other factors (including education, wine consumption, social environment, leisure activity and depression) did not modify the risk of AD for non-married. Very few studies directly examined the association between marital status and dementia mortality risk. One study using the U.S. deaths data during 1999-2004 concluded that the AD mortality rate ratio between un-married and married persons was 1.42 (95% CI =1.36-1.48), indicating that social isolation may also be a significant risk factor for dementia mortality (Steenland et al., 2009).

Although studies have examined differential mortality risks between population groups, investigation of the socio-spatial disparities in dementia mortality in the U.S. context is still lacking. Especially, how "upstream" factors operating in broader contexts may contribute to the differences in dementia mortality remains poorly understood. This dissertation aims to fill the gap.

CHAPTER 3: DETECTING SPATIOTEMPORAL CLUSTERS OF DEMENTIA MORTALITY IN THE UNITED STATES, 2000 - 2010

3.1 Introduction

Dementia refers to a range of neurodegenerative disorders characterized by progressive deterioration of cognitive abilities, such as memory and reasoning, and dysfunction of independent living among the affected. Studies of global prevalence of dementia point to the increasing challenge of dementia risk in all regions of the world (Ferri et al., 2005; Prince et al., 2013). The United States is no exception. Hebert and colleages (2003) projected that 13.2 million Americans will be living with AD by 2050, tripled from 4.5 million in 2000. The prevalence of all-cause dementia will be even greater. Absent effective curative treatments, mortality attributable to dementia has also been increasing dramatically. According to National Vital Statistics, the age-standardized AD mortality rate had increased from 18.0 per 100,000 population in 2000 to 29.4 in 2015, making it the 6th leading cause of mortality in all population and the 5th leading cause among older adults in the U.S. (Miniño et al., 2002; Murphy et al., 2017). If other forms of dementia are included, dementia is the 2nd largest contributor to death in older adults among individual common diseases (Tinetti et al., 2012). Due to the demographic shift toward an older population and increased average life expectancy, AD/dementia mortality in the U.S. is likely to escalate in future decades.

Despite its importance for etiological research and dementia care planning, geographical and temporal variation in AD/dementia mortality in the U.S. has received little attention. Among the few existing studies, most were carried out using the state, or a larger geography, as the analysis unit. For example, in comparing AD mortality risk between the U.S. and Puerto Rico, Figueroa and colleages (2008) found that, although the risk increased for both during 1999 and

2004, Puerto Rico had a higher age-standardized AD mortality rate than all of the U.S. and that Puerto Rican natives had a significantly higher age-standardized AD mortality rate than Puerto Ricans living in the U.S. Regional differences in AD mortality were also observed within Puerto Rico. At the census division level, Gillum and Obisesan (2011) examined geographical patterns of dementia mortality between Black and White older adults using 1999-2004 death certificates. They found that racial difference in the age-standardized rates ranged from -130 deaths per 100,000 population in the Middle Atlantic division (362 for Blacks and 492 for Whites) to 55 in the South Atlantic (731 for Blacks and 676 for Whites). At the state level, using 1999-2004 death certificates, Steenland et al. (2009) found that state mortality rates of AD as the underlying cause varied greatly, ranging from 8.2 per 100,000 population in New York and 33.7 in Washington. Using national vital statistics, Gillum and colleages (2011) found that in 2005-2006, the age-standardized mortality rate of dementia, as either the underlying or a contributing cause, among older adults varied by two-fold, ranging from 458 per 100,000 population in New York to 921 in Oregon. For AD alone, the mortality rate varied by three-fold, ranging from 133 per 100,000 population in New York to 419 in Washington. The 2005-2006 period had similar geographical patterns for all dementia mortality to those in 1999-2000; however, Arkansas, Louisiana, Mississippi and Arizona had marked increase in AD death rates. To my knowledge, only one study examined small area variations of AD/dementia mortality in the U.S. (Gillum et al., 2011). The county-level analysis was more informative compared to the ones based on larger geographical units; however, due to the short time periods (2 years), many counties were excluded as the aggregated death numbers in those counties were too small. While the studies mentioned above could not directly explain the sources of such variations, the authors suggested a few potential factors including differences in education, access to and quality of care, and

cardiovascular risk factors. It was also frequently stated that dementia diagnostic and reporting practices might vary between places and over time, potentially contributing to found patterns (Steenland et al., 2009; Gillum and Obisesan, 2011; Gillum et al., 2011).

Although these studies shed light on the geographical and/or temporal variations in AD/dementia mortality in the U.S., none of them investigated the patterns at a sub-state geography over a long period of time, potentially limiting the usefulness of their findings. Moreover, although areas with high and low dementia mortality rates were presented, no study above evaluated the statistical significance of those differences. Examining dementia mortality at a finer spatial resolution and over a long time may provide us with some etiological clues more relevant to epidemiological research (Russ et al., 2012). Moreover, these results may be especially useful for health policy makers to formulate more localized prevention and intervention strategies targeting communities at the highest risk. The purpose of this study, therefore, was to identify spatiotemporal clusters of both AD and all-cause dementia mortality in the U.S. at the county level during 2000 and 2010.

3.2 Data and methods

3.2.1 Data sources

This study used the U.S. multiple cause of death files for 2000-2010, county populations, and county location data to identify clusters of excess and deficit AD/all-cause dementia mortality during the decade. I requested the nation-wide individual death certificate data during 2000 and 2010 from the NCHS at the CDC under a data use agreement (NCHS, n.d.). This dataset consisted of all death certificate records in the U.S. during the study period. In this study, deaths occurred in states and territories outside the contiguous U.S. were excluded, as were

deaths of foreign residents. Figure 1 shows the trends of age-standardized mortality rates of AD/all-cause dementia during the study period. AD and all-cause dementia mortality rates had both steadily increased by year but all-cause dementia showed faster increase.

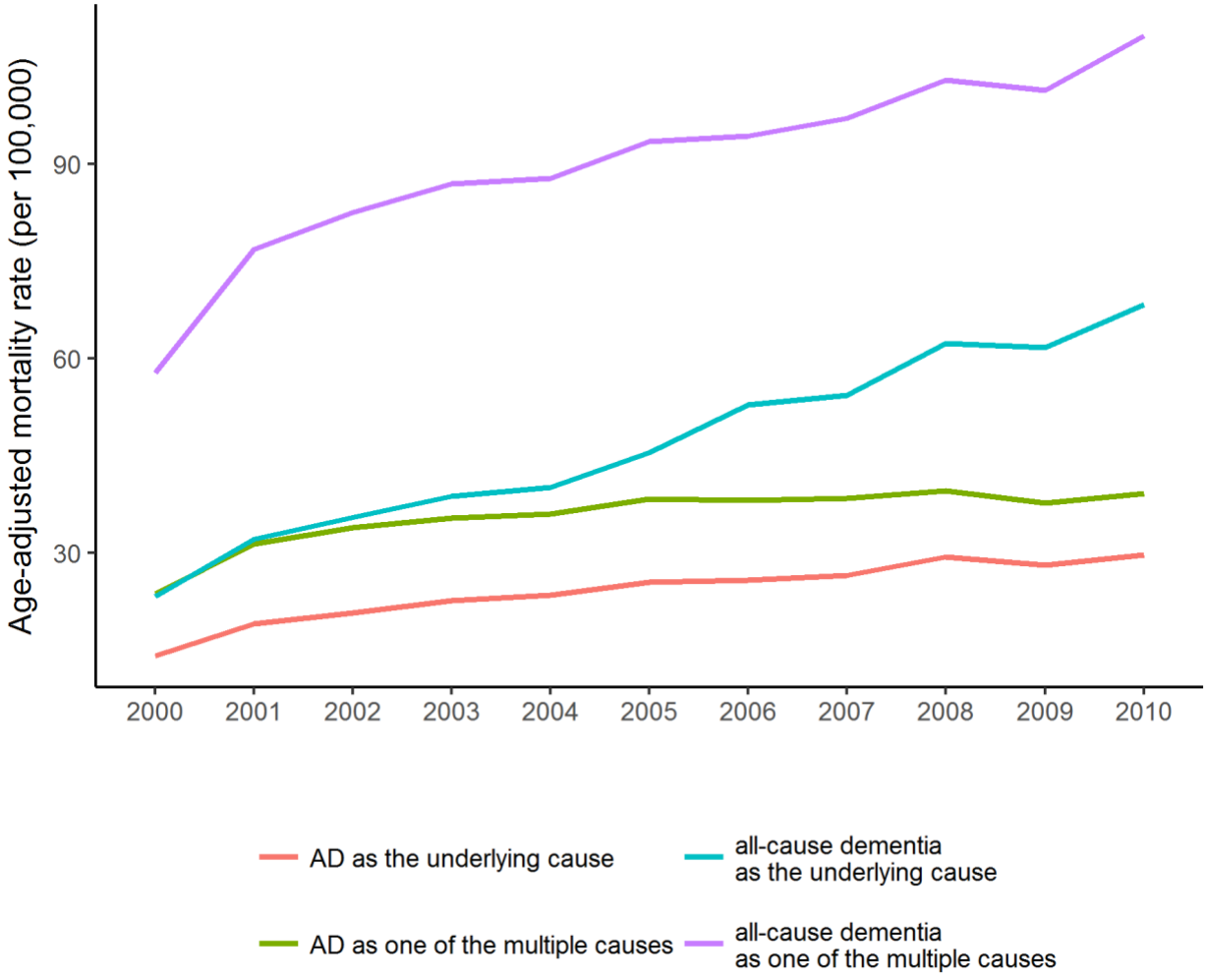

Figure 1 Temporal trend of annual age-adjusted Alzheimer's disease (AD) and all-cause dementia mortality in the U.S. during 2000 and 2010.

Information of the deceased were extracted from the death certificates, including sex, race, age at death, state of residence, county of residence, the underlying cause of death, and the multiple causes of death. Sex, race and age at death were used as covariates to adjust for the

differences in dementia mortality risk between population cohorts. State and county of residence were used to denote the place of residence. The underlying cause of death is the one disease that directly causes the death, while the multiple causes of deaths are a list of diseases that may all contribute to the death. In this study, both AD and all-cause dementia were used as the underlying cause and one of the multiple causes to create the "case file." All-cause dementia included AD (G30) and other dementia subtypes such as vascular dementia (F01), dementia in other diseases classified elsewhere (F02), and unspecified dementia (F03). The coding was according to the 10th revision of the International Classification of Disease (ICD-10) (World Health Organization, 1992). To create the "population file", county demographic data stratified by sex, race and five-year age groups were obtained from the Census Bureau, including Summary File 1 from the decennial censuses of 2000 and 2010 and intercensal yearly population estimates during the decade (data and methodology available at https://www.census.gov/data/datasets/time-series/demo/popest/intercensal-2000-2010-counties.html). The 2010 county TIGER/Line® Shapefiles were also obtained from the Census Bureau to create the "coordinates file", which used the latitude and longitude of county polygon centroids to indicate county localities (U.S. Census Bureau, 2012a).

It is worth noting that county vital and population statistics had spatial mismatch due to county boundary changes during the study period. To mitigate the problem, the geographical coding of some mortality cases and population data were modified. For example, if one county was split into two smaller counties, the two small counties were re-merged and recoded to make sure the area and code were identical to the original county. If a new county was created from parts of two neighboring counties, the resultant three counties were merged into one and all deaths occurred in the three counties were recoded to the code of the new county. In principle, all

counties involved in each boundary change (e.g., split, annexation, territory exchange, county status alteration, etc.) were merged into one county and recoded so that the geographical extent and coding system were consistent over time. 3103 counties were created after adjusting and recoding county boundary changes.

3.2.2 Space-time scan statistic

A retrospective space-time scan statistic was used to test for the existence of spatiotemporal clusters of significantly high and low AD/all-cause dementia mortality risk in the U.S. using SaTScan (version 9.4.4). The scan statistic has been used to examine the spatial and/or temporal patterns of infectious diseases outbreaks (Gaudart et al., 2005; Kulldorff et al., 2005), different types of cancer (Kulldorff et al., 1997, 1998; Hsu et al., 2004; Fukuda et al., 2005; Sheehan and DeChello, 2005; Henry et al., 2009; Amin and Burns, 2014), and other health outcomes such as accidental poisoning (Nkhoma et al., 2004), symptomatic pesticide exposure (Sudakin et al., 2002) and low birth weight (Ozdenerol et al., 2005).

The space-time scan statistic identifies clusters by imposing a series of cylindrical windows with circular bases centered at each county polygon centroid. The circular base of the scan window represents the spatial extent of potential clusters while the height represents the time interval. The radius of circular base continuously increases until the window reaches the maximum spatial cluster size and the height of the cylinders also increases until it reaches the maximum temporal cluster size. I chose to control the maximum spatial cluster size to 50% of the population at risk and the maximum temporal cluster size to 50% of the study period (5 years in this case) based on such rationale: if a high (low) risk cluster covers over 50% of the total population and over half of the study period, it is better to consider that there is a low (high) risk cluster outside the area and time interval. I additionally controlled the maximum radius of

circular clusters to a value of 500 kilometers. For each cylinder, the space-time scan statistic tested the null hypothesis that there was equal risk of AD/all-cause dementia death within the cylinder and the area and time interval outside. The two-sided alternative hypothesis was that the mortality risk of AD/all-cause dementia inside a cylinder was significantly different from outside. Considering that the spatiotemporal clusters may be confounded by the overall temporal trend in the data, I additionally adjusted for the log linear time trend automatically calculated by SaTScan (Nkhoma et al., 2004; Kulldorff, 2006).

It was assumed that the number of AD/all-cause dementia deaths in each county is distributed according to a Poisson model. Based on the assumption of Poisson distribution, the likelihood function of a potential cluster is formulated as

$$LR = \frac{L(c)}{L(null)} = \left(\frac{n}{E}\right)^n \left(\frac{N-n}{N-E}\right)^{N-n} \quad (1)$$

where *LR* is the likelihood ratio, *L(c)* is the likelihood that the cylinder is a cluster under the alternative hypothesis, *L(null)* is the likelihood under the null hypothesis, *n* is the observed number of deaths within the cylinder, *N* is the number of deaths in the total population, *E* is the expected number of death within the cylinder under the null hypothesis. The cylinder with the highest logarithm of *LR* (*LLR*) is considered the most likely cluster (Kulldorff, 1997; Kulldorff et al., 2003; Murray et al., 2014). To address the confounding effects of inhomogeneous local population structures, jointly defined by age, race and sex, on mortality risk measures, the *E* within each cylinder was standardized. First, a set of population cohorts were defined by five-year age groups, race, and sex. Then, cohort-specific mortality rates were calculated from the total population and used as the standard. The cohort-specific expected number of deaths within a cylinder was calculated by multiplying the number of cohort-specific populations within a cylinder and the corresponding standard cohort-specific mortality rates of the total population.

Finally, the cohort-specific expected numbers of deaths within the cylinder were combined to obtain the total expected number of deaths. With a given *N* and *E*, the likelihood value increases with *n*. The relative risk (*RR*), which measures the increased or decreased risk within the cylinder compared to the area and time outside, was also calculated for each cylinder with the following formula:

$$RR = \frac{n/E}{(N-n)/(N-E)} \quad (2)$$

999 random replications were generated in Monte Carlo stimulation to ensure the statistical stability of identified clusters. Using ArcGIS 10.3, the cluster *dbase* files were spatially joined with the county shapefile and maps showing the locations of detected clusters were created.

The scan statistic has several advantages over other cluster detecting methods. First, it adjusts for varying population density and potential confounders; second, it avoids preselection bias by not specifying window size or location before analysis; third, it takes into account multiple testing and returns a single *p*-value for accepting or rejecting the null hypothesis; and last, the approximate location of clusters, if detected, can be specified (Kulldorff et al., 1997). Prates, Kulldorff, and Assunção (2014) assessed the potential biases in relative risk estimates and concluded that the scan statistic has high power in correctly identifying clusters.

3.2.3 Sensitivity analysis

The default settings of maximum spatiotemporal cluster size in SaTScan (50% of total population and 50% of study period) tend to produce primary clusters occupying a large proportion of the study area, rendering non-informative results (Haining, 2003). Researchers have imposed additional controls by controlling maximum population at risk within clusters to a smaller percentage (Fukuda et al., 2005; Sherman et al., 2014), or by controlling the maximum number of cases within clusters (Sheehan and DeChello, 2005), or by controlling the maximum

radius of circular base or time period (Azage et al., 2015; Lefebvre et al., 2015). It is difficult to optimize the parameter settings as they may be dependent upon the geographical scale of processes leading to clustering, spatial and temporal resolutions, and others (Chen, Roth, Naito, Lengerich, & MacEachren, 2008; Jones & Kulldorff, 2012; Weisent, Rohrbach, Dunn, & Odoi, 2011). Indeed, there is insufficient knowledge on how the choice of maximum cluster size can influence results from the scan statistic (Weisent et al., 2011). To explore how the choice of maximum cluster size may affect cluster results, the SaTScan statistic was run post hoc with the maximum radius of cluster circles controlled to 300 kilometers and 700 kilometers, respectively, in addition to the default settings mentioned above. The cluster results according to these two alternate parameter settings were presented in Figure 5 and Figure 6.

3.3 Results

In 2000-2010 combined, AD was listed as the underlying cause for 741,745 residential deaths and as one of the multiple causes for 1,095,695 deaths. Meanwhile, all-cause dementia was listed as the underlying cause for 1,439,480 deaths and as one of the multiple causes for 2,770,094 deaths. All the statistically significant spatiotemporal clusters of AD/all-cause dementia mortality were shown in Figure 2. Because clusters with very small *LLR*s carry little useful information, only the most likely cluster and top 5 secondary clusters were presented in Table 1.

Figure 2 shows the spatiotemporal clusters of AD/all-cause dementia mortality, after adjusting for sex, race, age, and temporal trend. For AD as the underlying cause of death, 21 clusters were detected (Figure 2a). The most likely cluster was a low risk cluster located in the Northeast consisting of most counties in New York, Pennsylvania, and New Jersey. Compared to

the rest of the country, this area had a 43% lower risk of mortality directly from AD (*RR*=0.57, *LLR*=7012.4, 2006-2010) and the difference was statistically significant ($p<0.01$). The top 5 secondary clusters, ranked by their *LLR*s, were the large area in the Upper South consisting Kentucky, Tennessee and part of surrounding states (higher risk [+]), a northwestern region consisting of Washington, Oregon and west Idaho counties [+], south California and west Arizona [+], south Florida (lower risk [-]), and east Texas and Louisiana [+]. Among all clusters, the one with the highest mortality risk was the area encompassing a few counties in south Iowa (*RR*=1.96, *LLR*=274.2, 2006-2010) and the one with the lowest risk consisted of a few counties in south Texas (*RR*=0.36, *LLR*=278.6, 2000-2004).

For AD as one of the multiple causes of death, 19 clusters were detected (Figure 2b). The most likely cluster was in the same approximate location as in Figure 2a, but the size was slightly larger. This area had a 37% lower chance of mortality (directly and indirectly) from AD (*RR*=0.63, *LLR*=7999.3, 2006-2010) and the difference was statistically significant ($p<0.01$). Top 5 secondary clusters were the one in the Ohio River Valley region consisting of Kentucky, Tennessee and part of surrounding states [+], Florida [-], Washington, Oregon and west Idaho [+], central and south California [+], and one covering east Texas, Louisiana, Arkansas and Oklahoma [+]. Among all clusters, the highest risk lied in west Texas (*RR*=1.64, *LLR*=84.1, 2006-2010) while the lowest risk in south Texas (*RR*=0.50, *LLR*=224.2, 2000-2004).

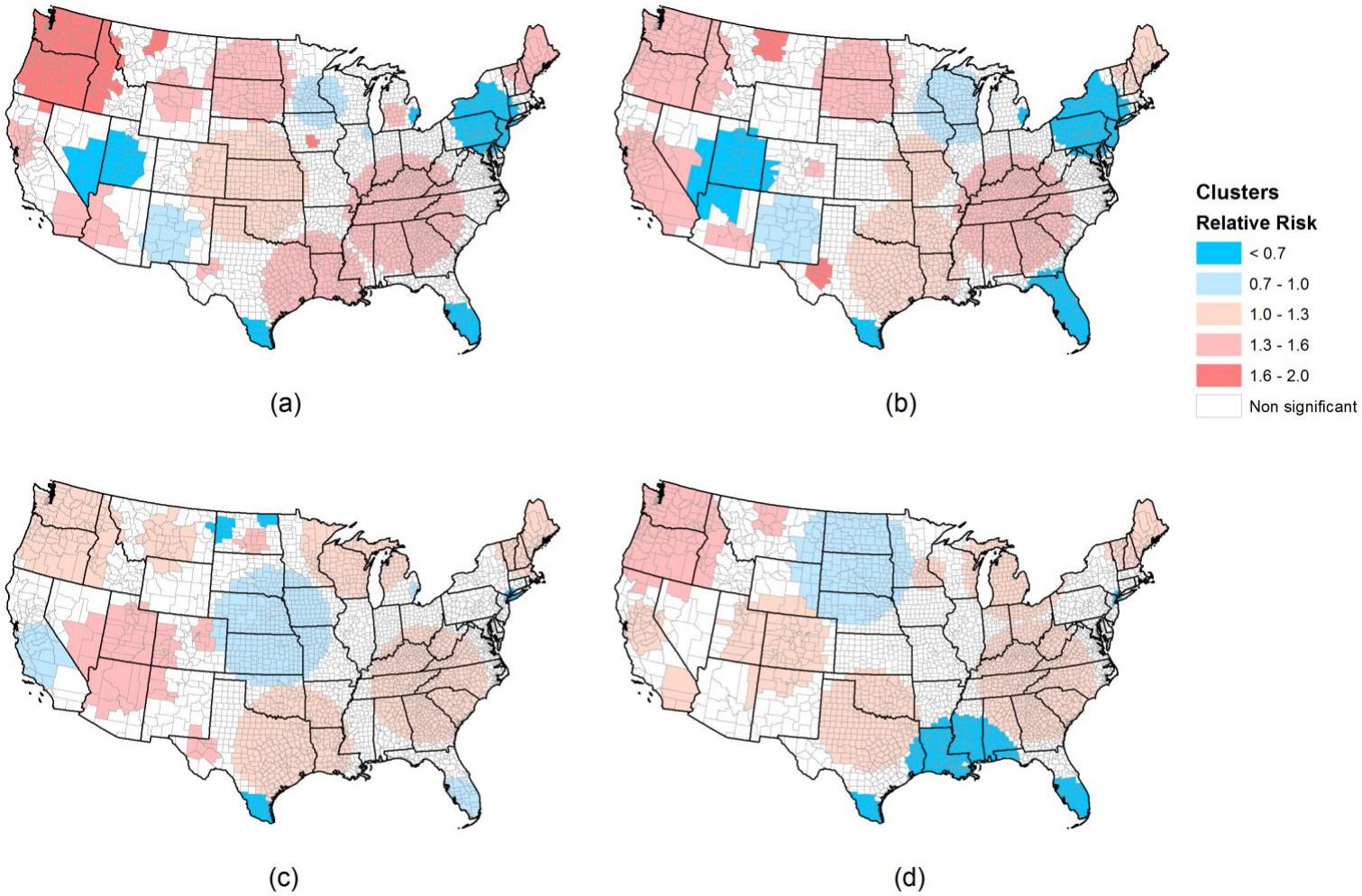

Figure 2 Spatiotemporal clusters of mortality attributable to (a) AD as the underlying cause (b) AD as one of the multiple causes (c) all-cause dementia as the underlying cause (d) all-cause dementia as one of the multiple causes, adjusted for sex, race, age and temporal trend.

For all-cause dementia mortality (Figure 2c and 2d), the most likely clusters were both located in downstate New York, northeast New Jersey, south Connecticut, with the lowest *RR*s among all clusters (for dementia as the underlying cause of death, *RR*=0.40, *LLR*=10462.2, 2006-1010; for dementia as one of the multiple causes, *RR*=0.47, *LLR*=11868.4, 2005-2009). The top 5 secondary clusters were almost identical in terms of location and size, 4 of which were the adjacent area between Kentucky, Tennessee, West Virginia, Virginia, North Carolina, South Carolina, and Georgia [+], south Florida [-], Washington, Oregon, west Idaho [+], Central California [-]. The only difference was that east Texas, Louisiana and part of Arkansas and Oklahoma [+] was a cluster for mortality of dementia as the underlying cause and north Texas and Oklahoma [+] was a cluster for mortality of dementia as one of the multiple causes.

Interesting findings were also observed regarding the temporal patterns of these clusters. For total population (Table 1) and population cohorts by sex (Table 2), most of the clusters with significantly lower *RR*s were in the second half of the decade; while most clusters with significantly higher *RR*s were in the first. The results implied that during the decade, the relative risk of AD/all-cause dementia mortality in most of the cluster areas listed in the tables had improved compared to the rest of the country. However, this change was not shared everywhere. California and south Nevada area had a higher *RR* of mortality of AD as one of the multiple causes (*RR*=1.31) during 2006-2010, and central California had a lower *RR* of mortality of dementia as the underlying cause (*RR*=0.74) during 2000-2004. The relative mortality risk of AD as one of the multiple causes in central California and south Nevada and of dementia as an underlying cause in central California residents might have worsened. For men, the Washington state

region joined central California as another area with worsened mortality risk of AD as one of the multiple causes (*RR*=1.70, 2006-2010) and of all-cause dementia as the underlying cause (*RR*=1.27, 2005-2009); however, for women, the Washington state region had lower *RR*s of mortality of both AD and all-cause dementia during the decade.

Table 1 Spatiotemporal clusters of AD and all-cause dementia mortality, adjusted for sex, race, age, and temporal trend.

Cluster	Approximate location	Time	Observed deaths	Expected deaths	*RR*	*LLR*	*p*-value
(a) AD as the underlying cause (adjusted for 3.93% annual increase)							
Most likely cluster	New York, New Jersey, Pennsylvania	2006-2010	39230	66284	0.57	7012.4	<0.01
Secondary cluster1	Ohio River Valley and Carolinas	2004-2008	58732	43390	1.35	2609.1	<0.01
Secondary cluster2	Pacific Northwest	2001-2005	18070	10786	1.68	2076.3	<0.01
Secondary cluster3	south California, east Arizona	2003-2007	16981	10787	1.59	1537.5	<0.01
Secondary cluster4	south Florida	2006-2010	14420	22021	0.65	1535.9	<0.01
Secondary cluster5	east Texas, Louisiana	2002-2006	23334	17547	1.34	887.2	<0.01
(b) AD as one of the multiple causes (adjusted for 1.41% annual increase)							
Most likely cluster	New York, New Jersey, Pennsylvania	2006-2010	69909	106940	0.63	7999.3	<0.01
Secondary cluster1	Ohio River Valley and Carolinas	2003-2007	82851	60927	1.38	3775.5	<0.01
Secondary cluster2	Florida	2006-2010	28230	42822	0.65	2930.2	<0.01
Secondary cluster3	Pacific Northwest	2001-2005	26220	16830	1.57	2276.1	<0.01
Secondary cluster4	Central and south California, south Nevada	2006-2010	69768	53962	1.31	2237.7	<0.01
Secondary cluster5	east Texas, Louisiana, Arkansas, Oklahoma	2002-2006	44753	36170	1.25	981.2	<0.01
(c) all-cause dementia as the underlying cause (adjusted for 7.58% annual increase)							
Most likely cluster	downstate New York, northeast New Jersey, south Connecticut	2006-2010	18653	45486	0.40	10462.2	<0.01
Secondary cluster1	Ohio River Valley and Carolinas	2006-2010	135886	107288	1.29	3821.1	<0.01
Secondary cluster2	south Florida	2006-2010	35010	46386	0.74	1571.8	<0.01
Secondary cluster3	east Texas, Louisiana, part of Arkansas and Oklahoma	2004-2008	62888	50550	1.26	1451.3	<0.01
Secondary cluster4	Pacific Northwest	2004-2008	31783	25172	1.27	816.2	<0.01
Secondary cluster5	Central California	2000-2004	15952	21527	0.74	804.9	<0.01
(d) all-cause dementia as one of the multiple causes (adjusted for 2.63% annual increase)							
Most likely cluster	downstate New York, northeast New Jersey, south Connecticut	2005-2009	33252	69298	0.47	11868.4	<0.01
Secondary cluster1	Ohio River Valley and Carolinas	2002-2006	201777	158200	1.30	5881.5	<0.01
Secondary cluster2	south Florida	2006-2010	52991	79567	0.66	5167.1	<0.01
Secondary cluster3	Pacific Northwest	2001-2005	55462	42508	1.31	1830.0	<0.01
Secondary cluster4	north Texas and Oklahoma	2002-2006	63836	50829	1.26	1569.2	<0.01
Secondary cluster5	Central California	2001-2005	47334	38419	1.24	977.0	<0.01

It has been reported that men and women may have different AD/dementia risk (Gao et al., 1998; Carter et al., 2012; Chêne et al., 2015). The difference may be due to sex(gender) differences in dementia risk factors (Azad et al., 2007; Mielke et al., 2014), or that sex modifies the associations between AD/dementia and its other risk factors (Fuhrer et al., 2003; Noale et al., 2013), or that clinical expression of AD pathology as dementia differs by sex (Barnes et al., 2005). Spatiotemporal cluster analysis was further carried out for men and women separately to test for any differential cluster patterns of AD/all-cause mortality by sex. Table 2 shows the most likely and top 5 secondary clusters by sex, adjusted for race, age and temporal trend (The cluster maps for men and women are Figure 3 and Figure 4, respectively). For men, the most likely cluster of AD as the underlying cause of death (Figure 3a) was in the Northeast region, consisting of large parts of New York, Pennsylvania, and New Jersey. This cluster had a statistically significant lower risk (*RR*=0.57, *LLR*=2063.1, 2006-2010) compared to the rest of the country. The most likely secondary cluster was in the Pacific Northwest, including most parts of Washington and Oregon (*RR*=1.72, *LLR*=622.1, 2001-2005). For AD as one of the multiple causes (Figure 3b), the most likely cluster (*RR*=0.64, *LLR*=2433.8, 2006-2010) was at the same approximate location as in Figure 2a; however, the most likely secondary cluster was in south Florida (*RR*=0.63, *LLR*=1088.8, 2006-2010). For all-cause dementia as the underlying cause of death (Figure 3c), the most likely cluster (*RR*=0.35, *LLR*=2934.1, 2006-2010) was a small area consisting of several counties in southeast New York and northeast New Jersey. The most likely secondary cluster (*RR*=1.30, *LLR*=1167.8, 2006-2010) was located in the Ohio River Valley and Carolinas. For all-cause dementia as one of the multiple causes (Figure 3d), the most likely cluster

(*RR*=0.48, *LLR*=3828.7, 2005-2009) was similar as in Figure 2c, but the most likely secondary cluster was in south Florida (*RR*=0.64, *LLR*=2008.0, 2006-2010).

Compared with men, women showed quite similar cluster patterns in AD/all-cause dementia mortality risk (Figure 4). The most likely clusters of AD/all-cause dementia mortality were both low risk clusters located in the Northeast region and the most likely secondary clusters were both high risk clusters in the Ohio River Valley and Carolinas region. One noticeable difference was that men had a much lower relative risk of mortality of AD as one of the multiple causes in Utah and New Mexico compared to women in the same area; while women had a relatively lower mortality risk of all-cause dementia as one of the multiple causes than men in Louisiana, south Mississippi, and southwest Alabama.

Table 2 Spatiotemporal clusters of AD/all-cause dementia mortality by sex, adjusted for race, age and temporal trend.

	AD as the underlying cause			AD as a multiple cause			Dementia as the underlying cause			Dementia as a multiple cause		
	Location	Time	*RR*	Location	Time	*RR*	Location	Time	*RR*	Location	Time	*RR*
Men												
Most likely cluster	New York, New Jersey, Pennsylvania	2006-2010	0.6	New York, New Jersey, Pennsylvania, Connecticut, Massachusetts	2006-2010	0.6	downstate New York, northeast New Jersey	2006-2010	0.4	downstate New York, northeast New Jersey	2005-2009	0.5
Secondary cluster1	Washington, Oregon	2001-2005	1.7	south Florida	2006-2010	0.6	Deep South	2006-2010	1.3	south Florida	2006-2010	0.7
Secondary cluster2	Ohio River Valley and Carolinas	2004-2008	1.4	Ohio River Valley and Carolinas	2003-2007	1.4	south Florida	2006-2010	0.7	Ohio River Valley and Carolinas	2001-2005	1.3
Secondary cluster3	south Florida	2006-2010	0.6	south and central California, southwest Nevada	2006-2010	1.3	Ohio River Valley and Carolinas	2004-2008	1.2	Washington, Oregon, west Idaho	2001-2005	1.3
Secondary cluster4	south California, west Arizona	2002-2006	1.6	Washington	2006-2010	1.7	Washington, Oregon, west Idaho	2005-2009	1.3	north Texas, Oklahoma	2002-2006	1.3
Secondary cluster5	east Texas, Louisiana	2002-2006	1.4	north Texas, Oklahoma, south Kansas, west Arkansas	2002-2006	1.3	central California	2000-2004	0.7	central California	2001-2005	1.3
Women												
Most likely cluster	New York, New Jersey, Pennsylvania	2006-2010	0.6	New York, New Jersey, Pennsylvania	2006-2010	0.6	south New York, northeast New Jersey	2006-2010	0.4	south New York, northeast New Jersey	2006-2010	0.5
Secondary cluster1	Ohio River Valley and Carolinas	2004-2008	1.4	Ohio River Valley and Carolinas	2003-2007	1.4	Ohio River Valley and Carolinas	2004-2008	1.3	Ohio River Valley and Carolinas	2002-2006	1.3
Secondary cluster2	Washington, Oregon, west Idaho	2001-2005	1.7	south Florida	2006-2010	0.6	east Texas, west Louisiana, southwest Arkansas, south Oklahoma	2004-2008	1.3	south Florida	2006-2010	0.7
Secondary cluster3	south California, west Arizona	2003-2007	1.6	Washington, Oregon, west Idaho	2001-2005	1.6	south Florida	2006-2010	0.8	Washington, Oregon, north California	2001-2005	1.3
Secondary cluster4	south Florida	2006-2010	0.7	south and central California, southwest Nevada	2006-2010	1.3	central California	2000-2004	0.8	North Texas, Oklahoma	2002-2006	1.3
Secondary cluster5	east Texas, Louisiana	2002-2006	1.3	east Texas, south Oklahoma	2002-2006	1.3	east Nevada, Utah, north Arizona	2002-2006	1.4	Central California	2001-2005	1.2

Note: All clusters are statistically significant at p=0.01. Clusters are ranked by their log likelihood ratios.

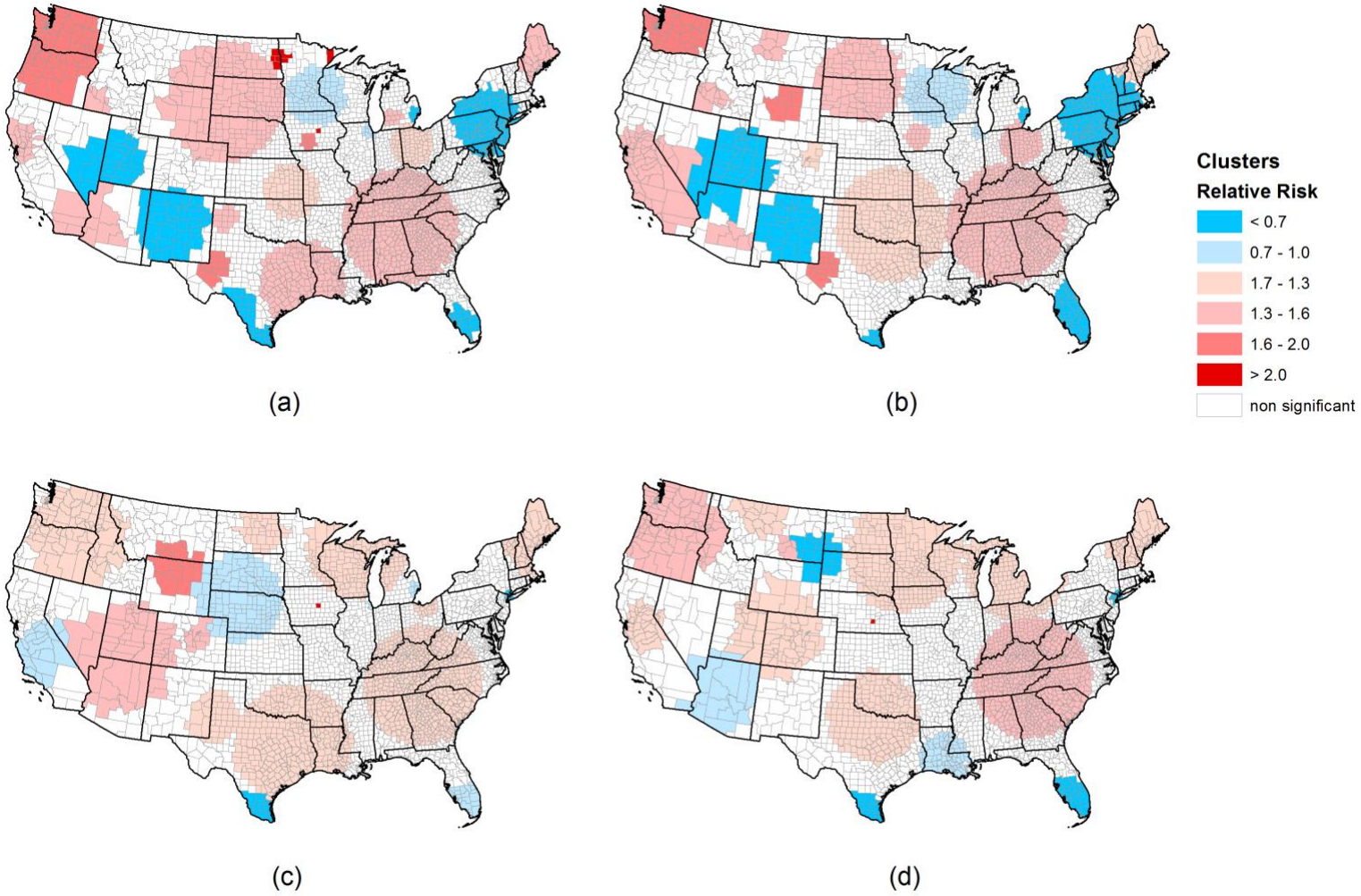

Figure 3 Spatiotemporal clusters of mortality attributable to (a) AD as the underlying cause (b) AD as one of the multiple causes (c) all-cause dementia as the underlying cause (d) all-cause dementia as one of the multiple causes in men, adjusted for race, age and temporal trend.

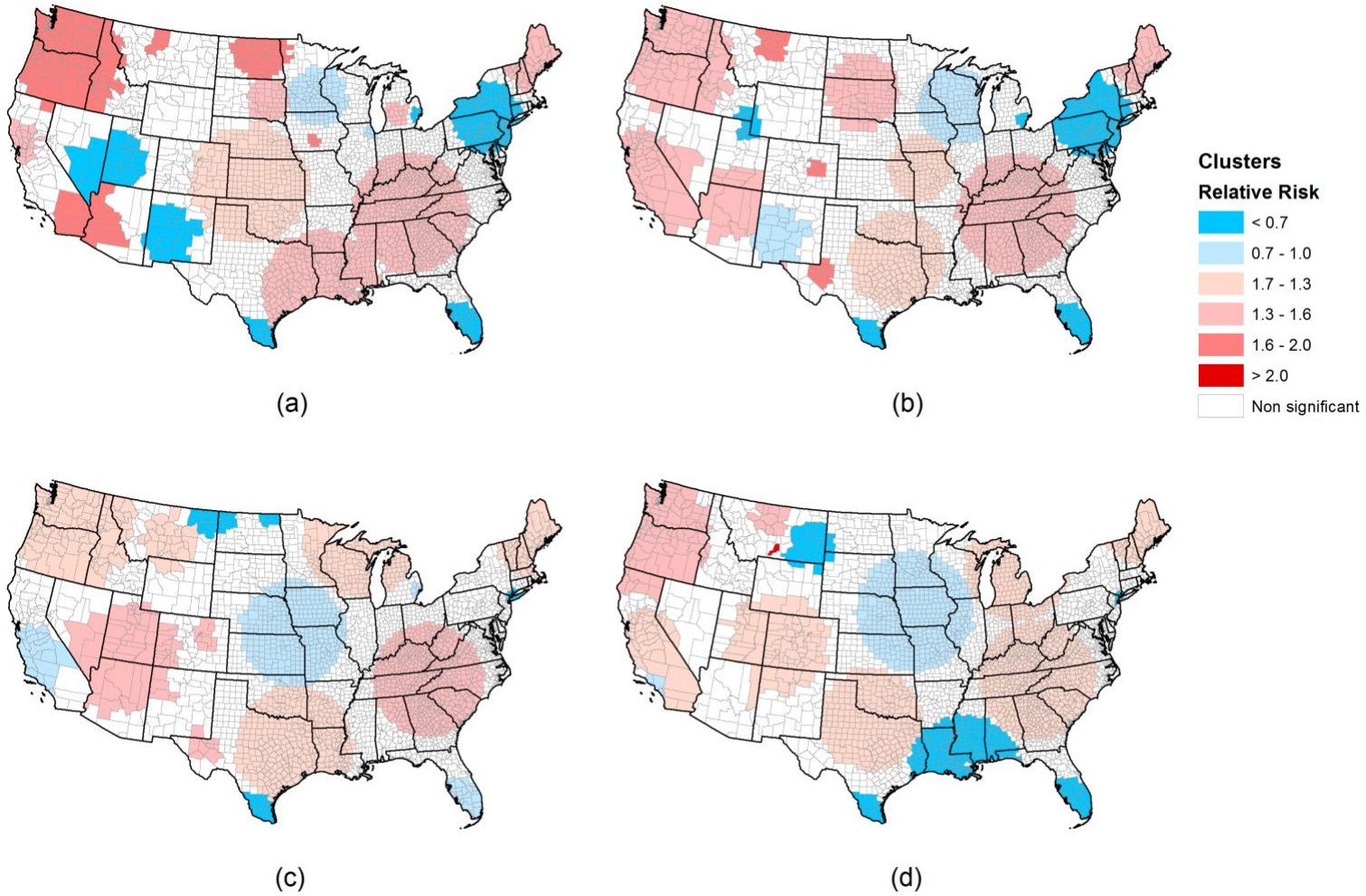

Figure 4 Spatiotemporal clusters of mortality attributable to (a) AD as the underlying cause (b) AD as one of the multiple causes (c) all-cause dementia as the underlying cause (d) all-cause dementia as one of the multiple causes in women, adjusted for race, age and temporal trend.

3.4 Discussion

This study provided evidence for spatiotemporal clusters of AD/all-cause dementia mortality in the U.S. during 2000 and 2010, suggesting both spatially and temporally uneven mortality risk. One of the highlights of this study is the use of complete national death certificate data. Compared to other community-based studies or population-based sample analyses, using exhaustive population death registry minimizes preselection bias (Thygesen and Ersbøll, 2014). Moreover, due to the fact that acute diseases such as pneumonia and heart disease are more likely to be listed on death certificate as the underlying cause of death, using multiple-cause data mitigated underestimation of the effects of chronical diseases such as AD and dementia on death (Gillum and Obisesan, 2011). Finally, improved disease diagnostic specificity in ICD-10 compared to previous versions makes the results of cluster analysis more accurate.

The implications of the results are twofold. First, one of the main reasons for examining geographical and temporal variations in disease risk is to facilitate the identification of modifiable risk and protective factors. The results suggest that apart from demographic structures, there may be some socio-environmental factors underlying the found clustering patterns. For example, socioeconomic deprivation and low education attainment in the South may be among the fundamental causes of high dementia mortality in that region. Other factors such as high prevalence of obesity, diabetes, tobacco use, and physical inactivity may elevate population dementia mortality risk in the region as well. However, Pacific Northwest being a consistent high-risk cluster suggests other possible factors at play. Indeed, given the multifactoriality of the diseases and various pathological pathways, other biological, behavioral and environmental factors (and their possible

interactions) might have also contributed to the clusters. For example, given the genetic features of AD and other types of dementia (Bekris and Yu, 2010; Srinivasan et al., 2016), concentration of persons with susceptible genes might partially explain the high-risk clusters. Moreover, spatiotemporal variations in local population health behaviors including dietary practices (Barberger-Gateau et al., 2007; Gu and Scarmeas, 2011; Shah, 2013) and social interactions (Kuiper et al., 2015) may also contribute to the cluster results. And finally, environmental factors including toxins (e.g., air pollution, lead exposure) and destination accessibility (e.g., access to health and social care) might have affected incidence risk or survival in dementia and thus mortality patterns as well. Although it is important not to conflate the risk of incident AD/dementia with ecological mortality risk from AD/dementia, factors associated with increased incident risk and shorter survival may partially explain the high-risk mortality clusters. To fully explain the causes of the clustering patterns, collaborative research efforts from multiple disciplines such as genetics, pathology, epidemiology and geography are required. The goal will not be achieved until we have a better understanding of AD/dementia etiologies.

Second, the results also have important implications for public health policies. As dementia patients at severe stages often show high levels of dependency and require around-the-clock care, federal and local health agencies should evaluate the capacities of health care systems (e.g., medical workforce, long term care facilities) to meet patient needs before death in those high-risk cluster areas. Moreover, as many dementia patients die from home (Mitchell et al., 2005), health policymakers should also evaluate the care gaps at homes and implement social care programs providing coping strategies and supporting resources for informal caregivers. The results suggest that communities in

Pacific Northwest and the Ohio River Valley and Carolinas region demand immediate attentions. Due to persistent socioeconomic deprivation, the latter region may bear additional obstacles in coping with the impacts of high dementia mortality. Federal and state health departments may employ the results to prioritize health and social care delivery to those communities. Actions plans should be in place in those areas to coordinate care management between familiar caregivers, community facilities and medical professionals.

I evaluated the effects of alternate maximum cluster sizes on cluster results. When the maximum radius decreased to 300 kilometers (see Figure 5), the large AD mortality clusters in the Ohio River Valley and Carolinas region in Figure 2 were forced to split into smaller clusters, although they fell inside the same *RR* interval. The large dementia mortality cluster in the same location, however, showed *RR* heterogeneity among resultant smaller clusters. Similar patterns appeared for the large clusters in the Pacific Northwest and east Texas and Louisiana. Other highly likely clusters in the Northeast, south Florida, central California did not change significantly. When the maximum radius increased to 700 kilometers (see Figure 6), the clusters located in the Ohio River Valley and Carolinas region and the northwest in Figure 2 became even bigger. However, increasing maximum radius did not significantly change the location, spatial and temporal extent of some highly likely clusters, such as the ones located in Pacific Northeast, south Florida and the region of east Texas and Louisiana (especially for dementia mortality). Indeed, there is a trade-off between large and small maximum cluster sizes in correctly identifying clusters. If the maximum size is too large, it can hide small clusters within larger, heterogeneous ones; yet, if the maximum size is too small,

significant regional clusters may not be detected (Chen et al., 2008). Although parameter settings of maximum cluster size affect cluster results, it was found that the approximate location/time and size of most of the highly likely clusters were consistent.

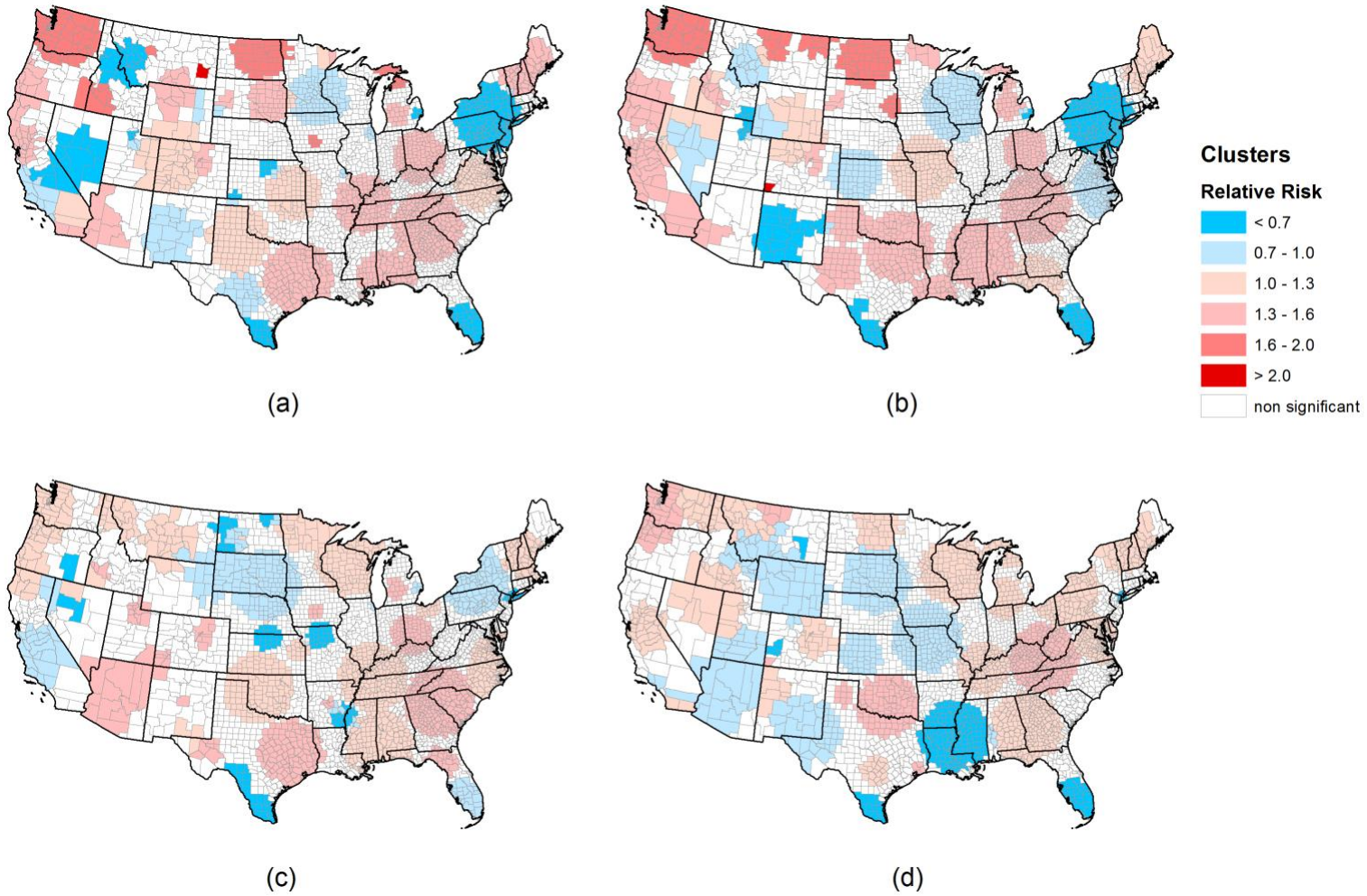

Figure 5 Spatiotemporal clusters of mortality attributable to (a) AD as the underlying cause (b) AD as one of the multiple causes (c) all-cause dementia as the underlying cause (d) all-cause dementia as one of the multiple causes, adjusted for sex, race, age and temporal trend. Maximum radius of cluster circle is 300 kilometers

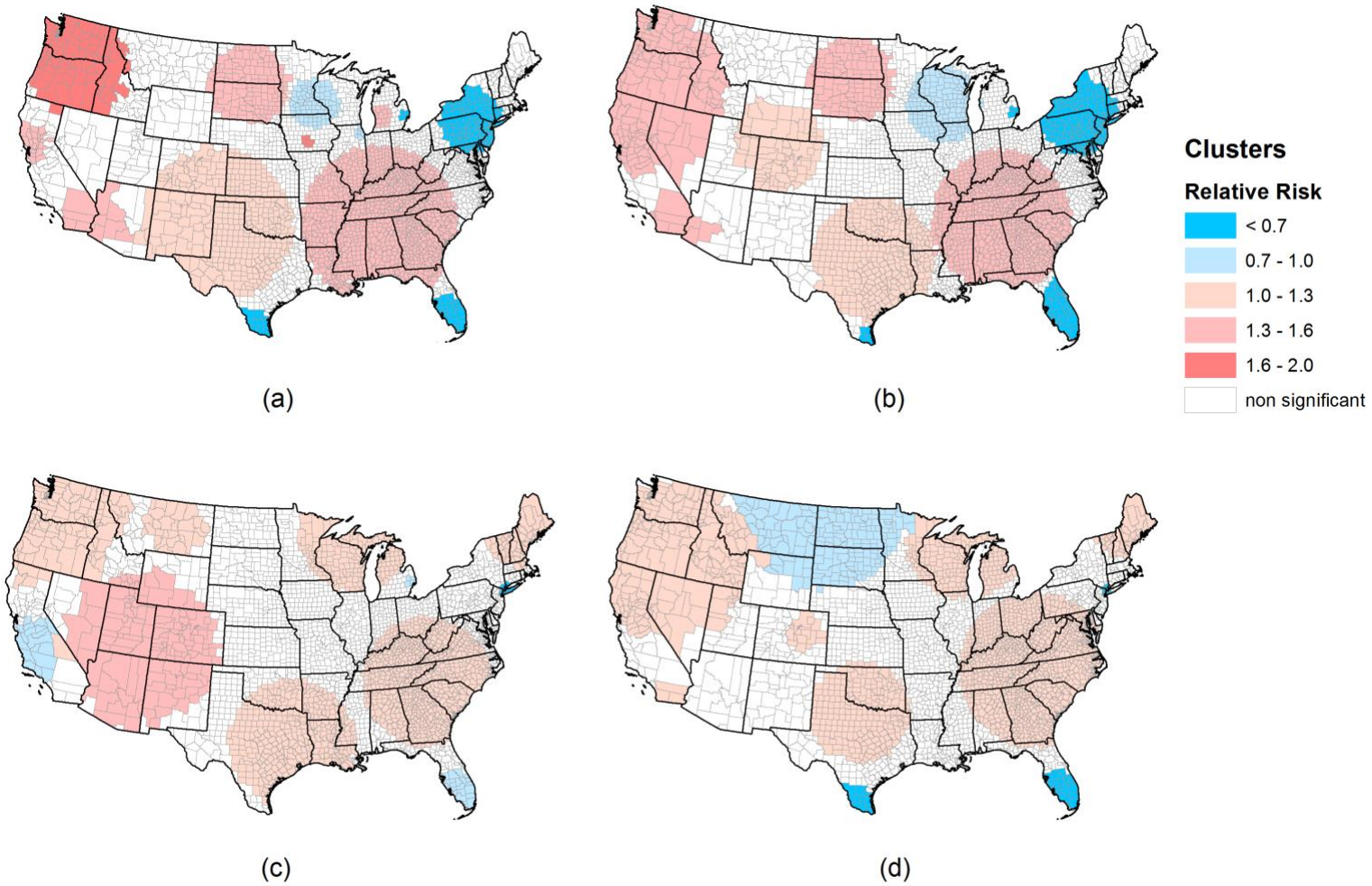

Figure 6 Spatiotemporal clusters of mortality attributable to (a) AD as the underlying cause (b) AD as one of the multiple causes (c) all-cause dementia as the underlying cause (d) all-cause dementia as one of the multiple causes, adjusted for sex, race, age and temporal trend. Maximum radius of cluster circle is 700 kilometers.

This study has some limitations, too. First, the under-reporting of AD/dementia in death registries is well documented (Morgan and Clarke, 1995; Olichney et al., 1995; Ganguli and Rodriguez, 1999; Romero et al., 2014). The real numbers of AD/dementia mortality may be greater than the vital statistics suggested. Second, geographical and temporal variations in disease coding and reporting practices may influence the cluster results. Those variations could stem from public awareness of AD/dementia, availability and accessibility of medical resources necessary for accurate case identification, certifying physicians' perception of AD/dementia as a (direct or indirect) contributing factor to death, among others (Gillum et al., 2011; Romero et al., 2014). Moreover, misclassification between dementia subtypes could also impact the results, especially for AD mortality. A more standardized and accurate reporting procedure of AD/dementia on death certificates is needed. Third, the scan technique can only identify the approximate location of risk clusters as the exact cluster peripheries should remain uncertain (Kulldorff, 2001, 2006; Boscoe et al., 2003). Fourth, given the study's ecological nature, the results cannot be used to extrapolate the risk of individuals dying from AD/dementia, as "ecological fallacy" may arise (Robinson, 1950). Ecological mortality risk from AD/dementia, other than individual risk for incidence, is discussed throughout the article, unless otherwise specified. Fifth, this study does not explicitly address the impact of population migration, especially of older adults, on the spatiotemporal clusters. However, the population files were created from the decennial censuses and the yearly estimates of county populations during the decade. It moderated the influence of demographic changes on the analysis results.

3.5 Conclusions

To my knowledge, this study is the first that used space-time scan statistics to identify AD/dementia mortality clusters in the U.S. Compared to other purely geographical studies, this article links varying dementia mortality risk to not only space but also time. It identified clusters of statistically significantly higher AD/all-cause dementia mortality risk in the Ohio River Valley and Carolinas region, the Northwest, central California, and east Texas, as well as clusters of statistically significantly lower risk in the Northeast and Florida. Temporal information showed improved relative risk of AD/dementia mortality in most of the highly likely clusters. Stratified analysis by sex revealed similar clustering results between men and women, with a few noticeable differences. Although causal inference of those clusters is beyond the scope of this study, the findings should propel researchers to focus on places and time periods with significantly different dementia mortality risk for etiological clues. More research is needed to uncover the mechanisms through which the biologies, behaviors and environmental exposures of local populations may interact to create and sustain differential AD/dementia mortality risk between places and time. Health policymakers should evaluate the medical and social care capacities and provide supporting resources in local areas, especially high-risk clusters, to ensure the quality of life of dementia patients at the end of their lives.

CHAPTER 4: SYNERGISTIC EFFECTS OF SOCIAL AND PHYSICAL ENVIRONMENTS ON DEMENTIA MORTALITY RISK

4.1 Introduction

Dementia is a major contributor to mortality in the United States. The term "dementia" consists of a number of neurodegenerative disorders (e.g. Alzheimer's disease, vascular dementia, dementia with Lewy bodies, mixed dementia, etc.) that can cause memory loss and other cognitive problems. Using a nationally representative sample, a recent study found that dementia is the second largest contributor to mortality among older adults in the U.S., following heart failure (Tinetti et al., 2012). According to the National Center of Health Statistics, Alzheimer's disease (AD), the most common form of dementia, is the 6th leading cause of death among all and the 5th leading cause of death among older adults in the U.S. (Murphy et al., 2017). In contrast to the declining mortality rates of other major causes of death (e.g. heart disease, cancer, HIV) over the recent years, the U.S. annual age-standardized AD mortality rate increased by 63.3% from 18.0 per 100,000 people in 2000 to 29.4 in 2015 (Miniño et al., 2002; Murphy et al., 2017). As the U.S. continues to shift towards an older population (Vincent and Velkoff, 2010), mortality attributable to dementia is likely to increase in the foreseeable future absent any curative treatments of the diseases.

Previous research revealed remarkable geographical variations in dementia/AD mortality risk in the U.S. (Figueroa et al., 2008; Steenland et al., 2009; Gillum and Obisesan, 2011; Gillum et al., 2011; Xu and Wu, 2018). It is generally reported that mortality rates in the Northwest Pacific region and the South were significantly higher compared to the rest of the nation; while those in the Northeast and Southeast were significantly lower. The mechanisms responsible for creating and sustaining such variations remain unclear. A large body of research has focused on

identifying individual-level risk factors for dementia, which is helpful in providing explanations. However, in recent years, researchers have begun to look beyond individual risk factors to explore the independent effects of social and physical environmental influences on cognitive ageing and dementia risk.

For instance, a recent review found that in studies examining the associations between neighborhood socioeconomic status (SES) and cognitive performance, the majority reported better cognitive functioning among older adults living in neighborhoods with higher SES compared to those living in neighborhoods with lower SES, independent of individual sociodemographic, behavioral and socioeconomic characteristics (Wu et al., 2015a). Studies have also found that residents living in areas with higher SES (Sheffield and Peek, 2009) or richer community resources (Clarke et al., 2015) had slower cognitive decline compared to their counterparts in areas that are more socioeconomically disadvantaged. Although studies of the relationship between neighborhood SES and cognitive functioning and decline are burgeoning, the results have not been conclusive. Some studies also found no independent effects of neighborhood SES on cognitive functioning (Sisco and Marsiske, 2012; Wörn et al., 2017), cognitive decline (Zeki Al Hazzouri et al., 2011; Rosso et al., 2016), or incident dementia (Menec et al., 2010; Wu et al., 2015b; Ouvrard et al., 2017), after adjusting for individual level factors.

Current evidence also suggests that strong social ties and interactions may protect individuals from incident cognitive decline (Bassuk et al., 1999b; Zunzunegui et al., 2003) or dementia (Fratiglioni et al., 2000; Wang et al., 2002; Crooks et al., 2008; Sörman et al., 2015). A recent review concluded that poor social interaction is comparable to other well-established risk factors of dementia such as low education, physical inactivity and late-life depression (Kuiper et

al., 2015). Although the majority of studies mentioned above measured social ties and social integration at the individual level, living in a socially integrated community may also have independent effects on cognitive functioning and dementia. Empirical studies have also shown that neighborhood social capital and social cohesion predict social and physical wellbeing and can serve as mediators between individual disadvantages and negative health outcomes in older adults (Cramm et al., 2013). Moreover, research has shown that area-based social capital is associated with risk factors for cognitive deterioration and/or dementia such as obesity (Cramm et al., 2013). In the cognitive ageing and dementia literature, the independent effects of area-based social integration remain under-explored.

Although more research is needed to establish a causal relationship, there is also mounting evidence linking the adverse effects of air pollution to neurobehavioral function (Power et al., 2016). Exposure to ambient air pollution, especially fine particulate matters (PM), may be associated with poorer cognitive function (Ranft et al., 2009; Zeng et al., 2010; Power et al., 2011; Ailshire and Clarke, 2014; Ailshire and Crimmins, 2014; Manjourides et al., 2017; Salinas-Rodríguez et al., 2018), faster cognitive decline (Weuve et al., 2012; Cacciottolo et al., 2017), and increased AD/dementia incidence (Wu et al., 2015; Oudin et al., 2016; Cacciottolo et al., 2017; Chen et al., 2017).

Available evidence indicates that social and physical environments may have independent effects on cognitive functioning and risk of dementia, above and beyond individual influences. What is lacking in current dementia risk factor literature is the investigation of the synergistic effects of social and physical environmental factors. Limited empirical studies have shown that social environmental factors (e.g. neighborhood disorder and decay, social integration) can either accentuate or mediate the adverse effects of physical environmental toxins

on cognitive health. For example, Ailshire et al. (2017) showed that the effect of $PM_{2.5}$ on cognitive errors was stronger among older adults living in neighborhoods with high social stressors. Similarly, Glass et al. (2009) found that residency in stressful neighborhoods accentuated the adverse effects of lead exposure on cognitive function. In the present study, I used a multilevel analysis framework to examine the associations between three contextual-level variables measured at the county level and individual risk of dementia mortality for older adults in Wisconsin. The three county-level variables are: 1) area socioeconomic deprivation (SED); 2) area social integration; and 3) air pollution. Multilevel logistic regression models were constructed to explore the synergistic effects of individual- and contextual-level factors in predicting the likelihood of dying from dementia. Figure 7 illustrates the conceptual framework of the multilevel mechanism underlying individual dementia mortality risk. It was hypothesized that individual dementia mortality risk was negatively associated with social integration and positively associated with area SED and air pollution. This study also aimed to test whether there were cross-level interaction effects between demographic characteristics and environmental factors on individual dementia mortality risk and whether area social integration might modify the effects of area SED and air pollution on individual dementia mortality risk.

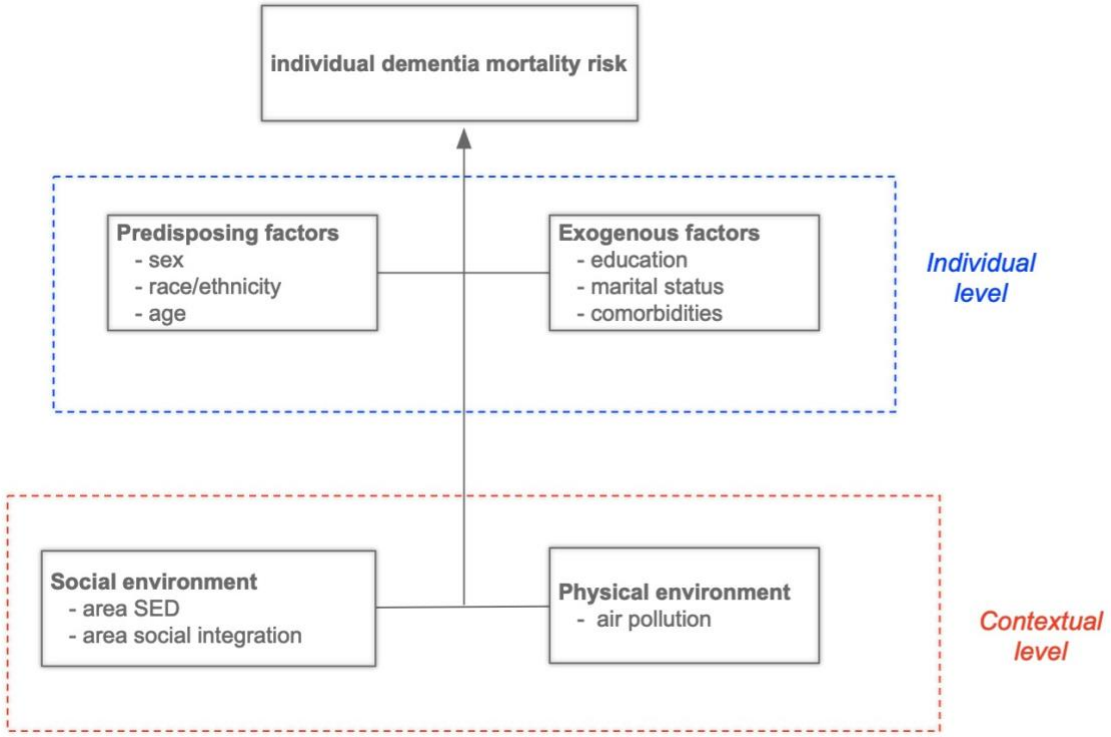

Figure 7 Conceptual framework of the multilevel socio-ecological mechanism underlying individual dementia mortality risk.

4.2 Data and methods

4.2.1 Data sources

Individual death certificates data were requested from the NCHS at the CDC. The sample consisted of all 36,394 residential deaths in the state of Wisconsin in 2010 for persons aged ≥ 65 years. These death certificates were then used to identify deaths attributable to dementia and to extract individual socio-demographic information. County-level social and physical environmental attributes were collected from a variety of sources. Data used for measuring county-level SED were obtained from the U.S. Census Bureau, 2006-2010 American Community Survey (U.S. Census Bureau, 2011). Area social integration measures were downloaded from County Health Rankings & Roadmaps (available at

http://www.countyhealthrankings.org). And air pollution data were obtained from Air National Environmental Public Health Tracking Network at the CDC website (available at https://ephtracking.cdc.gov). Individual death records and county data were joined by the Federal Information Processing Standard codes of counties.

4.2.2 Dependent variable

The dependent variable for all models was a binary variable to indicate a dementia attributable death. International Classification of Disease, 10th Revision (ICD-10) codes were used to identify dementia attributable deaths. The multiple causes of death were extracted from the *Entity-Axis conditions* field on death certificates, which lists up to 20 conditions contributing to a person's death. The value of the binary variable was assigned as 1 if any of the dementia codes (ICD-10 = F01, F02, F03, G30) were indicated as a cause of death on the death certificate; the value for all other deaths was equal to 0, indicating the death was not attributable to dementia.

4.2.3 Independent variables

Area socioeconomic deprivation. Counties were used as the spatial unit for measuring area socioeconomic deprivation. For each county, the Townsend Deprivation Index, a compositional measure of socioeconomic deprivation based on four variables: percentage of population 16 years and older who are unemployed, percentage of households without vehicle available, percentage of renter occupied households and percentage of households with more than 1 occupant per room (Townsend et al., 1988), was calculated. Originally developed in the United Kingdom, the index is a well-established and validated area deprivation index (Messer et al., 2006) and has been widely used to assess the relationships between area socioeconomic status and a number of health behaviors and outcomes (Araya et al., 2006; Bambra et al., 2014;

Dejardin et al., 2014; Remes et al., 2017; Blakey et al., 2018; Wilding et al., 2018). The four original variables were standardized and combined to create the index for each county. All counties were then grouped into quartiles based on index similarity. It was hypothesized that higher index values would be associated with elevated risk of dementia mortality.

Area social integration. The number of membership organizations (e.g. civic organizations, fitness centers, religious organizations, political organizations, and professional organizations) per 10,000 persons was used to measure the level of social integration in a county. These organizations were identified by North American Industry Classification System codes 813410, 713950, 713910, 713940, 711211, 813110, 813940, 813930, 813910 and 813920 from the original data drawn from the U.S. Census Bureau, County Business Patterns: 2010 (available at https://www.census.gov/data/datasets/2010/econ/cbp/2010-cbp.html). It has been stated that these membership organizations generate social capital by enabling interaction between members of a community (Rupasingha et al., 2006).

$PM_{2.5}$ concentration. Monitor and modeled annual average concentration of fine particulate matter that have a diameter of less than 2.5 micrometers ($PM_{2.5}$) was used to measure the overall air quality in Wisconsin counties in 2010. $PM_{2.5}$, instead of PM_{10}, was used because empirical evidence has shown that smaller fine particulate matters may be more detrimental to cognitive functioning (Underwood, 2017).

Individual-level Covariates. Covariates at the individual level include demographic factors which may predispose individuals to differential dementia mortality risk and exogenous variables which may modify such risk. These variables included sex, race/ethnicity, age at death, marital status, education attainment and comorbidities. Sex was categorized as male and female. Race/ethnicity was categorized as non-Hispanic White, non-Hispanic Black, non-Hispanic Other,

and Hispanic. Age at death was a continuous variable and accurate to month. A recent systematic review concluded that being married is associated with reduced risk of dementia (Sommerlad et al., 2017). Marital status was categorized as: Never married, single; Married; Widowed; Divorced; Marital Status not on certificate; Marital Status unknown. No records in the sample fell into the last two categories. Widowed and Divorced were combined into one category Widowed/Divorced for the analysis. Strong evidence suggests that higher education protects individuals from dementia (Sharp and Gatz, 2011) through "cognitive reserve" (Meng and D'Arcy, 2012). Education was also used as a proxy to control for the confounding effects of individual-level socioeconomic status on dementia mortality. Education was categorized as High school or less, Some college or college degree, and Advanced degree. Chronic diseases such as hypertension (Duron and Hanon, 2008; Kennelly et al., 2009; Nagai et al., 2010; Sharp et al., 2011) and diabetes mellitus (Cukierman et al., 2005; Biessels et al., 2006) are known risk factors of dementia. These two comorbidities were included as individual-level covariates in the regression models. The ICD-10 codes for hypertension are I10, I11.0, I11.9, I12.0, I12.9, I13.0, I13.10, I13.11, I13.2. The ICD-10 codes for diabetes mellitus are E08, E09, E10, E11, E13, O24, P70.2.

4.2.4 Statistical analysis

Descriptive statistics of all categorized individual- and contextual-level variables were prepared by the binary variable indicating dementia death. To test whether dementia mortality risk was associated with these variables, maximum likelihood estimates of crude odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated. Pearson's Chi-squared test was used to test the independence between dementia mortality risk and individual- and contextual-

level variables. Pearson correlation was used to test bivariate associations between continuous contextual-level variables.

Given that the outcome is a binary variable indicating whether a death is attributable to dementia, two-level logistic generalized linear mixed models (GLMM) based on a logit-link function were fitted to examine the associations between the risk of dementia mortality and social and physical environments. Using counties as the random effect cluster variable accounts for the hierarchical structure of individuals (level 1) nested within counties (level 2). Statistical analyses were carried out in several stages. First, a fully unconditional model was fitted (Raudenbush and Bryk, 2002); the variation in the individual risk of dementia mortality was modelled by a random intercept term for counties and an individual random error term. This model examines how much of the variance in the individual dementia mortality risk can be partitioned to level 2. In model 1-3, the three contextual-level variables as fixed main effects were gradually introduced at level 2. In model 4, the main effects of demographic variables including age (centered around its mean) as a continuous variable as well as sex and race/ethnicity as categorical variables were adjusted for at level 1. And finally, a fully-adjusted model 5 including all individual- and contextual-level variables was estimated to evaluate synergism of all variables. Four additional variables including education, marital status, hypertension and diabetes mellitus as categorical variables were controlled for. Model 5 evaluated whether adding exogenous compositional variables would modify the effects of contextual-level variables on dementia mortality risk. County level random variance was assessed after taking into account the compositional variations between these spatial units. Significance tests in all models were two-tailed and statistical significance was defined at the 5% alpha level. The results of fixed effects of individual- and contextual-level variables, except for

Age, are expressed as adjusted odds ratios (AOR) with 95% confidence intervals. All statistical analyses were conducted using the *glmer* package (Bates et al., 2014) in R version 3.4.0 (R Development Core Team, 2014).

4.3 Results

Table 3 presents the descriptive statistics for individual- and contextual-level variables for all residential deaths in Wisconsin in 2010. There were in total 36,394 deaths occurred in the state, among which 7,087 deaths were attributable to dementia. Approximately 54.7% of all deaths were female and the average age of all deaths was 83.0 ± 8.7 years. Pearson's Chi-Square Test showed that all individual- and contextual-level variables, except for education and diabetes mellitus, were significantly associated with the risk of dementia mortality. Correlation coefficients among the three contextual-level variables were also calculated (see Table 4). Area SED was negatively correlated with area social integration ($r = -0.02$) and $PM_{2.5}$ concentration ($r = -0.01$). Area social integration was negatively correlated with $PM_{2.5}$ concentration ($r = -0.43$). Only the correlation between area social integration and $PM_{2.5}$ concentration was statistically significant.

Table 3 Descriptive statistics of individual and contextual variables of all residential deaths among Wisconsin older adults in 2010.

Variables	All deaths		Dementia deaths		non-Dementia deaths		*p*- value†
	N	(%)	N	(%)	N	(%)	
Individual variables							
Sex							***
Male	16472	(45.3)	2358	(33.3)	14114	(48.2)	
Female	19922	(54.7)	4729	(66.7)	15193	(51.8)	
Race/ethnicity							*
non-Hispanic White	34854	(95.8)	6827	(96.3)	28027	(95.6)	
non-Hispanic Black	1022	(2.8)	186	(2.7)	836	(2.9)	
non-Hispanic Other	318	(0.9)	43	(0.6)	275	(0.9)	
Hispanic	200	(0.5)	31	(0.4)	169	(0.6)	
Age, yr							***
65-74 years old	7109	(19.5)	295	(4.1)	6814	(23.3)	
75-84 years old	12255	(33.7)	1805	(25.5)	10450	(35.6)	
85 years old and over	17030	(46.8)	4987	(70.4)	12043	(41.1)	
Marital status							***
Single	2129	(5.8)	401	(5.7)	1728	(5.9)	
Married	13445	(36.9)	1823	(25.7)	11622	(39.7)	
Widowed/Divorced	20820	(57.2)	4863	(68.6)	15957	(54.4)	
Education							
High School or Less	27039	(74.3)	5334	(75.3)	21705	(74.1)	
Some College or College Degree	7479	(20.6)	1397	(19.7)	6082	(20.7)	
Advanced Degree	1876	(5.2)	356	(5.0)	1520	(5.2)	
Hypertension							***
Yes	4471	(12.3)	969	(13.7)	3502	(12.0)	
No	31923	(87.7)	6118	(86.3)	25805	(88.0)	
Diabetes Mellitus							
Yes	1279	(3.5)	271	(3.8)	1008	(3.4)	
No	35115	(96.5)	6816	(96.2)	28299	(96.7)	
Contextual variables							
Area SED							***
Q1: Least Deprived	7551	(20.7)	1479	(20.9)	6072	(20.7)	
Q2	5437	(14.9)	864	(12.2)	4573	(15.6)	
Q3	7784	(21.4)	1589	(22.4)	6195	(21.1)	
Q4: Most Deprived	15622	(42.9)	3155	(44.5)	12476	(42.5)	
Area social integration							***
Q1: Most integrated	4721	(13.0)	830	(11.7)	3891	(13.3)	
Q2	6163	(16.9)	1157	(16.3)	5006	(17.1)	
Q3	9103	(25.0)	1876	(26.5)	7227	(24.7)	
Q4: Least integrated	16407	(45.1)	3224	(45.5)	13183	(45.0)	
PM2.5 concentration							***
Q1: Least polluted	2902	(8.0)	447	(6.3)	2455	(8.4)	
Q2	5882	(16.2)	1045	(14.7)	4837	(16.5)	
Q3	7967	(21.9)	1569	(22.1)	6398	(21.8)	
Q4: Most polluted	19643	(54.0)	4026	(56.8)	15617	(53.3)	

Note: Percentages may not add up to 1 due to round up.

†*p*- values were generated by Pearson's Chi-Square test of independence.

*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

Table 4 Descriptive statistics of and correlations between area SED, area social integration and $PM_{2.5}$ concentration among Wisconsin counties (n = 72).

	Range	Mean	Standard deviation	Correlation coefficient		
				(a)	(b)	(c)
(a) Area SED	(-4.32, 14.72)	0	2.94	1		
(b) Area social integration	(7.80, 23.40)	13.57	3.3	-0.02	1	
(c) PM2.5 concentration	(6.82, 11.28)	9.28	1.2	-0.01	-0.43***	1

Correlations coefficients represent Pearson's r.
*** p <0.001, ** p <0.01, * p <0.05

Figure 8 illustrates the differences in dementia mortality risk by individual- and contextual-level variables measured by crude ORs generated from univariate logistic regressions. Among individual-level variables, age had a significant impact on the risk. Compared to the youngest age group (65-74 years), people who were between 75 and 84 years old (OR = 3.99, 95% CI = 3.51-4.54) and who were 85 years old and over (OR = 9.56, 95% CI = 8.47-10.48) were much more likely to die with dementia. Being female was associated with higher risk of dementia mortality compared to being male (OR = 1.86, 95% CI = 1.76-1.97). Non-Hispanic Black (OR = 0.91, 95% CI = 0.77-1.07), non-Hispanic Other (OR = 0.64, 95% CI = 0.45-0.89), and Hispanic (OR = 0.75, 95% CI = 0.5-1.11) had lower risks compared to non-Hispanic White. However, only the difference between non-Hispanic White and non-Hispanic Other was statistically significant. Although more education was associated with lower risk of dementia mortality, the difference was minimal and statistically non-significant. Compared to being single, being married was associated with decreased risk of dementia mortality (OR = 0.68, 95% CI = 0.6-0.76) while being widowed or divorced was associated with higher risk (OR = 1.31, 95% CI = 1.17-1.47). Having diabetes mellitus (OR = 1.12, 95% CI = 0.97, 1.28) and hypertension (OR = 1.17, 95% CI = 1.08-1.26) were both associated with higher risk of dementia mortality but only the latter reached statistical significance. Among all contextual-level variables, area SED was significantly associated with risk of dementia death. Specifically, living in the second least

deprived areas (Q2) was associated with 22% less risk of dementia death compared to living in the least deprived areas (Q1). The risks associated with living in more deprived areas (Q3 and Q4) were slightly higher than in least deprived areas (Q1) and the differences were not statistically significant. In terms of area social integration, less socially integrated areas were associated with higher risk (Q2 vs. Q1, OR = 1.08, 95% CI = 0.98, 1.12; Q3 vs. Q1, OR = 1.22, 95% CI = 1.11-1.33; Q4 vs. Q1, OR = 1.15, 95% CI = 1.05-1.25, respectively) compared to most integrated areas (Q1). $PM_{2.5}$ concentration appeared to have a dose-response effect on the risk of dementia death. The most polluted areas (Q4) were associated with 43% more risk of dementia death (OR = 1.42, 95% CI = 1.27-1.58) compared to the least polluted areas (Q1).

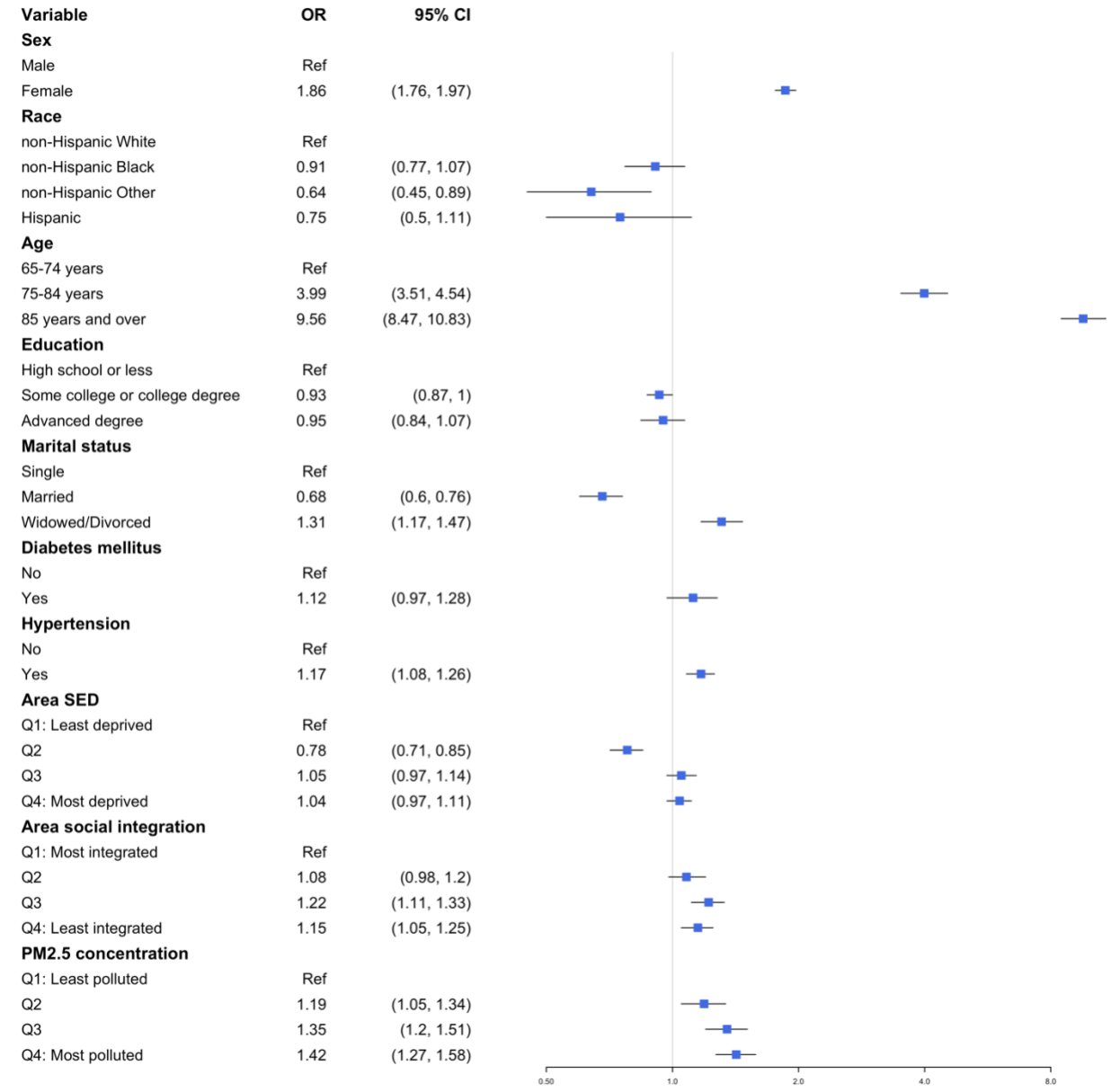

Figure 8 Forest plot of crude odds ratios in dementia mortality risk by individual- and contextual-level variables.

In the null multilevel model, the estimated intercept was -1.56 and the variance of random effect was 0.06 and statistically significant. In an average county in Wisconsin in 2010, the probability of dementia mortality among older adults was 0.17 (95% CI = 0.12-0.25). The results from multilevel logistic regression models with predictors are presented in Table 5. In

model 1, which only included area SED, the second quartile of area SED (Q2) was associated with significantly lower dementia mortality risk (Q2 vs. Q1: AOR = 0.81, 95% CI = 0.68-0.97). Q3 and Q4 were associated with elevated dementia mortality risk but the effects were minimal and not statistically significant. Model 2 included area social integration as an additional contextual explanatory variable. Results showed that the gradient in the relationship between area SED and dementia mortality risk did not change significantly when area social integration was accounted for. The third quartile of area social integration (Q3) was associated with significantly higher dementia mortality risk compared with Q1 (AOR = 1.28, 95% CI = 1.08-1.51). Model 3 incorporated all three contextual variables. The second quartile of area SED (Q2) was still associated with lower dementia risk; however, the third quartile appeared to be associated with significantly higher risk (AOR = 1.16, 95% CI = 1.00-1.23). Area social integration showed no relationship between dementia mortality risk when $PM_{2.5}$ concentration was introduced to the model. $PM_{2.5}$ concentration still maintained the dose-effect relationship between dementia mortality risk; however, only the coefficient estimates for Q3 and Q4 were statistically significant (Q3 vs. Q1, AOR = 1.28, 95% CI = 1.08-1.51; Q4 vs. Q1, AOR = 1.34, 95% CI = 1.12-1.60).

Table 5 Associations between individual- and contextual-level variables and risk of dementia mortality: multilevel logistic generalized linear mixed models.

	Model 1		Model 2		Model 3		Model 4		Model 5	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Fixed effects										
Individual variables										
Age, yr (continuous, centered)							2.08***	(2.01, 2.14)	2.07***	(2.01, 2.14)
Sex										
Male							1		1	
Female							1.41***	(1.33, 1.49)	1.41***	(1.32, 1.50)
Race/ethnicity										
non-Hispanic White							1		1	
non-Hispanic Black							1.2*	(1.00, 1.43)	1.19	(1.00, 1.42)
non-Hispanic Other							0.91	(0.65, 1.27)	0.90	(0.64, 1.27)
Hispanic							0.98	(0.66, 1.46)	0.97	(0.65, 1.44)
Marital status										
Single									1	
Married									0.96	(0.85, 1.09)
Widowed/Divorced									0.98	(0.87, 1.11)
Education										
High School or Less									1	
Some College or College Degree									0.97	(0.90, 1.03)
Advanced Degree									1.10	(0.96, 1.24)
Hypertension										
No									1	
Yes									1.01	(0.93, 1.10)
Diabetes mellitus										
No									1	
Yes									1.28***	(1.11, 1.48)
Contextual variables										
Area SED										
Q1: Least Deprived	1				1		1		1	
Q2	0.81*	(0.68, 0.97)	0.82*	(0.69, 0.97)	0.85*	(0.73, 1.00)	0.85*	(0.74, 0.98)	0.85*	(0.74, 0.98)
Q3	1.08	(0.91, 1.29)	1.11	(0.95, 1.31)	1.16*	(1.00, 1.33)	1.18*	(1.03, 1.34)	1.17*	(1.03, 1.34)
Q4: Most Deprived	1.05	(0.88, 1.24)	1.06	(0.90, 1.24)	1.07	(0.93, 1.23)	1.08	(0.95, 1.22)	1.07	(0.95, 1.22)
Area social integration										
Q1: Most integrated			1		1		1		1	
Q2			1.12	(0.90, 1.24)	1.04	(0.89, 1.22)	1.02	(0.88, 1.18)	1.02	(0.88 1.18)
Q3			1.28**	(1.08, 1.51)	1.14	(0.97, 1.34)	1.12	(0.97, 1.30)	1.12	(0.96, 1.30)
Q4: Least integrated			1.10	(0.93, 1.29)	0.96	(0.81, 1.13)	0.97	(0.83, 1.13)	0.97	(0.84, 1.13)
PM2.5 concentration										
Q1: Least polluted					1		1		1	
Q2					1.12	(0.95, 1.32)	1.06	(0.90, 1.24)	1.06	(0.91, 1.25)
Q3					1.28**	(1.08, 1.51)	1.20*	(1.03, 1.41)	1.21*	(1.03, 1.42)
Q4: Most polluted					1.34**	(1.12, 1.60)	1.29**	(1.09, 1.53)	1.29**	(1.10, 1.53)
Random effects										
Intercept variance	0.044***		0.035***		0.023***		0.015***		0.015***	
(SD)	(0.21)		(0.19)		(0.15)		(0.12)		(0.12)	
Diagnosis										
Log-likelihood	-17883.8		-17879.7		-17873.8		-16426.7		-16419.1	
AIC	35777.7		35775.4		35769.6		32885.4		32882.1	
ICC	0.01		0.01		0.01		0.005		0.005	

OR: odds ratio, CI: confidence interval, SD: standard deviation, SED: socioeconomic deprivation, PM: particulate matter, AIC: akaike information criterion, ICC: intraclass correlation.

*** $p<0.001$, ** $p<0.01$, * $p<0.05$

After accounting for the individual-level covariates (model 4 and 5), the direction, size and statistical significance of the main fixed effects of contextual-level predictors changed little from those estimated in model 3. Model diagnostics suggested that model 5 performed the best among all the models. In the fully-adjusted model (model 5), the 2nd quartile of area SED was associated with significantly lower dementia mortality risk (AOR = 0.85, 95% CI = 0.74-0.98); while the 3rd quartile of area SED was significantly associated with higher dementia mortality risk (AOR = 1.17, 95% CI = 1.03-1.34). Although people in the most deprived areas had higher dementia mortality risk compared to those in the lease deprived areas, the difference was statistically insignificant. Area social integration showed no statistically significant relationship with dementia mortality risk. $PM_{2.5}$ concentration remained a significantly factor, with individuals residing in the most polluted areas (Q4) 29% more likely to die from dementia (AOR = 1.29, 95% CI = 1.10-1.53) compared to those in the least polluted areas (Q1). To test whether the associations between environmental factors and dementia mortality risk differed by demographic cohort, cross-level interaction terms (e.g. sex*area SED) were added separately to the fully adjusted model. The results did not suggest any significant interaction effects between all three environmental factors with age (as a continuous variables), race/ethnicity or sex.

Due to reduced physical mobility, older adults have increased reliance on the social connections or resources in their communities to maintain health. It is reasonable to assume that local contexts are more important on the health and wellbeing of older people, especially the oldest old. To test whether the associations between socio-physical environments of interest and dementia mortality risk vary by age, the sample was stratified into three age groups (65-74 years, 75-84 years, 85 years and over) and the full-adjusted multilevel logistic regression analysis was carried out on the cohorts separately. Results presented in Table 6 showed that $PM_{2.5}$

concentration was strongly associated with dementia mortality risk for people in the 65-74 years age cohort, with people residing in the most polluted areas (Q4) more than two times more likely (AOR = 2.12, 95% CI = 1.17-3.84) to die from dementia compared to their counterparts in the least polluted areas (Q1). However, area SED and social integration did not seem to be associated with the risk for this cohort. For people aged 85 years and over, while $PM_{2.5}$ concentration remained a significant factor, the association was not as eminent as it was for the youngest cohort. It could be that the younger individuals in the sample were able to participate in more outdoor activities, and thus were more vulnerable to the influences of air pollution. Also, the association between area SED and dementia mortality risk emerged for the oldest old. Specifically, individuals residing in the 3rd quartile of area SED had much higher risk (Q3 vs. Q1, AOR = 1.21, 95% CI = 1.06-1.38). For the oldest old, they tend to retrieve from public life due to diminished physical abilities and become more tethered to their home environments. Social isolation hence had a stronger effect compared to their younger counterparts. Although people living in less socially integrated areas had higher risk of dementia mortality, the differences were not statistically significant.

Table 6 Associations between contextual-level variables and risk of dementia mortality by age group.

Variable	65-74 years		75-84 years		85 years and over	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Area SED						
Q1: Least Deprived	1		1		1	
Q2	0.83	(0.53, 1.30)	0.76**	(0.63, 0.91)	0.86	(0.75, 1.00)
Q3	1.12	(0.78, 1.62)	1	(0.86, 1.17)	1.21**	(1.06, 1.38)
Q4: Most Deprived	0.98	(0.71, 1.35)	0.96	(0.84, 1.10)	1.08	(0.96, 1.22)
Area social integration						
Q1: Most integrated	1		1		1	
Q2	1.02	(0.62, 1.70)	0.88	(0.72, 1.07)	1.07	(0.92, 1.25)
Q3	1.08	(0.66, 1.77)	1.02	(0.84, 1.24)	1.13	(0.97, 1.32)
Q4: Least integrated	0.89	(0.55, 1.45)	0.84	(0.69, 1.03)	1.04	(0.89, 1.22)
PM2.5 concentration						
Q1: Least polluted	1		1		1	
Q2	0.95	(0.50, 1.80)	1.04	(0.82, 1.32)	1.09	(0.91, 1.30)
Q3	1.85*	(1.04, 3.31)	1.19	(0.95, 1.49)	1.21*	(1.02, 1.44)
Q4: Most polluted	2.12*	(1.17, 3.84)	1.23	(0.97, 1.55)	1.25*	(1.04, 1.49)

OR: odds ratio, CI: confidence interval, SED: socioeconomic deprivation, PM: particulate matter

All models were adjusted for sex, age (centered), race/ethnicity, marital status, education, hypertension and diabetes mellitus.

*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

4.4 Discussion

Using the death certificates of Wisconsin residents in 2010 as a sample, this study investigated the associations between three socio-physical environmental factors and individual dementia mortality within a multilevel framework. It was found that there was a significant association between area socioeconomic deprivation and dementia mortality risk, net of individual-level covariates and other contextual level variables. Specifically, living in the least deprived areas was associated with the lowest risk of dementia death; however, only the 3rd quartiles of area social deprivation was associated with significantly higher risk. Area social integration showed a non-linear association with individual dementia mortality risk, too. Mid-level area social integration was linked with significantly higher individual dementia mortality risk; while the risk in areas that were the least and most integrated did not differ significantly. Ambient air pollution, measured by $PM_{2.5}$ concentration, was significantly associated with

individual dementia mortality risk with a positive gradient, independent of individual and other contextual covariates.

There are a number of ways in which living in a socio-economically deprived area can "get in our brain." Community studies of the effects of socio-environmental factors on cognitive health emphasize the role of psychosocial and physiological stress responses. Studies have shown that chronical exposure to social stressors such as neighborhood socioeconomic disadvantage and social disorders may prompt a psychosocial stress response commonly found in people with cognitive impairments (Oei et al., 2006; Ailshire et al., 2017). Meanwhile, living in a socio-economically deprived neighborhood may also induce several neuro-damaging physiological changes in our brain. First, short-term exposure to stressors increases the production of stress hormones, which may help individuals to adapt to adverse situations (Taylor et al., 1997). However, when activation of such stress response is prolonged and chronic, it can result in the overproduction of glucocorticoid hormones (e.g., cortisol) and cytokines (McEwen & Tucker, 2011), which has been associated to damage in the brain structures involved in cognition and mental health (De Kloet et al., 1999; Sapolsky, 1999; Forget et al., 2000; Landfield et al., 2007; Lupien et al., 2009). Second, repeated and chronic activation of stress responses may contribute to vascular problems such as hardening of arteries and hypertension (Plante, 2002; Spruill, 2010), both of which may increase the risk for cognitive impairment and dementia (Nash and Fillit, 2006; Nagai et al., 2010). And finally, overproduction of those stress hormones may increase one's susceptibility to environmental toxins detrimental to cognition (McEwen, 1992). The results did not show a gradient in dementia mortality risk by area SED. Living in the 2nd quartile of area SED was associated with significantly lower risk of dementia death while living in the 3rd quartile was associated with significantly higher risk. The reasons are unclear. It is

possible that living in the most deprived areas increases the chance of dying from other fatal diseases such as heart disease and stroke at early ages, before dementia could be even developed.

The hypothesis that living in more socially integrated areas may be associated with lower risk of dementia death was not confirmed by the results. Instead, the coefficient estimates suggested that intermediate level area social integration was associated with higher risk of dementia death, although the differences were not statistically significant. Why the relationship between area social integration and dementia mortality risk shows such pattern is unclear. In examining the effects of community social environment on the mortality of individuals with serious illness, Wen and colleagues (Wen et al., 2005) also found that higher levels of social network density was detrimental, as it was associated with lower probability of survival. The authors found in their data that areas with higher levels of social integration also had more crime and violence and were more socioeconomically deprived. Morenoff and colleagues also found a relationship between high levels of social integration and low community socioeconomic status (Morenoff et al., 2001). The social disorganization theory posits that when large scale social disorders emerge, residents tend to form groups or alliances with other members in the community to cope with these problems. In the social capital literature, the structural social capital, often measured by the density of social networks or civic engagement patterns (Islam et al., 2006), only captures one dimension of the concept. Cognitive social capital, referred to as residents' perceptions of their local communities including the sense of belonging, trust, and satisfaction (Uphoff et al., 2013), may be more important to cognitive health. It is possible that individuals living in areas of higher levels of structural social capital may be more exposed to various unfavorable community environment conditions, and thus possess more negative cognitive social capital towards their local communities that could be detrimental to cognitive

health. Using the density of social networks may not be adequate in capturing the dynamics and processes that community social integration may influence dementia mortality risk.

The direction of the relationship between air pollution and risk of dementia mortality was within expectations. Higher level of $PM_{2.5}$ concentration was associated with higher risk of dementia mortality, in a dose-response manner. As shown in Table 5, in the model that only accounted for contextual variables, the highest quartile of $PM_{2.5}$ concentration was associated with 34% more likely of a death attributable to dementia compared to the lowest quartile. Controlling for individual level socio-demographic and comorbidities variables and other contextual variables slightly reduced the elevated risk. Living in the most polluted areas was still associated with significantly higher risk of dementia death (29% more likely). Age-stratified analysis showed that air pollution was associated with significantly greater risk of dementia mortality among the 65-74 years age cohort. The mechanisms through which exposure to air pollution may cause cognitive damage may be multifaceted. It has been reported that long-term air pollution is associated with increased biomarkers of neuroinflammation (Calderón-Garcidueñas et al., 2008), an altered innate immune response in the brain and disruption of the blood-brain barrier (Calderón-Garcidueñas et al., 2008), smaller total cerebral brain volume and greater risk of covert brain infarcts (Wilker et al., 2015), and smaller deep-gray brain volumes (Power et al., 2018). All of these physiological changes in the brain may contribute to the differential risks associated with $PM_{2.5}$ concentration.

To the author's knowledge, this is the first study to examine the combined effects of three socio-physical environmental factors and the risk of dementia mortality. Informed by current literature on environmental influences on cognitive impairment and dementia, it examined the associations between area socioeconomic deprivation, area social integration and air quality of

local communities and residents' risk of dementia death. The results added new evidence supporting significant associations between all three environmental factors and dementia mortality risk, despite that some associations were in unexpected directions. Another strength is the large multiethnic sample in the study. The sample ensured that different population cohorts were adequately represented and that there were considerable variabilities in the values of environmental measurements. At last, multilevel logistic regression models were used to account for the nesting of individuals within places of residence. Based on the assumption that disease determinants are best conceptualized and measured at the individual level, most epidemiological research on dementia risk so far tend to explain individual-level outcomes with individual-level variables only. By simultaneously taking into account individual- and contextual-level variables, the multilevel models reduced the estimation biases stemmed from the false assumption that individuals are independent even they may share common environmental influences. The results help better differentiate the "independent" effects of contextual factors on dementia mortality risk.

Major implications from the results suggest that areas with intermediate SED and social integration had higher risk of death attributable to dementia. Although the mechanisms responsible for such patterns are not entirely clear, I argue that by continuing improving the socioeconomic conditions of local communities, it may have positive effects on reducing dementia mortality risk of residents. The result that mid-level area social integration is associated with higher dementia mortality risk is surprising. Further research is needed to examine the effects of other dimensions of social capital on dementia mortality risk. Moreover, we need to look deeper into community processes to see whether social integration is related (as a response mechanism) to other social stressors other than socioeconomic deprivation that may increase

dementia risk. Current recommendations for dementia prevention include physical exercise (Middleton and Yaffe, 2009; Livingston et al., 2017). However, the results suggest that the benefits of physical activity may be greatly discounted if the environment in which we exercise is abundant with pollutants. The relatively younger age cohort in the sample was more effected by its negative effects, as illustrated in the results, possibly because they are more exposed to air pollution. The monitoring and regulation of air pollution, particularly fine particulate matters, in our living environments should be integrated as part of the dementia prevention framework.

This study has several limitations, too. First, the under-diagnosis and under-reporting of dementia are well documented (Falagas et al., 2007; Connolly et al., 2011; Romero et al., 2014). The lack of medical facilities and personnel necessary for accurate diagnosis and reporting of dementia in highly socioeconomically deprived areas might contribute to the findings that living in those areas was associated with lower risk of dementia mortality. Second, hypertension and diabetes mellitus were used to adjust for comorbidity risk factors. However, empirical studies have shown that community environments may affect the prevalence/incidence of both diseases (Mujahid et al., 2008; Forest et al., 2009). The indirect effects of the three socio-physical environmental factors on dementia mortality risk through those comorbidity risk factors were not examined in the study. The total effects of the environmental factor might be greater than the main effects estimated in the models. Third, contextual effects on health is best examined at the geography at which those factors are operating (Pickett and Pearl, 2001), meaning that the choice of areal unit of analysis by which context is conceptualized and measured should be informed by theories and empirical research on the mechanisms by which context may affect the health outcome of interest. These arguments are compelling on theoretical grounds. However, more often in place effects on health research, administrative units such as census tract or block group

are frequently used as the areal unit of analysis, due to the fact that ecological data for those units are routinely collected and published. For dementia mortality, it is extremely difficult to justify an optimal areal unit of analysis, partly because we still lack knowledge of how environments may affect the risk. county was chosen as the areal unit because it is the finest geography at which all death certificates can be geocoded. Fourth, the associations between environmental factors and the risk of dementia mortality presented in the results could not be used to infer causality due to the cross-sectional nature of the study. The processes leading to dementia death are gradual and cumulative. This issue is accentuated by the fact that people move throughout their lives and thus environmental exposures may vary significantly at different life stages. Examining the histories of exposures to the three environmental factors over the life course might be more informative than exposures at a given time. Future work will need to investigate lifelong exposure of relevant environmental factors and its effects on dementia mortality risk.

4.5 Conclusion

This study investigates whether socio-physical environments are associated with individual dementia mortality risk. In contrast to conventional cohort studies, it was able to assess the independent effects of three environmental factors (area socioeconomic deprivation, area social integration and air pollution) while accounting for individual-level socio-demographic and comorbidity factors. The results provided cross-sectional evidence that all three environmental factors were significantly associated with disparities in dementia mortality risk. Future work is needed to investigate why mid-level area socioeconomic deprivation and social integration are associated with increased risk of dementia mortality. Among the three environmental factors, $PM_{2.5}$ concentration might have the most significant effects. Public health

policies aiming at dementia prevention and intervention need to address the air quality issue in local communities. Compared to other measures that improve our living environment, reducing air pollution, especially fine particulate matters, might be an effective strategy to reduce dementia mortality.

CHAPTER 5: ASSESSMENT OF CHANGES IN THE PLACE OF DEATH OF OLDER ADULTS WHO DIED FROM DEMENTIA IN THE UNITED STATES, 2000-2014

5.1 Introduction

Largely due to population ageing and increasing longevity, mortality among older adults (defined as persons aged 65 years and older) from a dementia-related disease in the U.S. is expected to increase drastically in the near future (Weuve et al., 2014). This trend, showing no sign of deceleration, tests the federal and state health care systems' capability to adequately and efficiently provide quality end-of-life care for this population (Houttekier et al., 2010). Many empirical studies have suggested that the place of death is an indicator of the quality of end-of-life care because it is associated with the types of care that are available to patients, health and social care utilization, and life satisfaction (Lane et al., 1998; Volicer et al., 2003; Teno et al., 2004; Houttekier et al., 2010; Wright et al., 2010). It is generally reported that, compared with those who died at other places, patients who died at home, especially with hospice services, had better quality of life, experienced fewer symptoms and less discomfort, and their caregivers were less likely to develop psychiatric illness (Volicer et al., 2003; Teno et al., 2004; Wright et al., 2010). For reasons mentioned above, most people prefer to die at home (Deliens et al., 2013; Fischer et al., 2013).

Existing studies of place of death in the U.S. and other countries predominately focused on all-cause or cancer-specific deaths (Gruneir et al., 2007). Only a few studies examined patients who died from a dementia-related disease. For example, using Medicaid-eligible persons with dementia (in the cited study, dementia is not necessarily the underlying cause of death) in the South Carolina Alzheimer's Disease Registry between 1988 and 1994, Lane et al. (1998) found that 8% of the study group died at home, 13% died at mental health nursing facilities, 27%

died in nursing homes, and 51% died in hospitals (including hospice). Analysis between place of residence near death and place of death indicated that a substantial number of people transitioned from residential homes to hospital and nursing homes at the end of life. A national study of the location of death for U.S. older persons whose underlying cause of death was dementia showed that in 2011, the most common place of death was nursing home (66.9%), followed by hospital (15.6%), home (12.7%) and other (4.7%) (Mitchell et al., 2005). Using a random 20% sample of fee-for-service Medicare beneficiaries in 2000, 2005 and 2009, Teno et al. (2013) found that decedents with a dementia diagnosis were less likely to die at home and in acute care hospitals and more likely to die in nursing homes, compared to those with a diagnosis of cancer and chronic obstructive pulmonary disease. Also, decedents with a dementia diagnosis were more likely to die at home and nursing home and less likely to die in an acute care hospital in 2009, as compared to 2000.

The distributions of place of death of dementia patients in European countries were quite different. In Finland, primary care hospital (39.8%) was the most common place of death among people with dementia in 2013, followed by sheltered housing with 24-hour assistance (24.7%) and nursing home (20.8%). Home death was rare (8.1%). Over the study period, the proportion of deaths in primary care hospitals decreased while the proportion of home deaths increased (Masuchi et al., 2018). In Belgium, 58.2% of dementia patients died in a care home in 2008, compared to 24.6% in hospital, 13.4% at home, and 3.0% in a palliative care unit (Meeussen et al., 2012). In England, Sleeman et al. (2014) found that the trend towards increasing hospital deaths of dementia patients had reversed during 2001 and 2010 and that nursing home bed availability was a key factor. Houttekier et al. (2010) examined the place of death of older persons with dementia in five European countries: Belgium, the Netherlands, England, Scotland,

and Wales. They found that between 50% (Wales) and 92% (Netherlands) of patients with dementia died in a nursing home and between 3% (Netherlands) and 46% (Wales) died in hospital. Home death was rare (3–5%), except in Belgium (11%). In another study of international variation in place of death of older people who died from dementia in 14 European and non-European countries, Reyniers et al. (2015) found substantial differences in the frequency distributions of places of death (proportion of home death: from 3.4% in Canada to 69.3% in Mexico; hospital death: from 1.6% in the Netherlands to 73.6% in South Korea; long-term care setting: from 5.5% in South Korea to 93.1% in the Netherlands).

A multitude of factors can influence the place of death of dementia patients, including age (Mitchell et al., 2005; Masuchi, 2013; Badrakalimuthu and Barclay, 2014; Sleeman et al., 2014; Reyniers et al., 2015), sex/gender (Masuchi, 2013; Badrakalimuthu and Barclay, 2014; Sleeman et al., 2014; Reyniers et al., 2015), marital status (Sleeman et al., 2014; Reyniers et al., 2015), education level (Reyniers et al., 2015), living with a relative (Escobar Pinzon et al., 2013), hospice enrollment (Badrakalimuthu and Barclay, 2014), urbanization of place of residence (Sleeman et al., 2014; Reyniers et al., 2015), area deprivation (Sleeman et al., 2014), and availability of health care resources (e.g. general practitioners and hospital/nursing home bed) (Mitchell et al., 2005; Badrakalimuthu and Barclay, 2014; Sleeman et al., 2014; Reyniers et al., 2015), although the relationships may vary between countries.

The distribution of place of death of U.S. older adults who died from dementia has not been updated since the publication of Mitchell et al. (2005) and how the changes were related to the provision of health care resources is unknown. To bridge this knowledge gap, this article examines the trends in place of death among U.S. older adults who died from dementia-related diseases during 2000 and 2014. It aims to address the following questions:

1) What is the frequency distribution of place of death among older adults who died from dementia in the U.S.? How has it changed over time?

2) What are the interstate variations in the changes?

3) What are the associations between place of death and structure of social and health service delivery at the state level?

4) What are the implications for national and state health policies aimed at improving the quality of end-of-life care for dementia patients?

5.2 Data and methods

5.2.1 Data

The data for this study were drawn from all death certificates completed during 2000 and 2014 in the United States (NCHS, n.d.). The NCHS uses the *International Classification of Diseases, Tenth Revision* (ICD-10) to select the causes of death of each decedent. Among all death certificates, those of older adults with a dementia-related disease (ICD-10 codes: F01, F02, F03, G30) as the underlying cause of death were examined in this study. The place of death includes decedent's home, nursing home/long-term care, hospital and other.[1] Sociodemographic characteristics (including sex, race/ethnicity, age at death, marital status, and educational attainment) and the state of residence of the decedents were extracted. These data were used to examine the disparities in place of death between different population cohorts and states.

[1] The National Center for Health Statistics started to record *Hospice facility* as a stand-alone *Place of death* category on death certificates in 2003. In that year, only 178 deaths (1.8‰ of all dementia deaths) occurred at hospice facilities in the United States and those deaths were concentrated in 5 states, including Arkansas, California, Idaho, Montana, and New York. Also, according to the National Hospice and Palliative Care Organization, only 1.3% of days of hospice care were provided at Hospice Inpatient Facility in 2016 (https://www.nhpco.org/sites/default/files/public/Statistics_Research/2017_Facts_Figures.pdf). Using *Hospice facility* as a category of *Place of death* in this study does not reflect the actual use of hospice care among dementia patients. Thereby, *hospice facility* was combined into the *Other* category.

I examined associations between three state health system factors and the place of death of U.S. older adults who died from dementia:

1) *Socio-demographic structure of decedents from dementia (SDS).* A patient's socio-demographic attributes can affect his/her place of death. The socio-demographic structure of decedents who reported dementia as the underlying cause of death was included in the panel data regression models. The structure was measured by variables including percentage of decedents who were aged 85 years and older, percentage of decedents who were female, percentage of decedents who were non-Hispanic White, percentage of decedents who were married, and percentage of decedents who had high school or lower educational attainment. These percentages were generated from the death certificates.

2) *Care facility resources*. Two variables indicating the availability of care facility resources, including the number of hospital beds (HB) per 1,000 population and the number of nursing home beds per 1000 older adults (NHB), were included in this study. The yearly hospital beds per 1,000 population were generated by Henry J Kaiser Family Foundation with the American Hospital Association Annual Survey data. (Henry J Kaiser Family Foundation, n.d.). The yearly numbers of nursing home beds by state were obtained from the NCHS website (NCHS, 2018). Census and intercensal estimates of state population by age groups were used to calculate the yearly number of nursing home beds per 1000 older adults across the years (U.S. Census Bureau, 2012b, 2018).

3) *Public care financing*. The structure of federal and state spending on long-term care may affect where dementia patients die. This study included yearly state price-, age-, sex-, and race-adjusted Medicare reimbursement per enrollee (Part A and Part B) (CMHS (Continuous Medicare History Sample)- or claim-based home health agencies (HHA) reimbursement, CMHS-

or claim-based hospital and skilled nursing facility (HSNF) reimbursement[2]) and yearly state Medicaid expenditures (total federal and state Medicaid expenditure on institutional long-term services and supports[3] (LTSS), Medicaid expenditure on home and community based services (HCBS)). State population mentioned above was also used to calculate the Medicaid expenditures on institutional LTSS and HCBS per older adults by year and state.

5.2.2 Analytical approach

Multivariate regression analysis was used to examine the relationships between various state factors on place of death of dementia patients. One of the advantages of the dataset is that it is a time series/panel data. Using fixed-effects panel models allows for control of the confounding of unobserved factors on the effects of variables of interest on place of death. The dependent variable was logit-transformed percentage of deaths at a certain place among all

---

[2] CMHS-based Medicare reimbursement rate was calculated from 5% sample of Medicare beneficiaries provided in the Continuous Medicare History Sample (CMHS) file. As the Medicare payment shifted toward the claim-based method, the CMHS-based method was discontinued by the Centers of Medicaid and Medicare (CMS). The Dartmouth Atlas (https://atlasdata.dartmouth.edu) provides state level CMHS-based Medicare reimbursement for years 1992-2007 and started calculating claim-based reimbursement from 2003 (discussions of the differences between the 5% CMHS sample and the 20% claim sample can be found at https://atlasdata.dartmouth.edu/pdf/PA_Spending_Report_0611.pdf). As the website states, "The availability of comprehensive claims files and the greater number of patients represented in a 20% sample (20% of patients included in the CMS physician/Supplier Part B file) have made it feasible to calculate per capita spending directly from the claims data." By comparing the 2007 CMHS-based sample and claims-based sample, the researchers found that the two hospital referral regions (HRR) level per capita Medicare spending, as well as spending growth rates, calculated from the two samples were highly correlated. They conclude that it is acceptable to "chain" the two datasets to construct a dataset covering a longer period. In this study, data for years 2000-2003 were CMHS-based and data for years 2004 and afterward were claims-based.

[3] According to Centers for Medicare & Medicaid Services, the term "institution", in the context of federal Medicaid requirements, refers to residential facilities that "assume total care of the individuals who are admitted." The services provided are "hospital services, Intermediate Care Facilities for People with Intellectual disability (ICF/ID), Nursing Facility (NF), Preadmission Screening & Resident Review (PASRR), Inpatient Psychiatric Services for Individuals Under Age 21, and Services for individuals age 65 or older in an institution for mental diseases." For more details, see https://www.medicaid.gov/medicaid/ltss/institutional/index.html

dementia deaths. The independent variables were state factors mentioned in the data section. The state was the unit of analysis. The fixed-effects panel models can be specified as following:

$$\text{logit}(Pr_{it}) = \beta_0 + \beta_1 SDS_{it} + \beta_2 HB_{it} + \beta_3 NHB_{it} + \beta_4 HHA_{it} + \beta_5 HSNF_{it} + \beta_6 ILTSS_{it} + \beta_7 HCBS_{it} + \varepsilon_{it} \quad (3)$$

where Pr_{it} is the outcome variable for state *i* at year *t*, such as the percentage of home deaths in the year 2000. β_0 is the intercept. β_1 ... β_7 are the coefficients of interest. And ε_{it} is the random error term. Since Pr_{it} is a percentage, using it directly as the dependent variable in the regression models could result in the problem that the predicted outcome/percentage falling outside the [0, 1] range. To mitigate this issue, the percentage variable was logit-transformed.

5.3 Results

5.3.1 National trends

There were 75,442 older adults who died from a dementia-related disease as the underlying cause in year 2000, of which 9,375 (12.4%) died at decedent's home, 11,801 (15.6%) died at hospital, 51,209 (67.9%) died at nursing home/long-term care, and 3,057 (4.1%) died at other places. In the year 2014, 223,011 older adults died from a dementia-related disease as the underlying cause, of which 46,802 (21.0%) died at decedent's home, 21,626 (9.7%) died at hospital, 123,981 (55.6%) died at nursing home/long-term care, and 30,602 (13.7%) died at other places. Figure 9 shows the yearly proportions of different places of death during the study period. As one can observe, there was a steady increase in the proportions of deaths at the decedent's home and other places during the study period; while the proportions of deaths at institutional settings such as nursing home/long-term care facilities and hospitals had decreased. Chi-squared

($\chi 2$) testing for trend in proportions showed that the proportions of death across settings had changed significantly over the years ($p<0.01$ for all four categories).

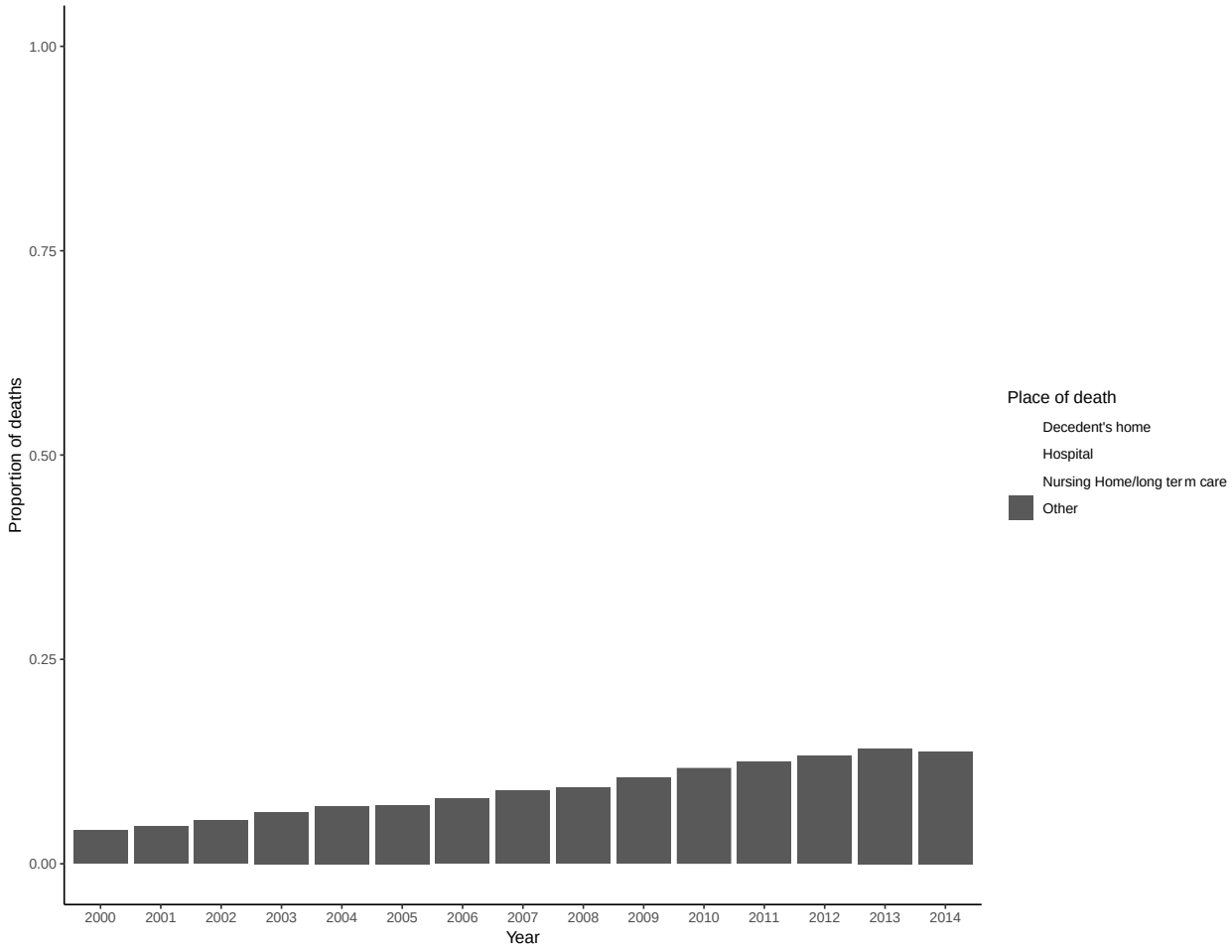

Figure 9 National trends in the place of death of older adults with dementia as the underlying cause in the United States, 2000-2014.

Table 7 shows the numbers and percentages of dementia deaths at different places of death in the years 2000 and 2014, by socio-demographic characteristics. In 2000, the percentage of nursing home/long-term care death was much higher in females compared to males (female: 70.8% vs. male: 60.9%) whereas the proportion of hospital death in females was significantly lower (female: 12.8% vs. male: 22.6%). Percentages of deaths at decedent's home as well as other places did not differ significantly between the sexes. Non-Hispanic whites were less likely

to die at their home and hospital compared with other racial/ethnic groups; while they were much more likely to die at nursing home/long-term care facilities (approximately 7 out of 10 non-Hispanic whites versus less than half for other race/ethnicity groups). Hispanics had the highest percentage of home death while non-Hispanic blacks had the highest percentage of hospital death. Age as also significantly associated with where people died. Decedents who died at earlier ages were more likely to die at home and hospital; those who died at older ages were increasingly more likely to die in a nursing home/long-term care setting. Decedents who were married were more likely to die at their home and hospital and less likely to die at nursing home/long-term care. In terms of education attainment, those who were more educated were more likely to die at home and less likely to die at nursing home/long-term care.

Decedents in 2014 were more likely to die at home and other places and less likely to die at hospital and nursing home/long-term care settings across population cohorts. Moreover, the differences between population cohorts for the year 2000 persisted into 2014. Compared with males, females were still more likely to die at nursing home/long-term care facility (57.8% vs. 51.0%) and less likely to die at hospital (8.2% vs. 13.0%), although the difference between sexes was not as pronounced as in 2000. Non-Hispanic Whites had the smallest increase (7.6%) in the proportion of home deaths and the largest decrease (11.7%) in the proportion of nursing home/long-term care deaths compared with other racial/ethnic groups. Hispanics were equivalently split between home and nursing home/long-term care deaths (34.8% vs. 34.5%); however, non-Hispanic white decedents were much more likely to die at a nursing home/long-term care setting rather than at home (58.2% vs. 19.4%). Older age was still associated with dying in a nursing home/long-term care facility rather than at home or hospital. The oldest old age group (85 years and over) had the largest increase in the proportion of home death and

largest decrease in the proportion of nursing home/long-term care facility death. Decedents who were married at death were much more likely than their counterparts to die at home and much less likely to die at a hospital in 2014. Decedents who were widowed/divorced had the largest decrease in the proportion of nursing home/long-term care death. Lastly, the decrease in the proportion of nursing home/long-term care death was slightly more pronounced for decedents who had some college education or a college degree; the increase in the proportion of home death was less pronounced for decedents who had advanced degree education.

Table 7 Distribution of place of death for US older adults whose underlying cause of death was a dementia-related disease in 2000 and 2014, n(%).

	2000				2014			
	Decedent's home	Hospital	Nursing home / long term care	Other	Decedent's home	Hospital	Nursing home / long term care	Other
All deaths	9375 (12.4)	11801 (15.6)	51209 (67.9)	3057 (4.1)	46802 (21.0)	21626 (9.7)	123981 (55.6)	30602 (13.7)
Sex								
Male	2704 (12.3)	4949 (22.6)	13341 (60.9)	925 (4.2)	14894 (21.3)	9106 (13.0)	35622 (51.0)	10290 (14.7)
Female	6671 (12.5)	6852 (12.8)	37868 (70.8)	2132 (4.0)	31908 (20.8)	12520 (8.2)	88359 (57.8)	20312 (13.3)
Race/ethnicity								
non-Hispanic White	8142 (11.8)	9799 (14.2)	48174 (69.9)	2818 (4.1)	37093 (19.4)	16390 (8.6)	111365 (58.2)	26424 (13.8)
non-Hispanic Black	710 (16.8)	1345 (31.8)	2041 (48.2)	139 (3.3)	4808 (28.3)	2931 (17.3)	7188 (42.4)	2045 (12.0)
non-Hispanic Other	116 (18.2)	188 (29.4)	301 (47.1)	34 (5.3)	1290 (29.3)	715 (16.3)	1850 (42.1)	544 (12.4)
Hispanic	407 (24.9)	469 (28.7)	693 (42.4)	66 (4.0)	3611 (34.8)	1590 (15.3)	3578 (34.5)	1589 (15.3)
Age group								
65-74 years	839 (17.6)	1057 (22.2)	2665 (56.0)	194 (4.1)	2864 (23.6)	1666 (13.7)	5879 (48.5)	1717 (14.2)
75-84 years	3512 (14.2)	4502 (18.2)	15641 (63.2)	1084 (4.4)	13020 (22.6)	6567 (11.4)	29872 (51.9)	8132 (14.1)
85 years and over	5024 (10.9)	6242 (13.6)	32903 (71.6)	1779 (3.9)	30918 (20.2)	13393 (8.7)	88230 (57.6)	20753 (13.5)
Marital status								
Single	317 (7.8)	612 (15.1)	3008 (74.0)	128 (3.1)	1345 (13.3)	1159 (11.5)	6542 (64.6)	1076 (10.6)
Married	3466 (16.9)	4156 (20.3)	11973 (58.5)	859 (4.2)	16208 (27.7)	6822 (11.6)	27109 (46.3)	8462 (14.4)
Widowed/Divorced	5592 (11.0)	7033 (13.8)	36228 (71.1)	2070 (4.1)	29249 (19.0)	13645 (8.8)	90330 (58.5)	21064 (13.7)
Education attainment								
High School or Less	6645 (11.9)	8950 (16.0)	38369 (68.5)	2038 (3.6)	31052 (20.4)	15231 (10.0)	86124 (56.7)	19598 (12.9)
Some College or College Degree	2159 (13.6)	2303 (14.5)	10612 (66.8)	820 (5.2)	12542 (21.8)	5142 (9.0)	30933 (53.9)	8797 (15.3)
Advanced Degree	571 (16.1)	548 (15.5)	2228 (62.8)	199 (5.6)	3208 (23.6)	1253 (9.2)	6924 (50.9)	2207 (16.2)

5.3.2 State variations

There were significant interstate and temporal variations in the percentages of dementia death at different places, the socio-demographic structures of decedents, and state health care resources (see Table 8). Among all states and the District of Columbia, the percentage of decedents who died at home averaged at 15.8%, with a range between 0% and 54.1%. The average yearly percentages of decedents who died at hospital, nursing home/long-term care and other places were 12.7%, 63.4% and 8.1%, respectively. The percentages of decedents who died at home and hospital peaked around 50%; however, the highest percentage of deaths at nursing home/long-term care reached 100% (South Dakota, years 2000-2002).

States also varied in terms of the socio-demographic structure of their dementia decedents across the years. The average percentage of decedents who were age 85 years and older was 64.9%; the average percentage of those who were female was 69.7%; the average percentage of those who were non-Hispanic white was 88.8%; an average of 26.4% of decedents were married at the time of death; an average of 70.9% of decedents had an education attainment of high school or less.

As for state care facility resources, the average number of hospital beds per 1000 population was 2.9 and the average number of nursing home beds per 1000 older adults was 9.8. The average number of hospital beds per 1000 population ranged from 1.7 to 6.2. There was substantial variability between states in nursing home bed resources, as the highest number (37.3, Iowa in 2012) was nearly 25 times greater than the lowest (1.5, Alaska in 2010). Figure 10 and Figure 11 show the trends in hospital bed and nursing home bed availability between 2000 and 2014 by state.

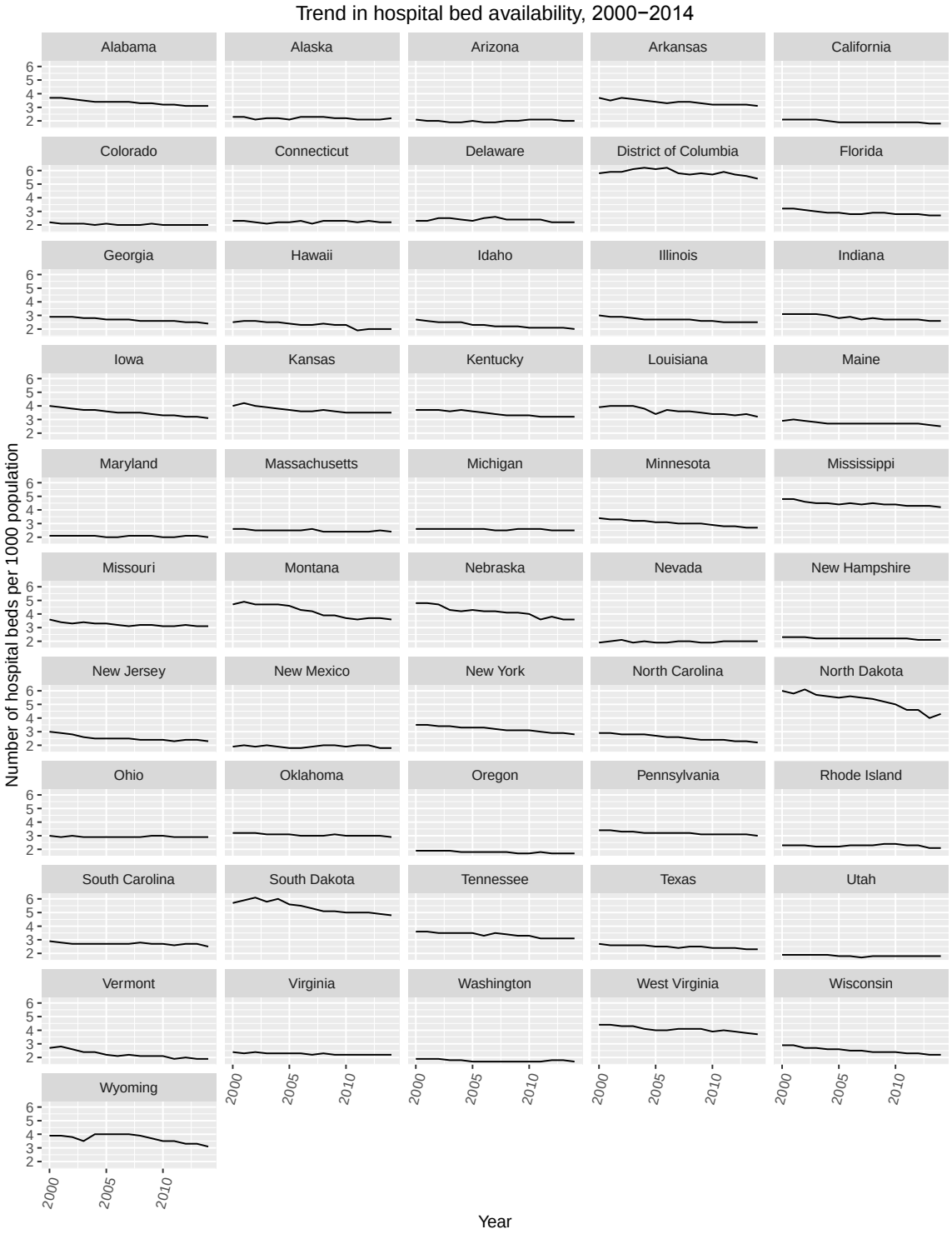

Figure 10 Trend in the number of hospital beds per 1000 population between 2000 and 2014 by state.

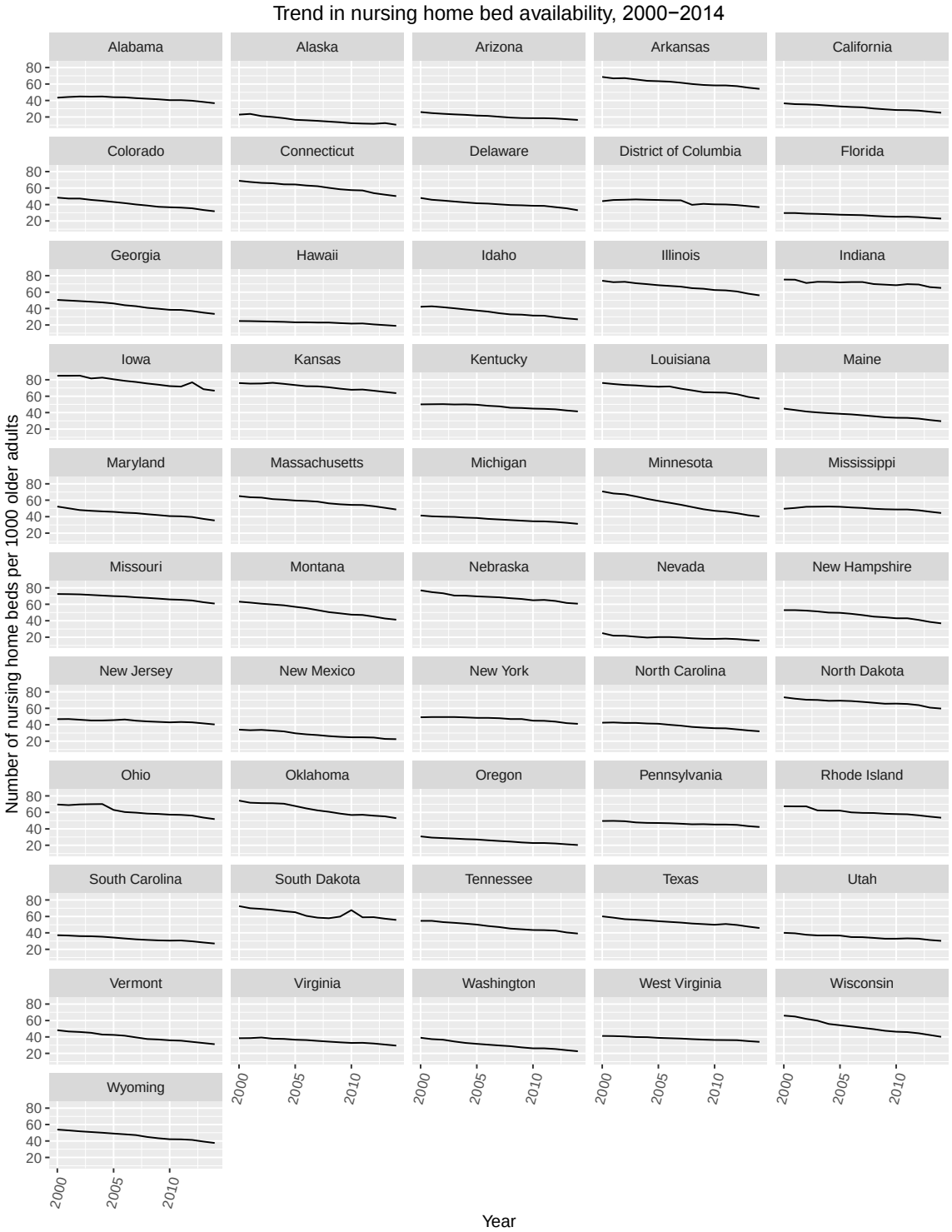

Figure 11 Trend in the number of nursing home beds per 1000 older adult between 2000 and 2014 by state.

Medicare reimbursement rates were also considerably different between states. The reimbursement rate on home health agency (HHA) averaged at 400 U.S. dollars, with a range of 100 and 1,400; while the reimbursement rate on hospital and skilled nursing facility (HSNF) had an average value at 4,000 dollars, with the range of 2,400 and 5,700. Medicaid expenditure on institutional long-term services and supports (LTSS) per older adults in 1000 dollars averaged at 0.38, with a range of 0 and 2.5; while the expenditure on home and community-based services (HCBS) averaged at 0.34, ranging from 0 to 3.2. Figure 12 to Figure 15 show the trends in state Medicare reimbursement rates on HHA and HSNF and Medicaid expenditures on institutional LTSS and HCBS between 2000 and 2014.

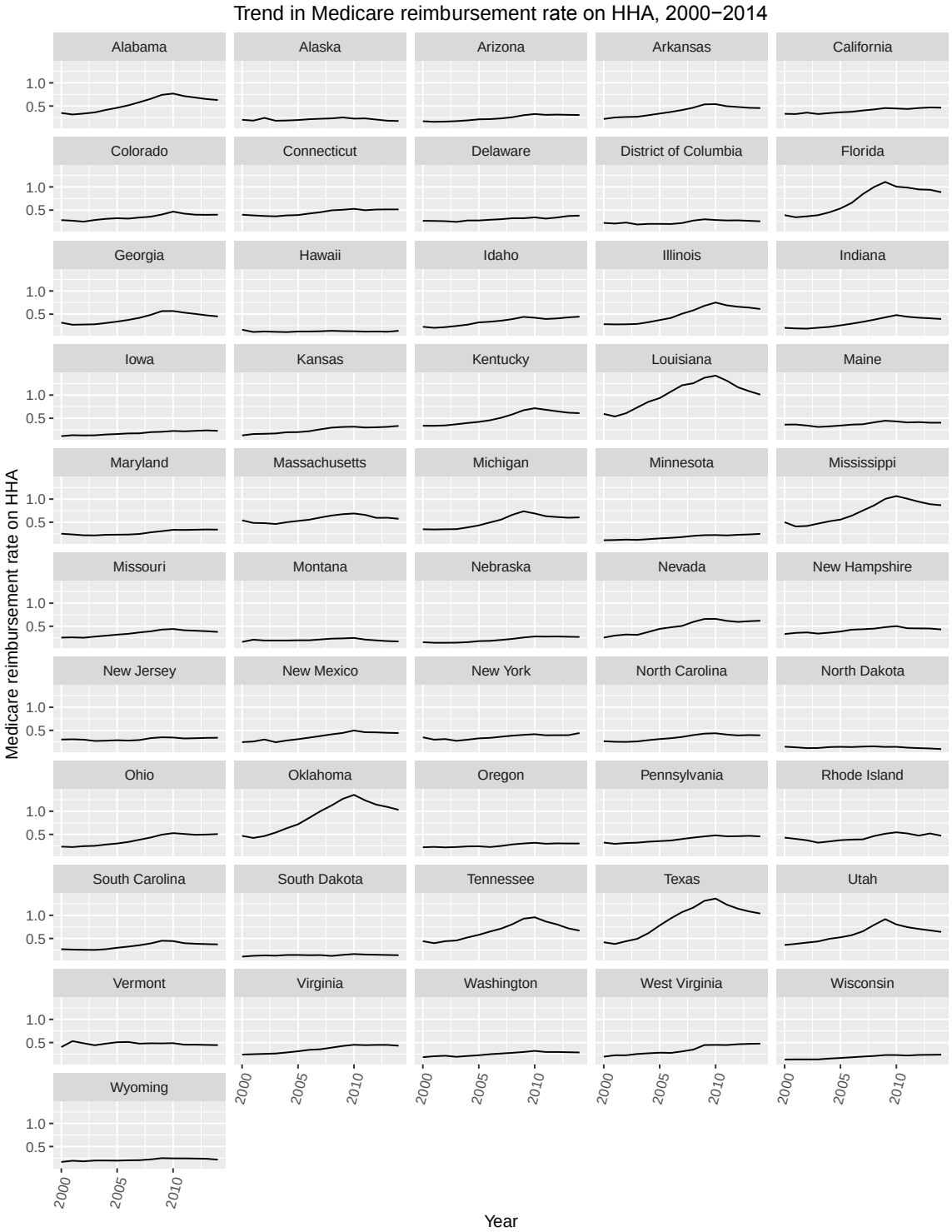

Figure 12 Trend in Medicare reimbursement rate on home health agencies (HHA) between 2000 and 2014 by state.

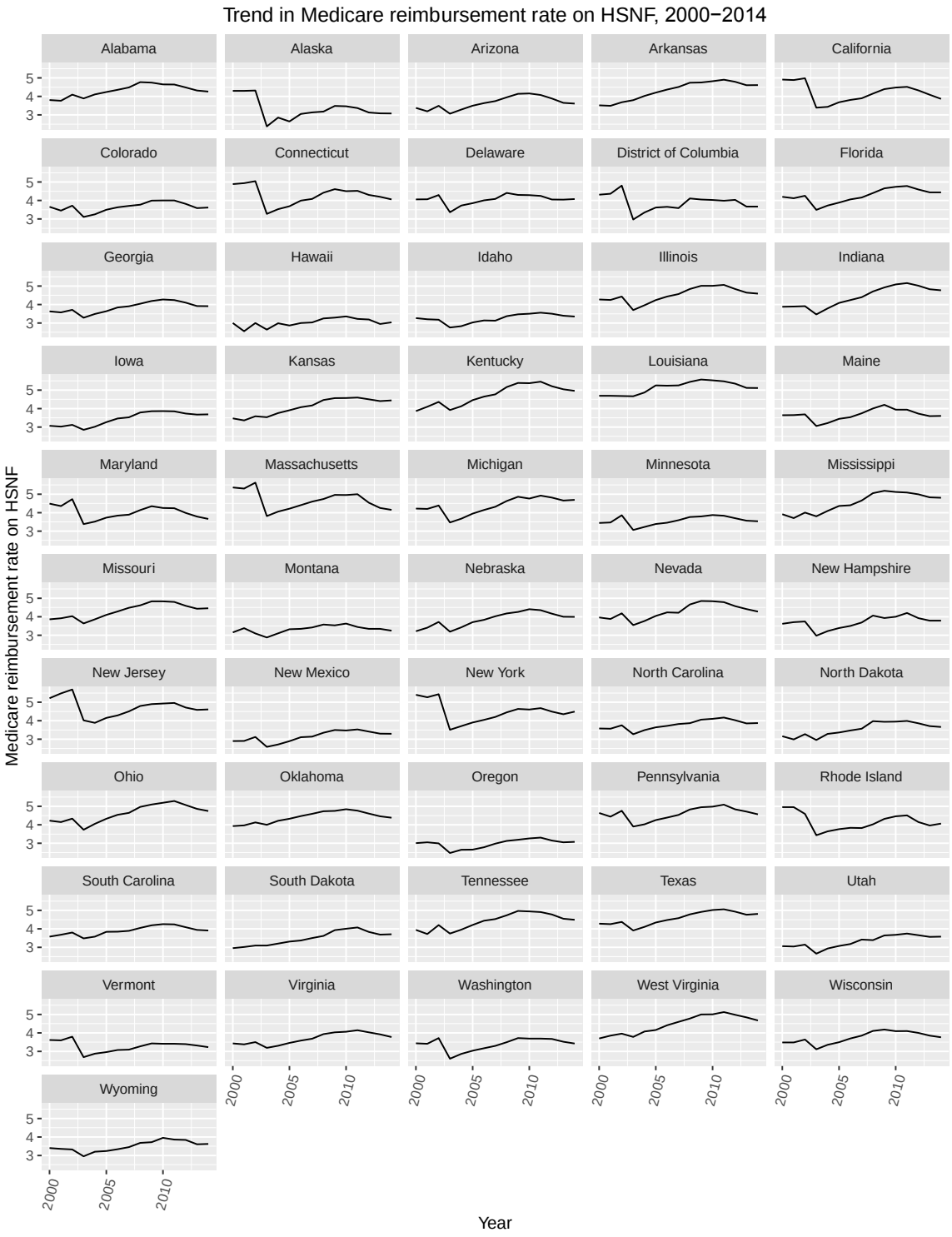

Figure 13 Trend in Medicare reimbursement rate on hospital and skilled nursing facilities (HSNF) between 2000 and 2014 by state.

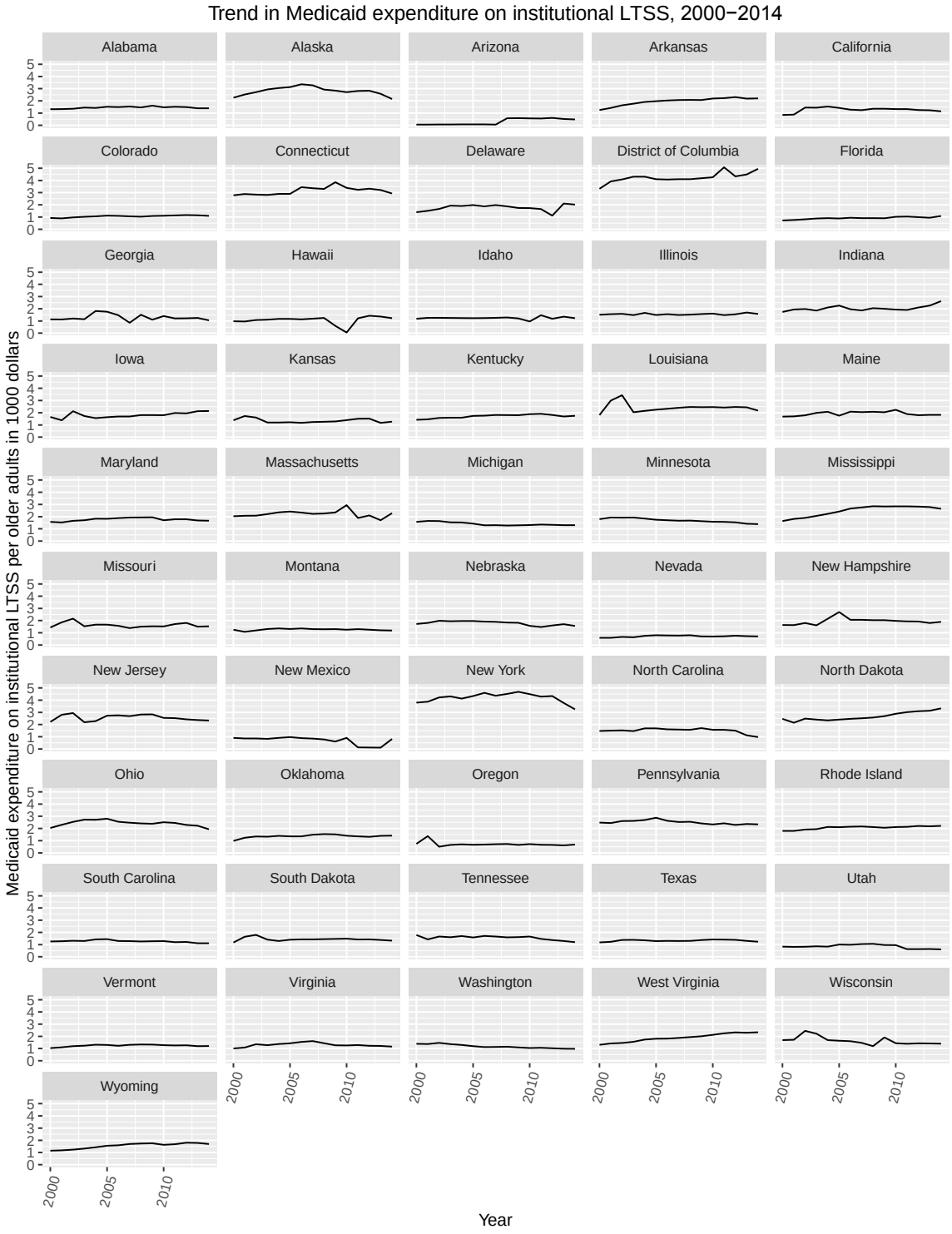

Figure 14 Trend in Medicaid expenditure on institutional long-term services and supports (LTSS) per older adult between 2000 and 2014 by state.

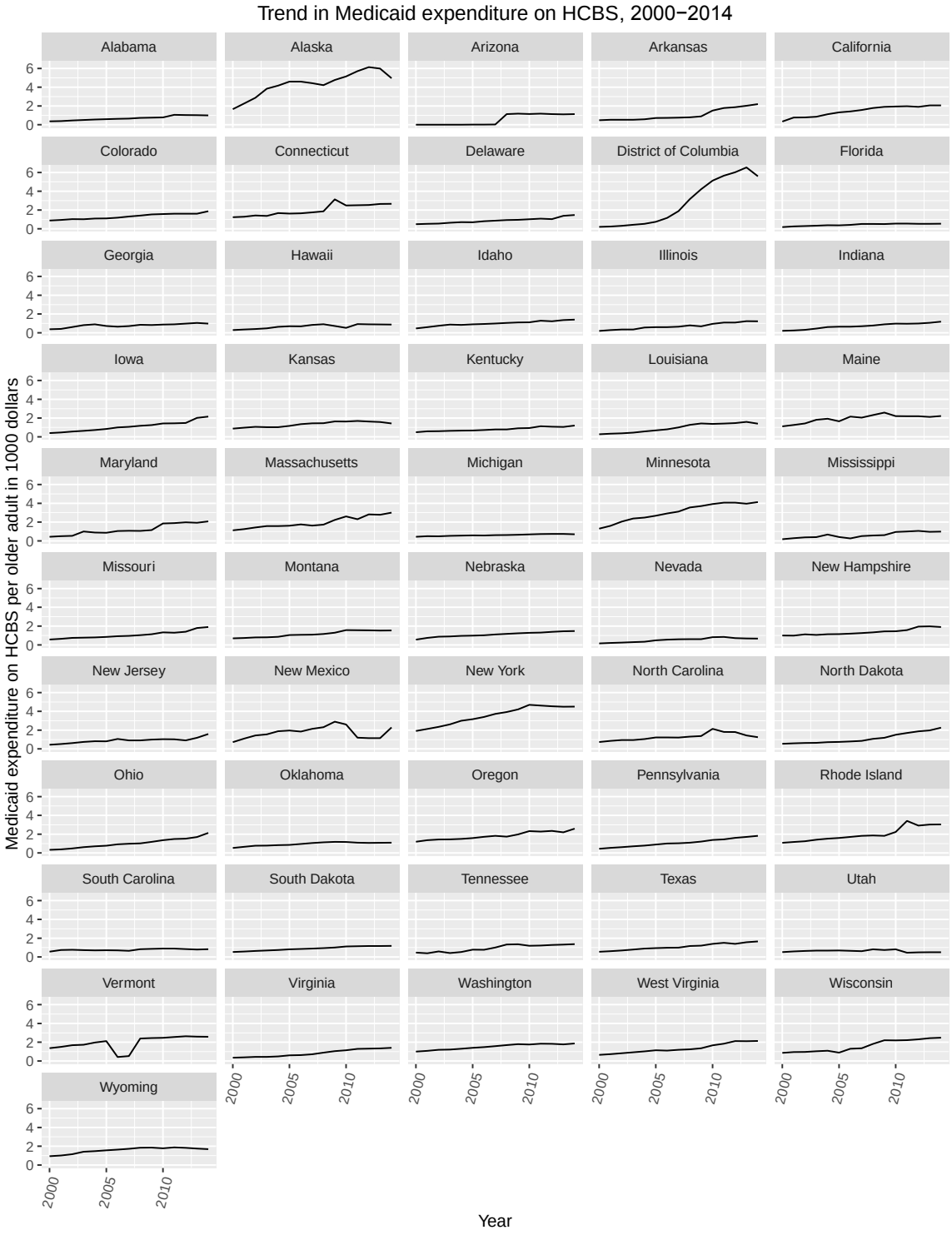

Figure 15 Trend in Medicaid expenditure on home and community-based services (HCBS) per older adult between 2000 and 2014 by state.

Figure 16 shows the state changes in the percentage of deaths at difference places between 2000 and 2014 (Red dots represent the year 2000 and blue dots represent the year 2014. All states and District of Columbia are ordered by the percentage in 2014.). Utah had the highest percentage of deaths at home (54.1%) in 2014 among all, followed by Alabama (40.3%), New Mexico (31.4%), Hawaii (30.7%), and Louisiana (29.5%). The states with the lowest percentages of home death in 2014 were South Dakota (5.4%), North Dakota (6.5%), Iowa (7.2%), Nebraska (9.3%), and Wisconsin (10.4%). Utah also had the largest increase in the percentage of home deaths among all states and DC, from 21.7% in 2000 to 54.1% in 2014. For hospital death, the highest percentages in 2014 were in Alaska (20.4%), New York (17.4%), District of Columbia (16.3%), Mississippi (15.0%), and Hawaii (15.0%) and the lowest were in Utah (4.2%), Minnesota (4.4%), Arizona (5.1%), Wisconsin (5.1%) and Idaho (5.6%). The largest decrease occurred in Louisiana, from 31.1% in 2000 to 9.4% in 2014. For deaths at nursing home/long-term care, the highest percentages in 2014 were in North Dakota (85.6%), South Dakota (82.7%), Iowa (78.9%), Maine (76.4%), and Montana (76.2%); and the lowest were in Arizona (32.1%), Hawaii (33.1%), Florida (34.1%), Utah (36.0%), and Georgia (37.1%). The largest decease was in Arizona, from 68.1% in 2000 to 32.1% in 2014. Contradictory to the overall trend, a few states had an increase in the percentage of nursing home/long-term care deaths during the study period, including West Virginia, Louisiana, Mississippi and District of Columbia. For deaths at other places, the highest percentages in 2014 were in Arizona (40.0%), Florida (35.4%), Wisconsin (33.7%), Georgia (26.5%), and Maryland (24.6%) and the lowest were in North Dakota (1.0%), Alaska (1.1%), West Virginia (3.0%), Massachusetts (3.5%), and Vermont (3.6%). Arizona had the largest

increase in the percentage of deaths at other places, from 9.2% in 2000 to 40.0% in 2014. It should be noted that from death certificates, a few states had very small numbers of deaths from dementia over the study period. For example, Rhode Island reported only 12 home deaths, 31 hospital deaths, 109 nursing home/long-term care deaths, and 15 other deaths in the 15-year span. The Dakotas also had the same issue. The percentages of deaths at different places generated from smaller numbers may have greater variability and are more likely to become outliers. To address the small number problem, states with the reported number of deaths at any place in any year smaller than 30 were excluded from the panel data analysis to ensure that parametric coefficient estimates were more resilient to the influence of those outliers.

Table 8 Summary statistics of panel data, including all states and DC.

Variable	Min	Max	Mean	Standard Deviation
Place of death				
% of decedents who died at home	0	54.1	15.8	7.9
% of decedents who died at hospital	0	50	12.7	6.6
% of decedents who died at nursing home/long term care	26	100	63.4	14.1
% of decedents who died at other places	0	44.1	8.1	7.8
Socio-demographic structure				
% of decedents who were aged 85 years and older	0	100	64.9	6.2
% of decedents who were female	33.3	100	69.7	3.6
% of decedents who were non-Hispanic White	22.7	100	88.8	13.8
% of decedents who were married	0	55.6	26.4	3.8
% of decedents who had high school or less education	0	88.9	70.9	6.8
Care facility resources				
# of hospital beds per 1000 population	1.7	6.2	2.9	0.95
# of nursing home beds per 1000 older adults	10.5	85	46.5	15.8
Public care financing				
Medicare reimbursement rate on home health agencies (HHA) in 1000 dollars	0.1	1.4	0.4	0.23
Medicare reimbursement rate on hospital and skilled nursing facilities (HSNF) in 1000 dollars	2.4	5.7	4	0.64
Medicaid expenditure on institutional long term services and supports (LTSS) per older adults in 1000 dollars	0.1	5.1	1.7	0.8
Medicaid expenditure on home and community-based services (HCBS) per older adults in 1000 dollars	0	6.5	1.3	1

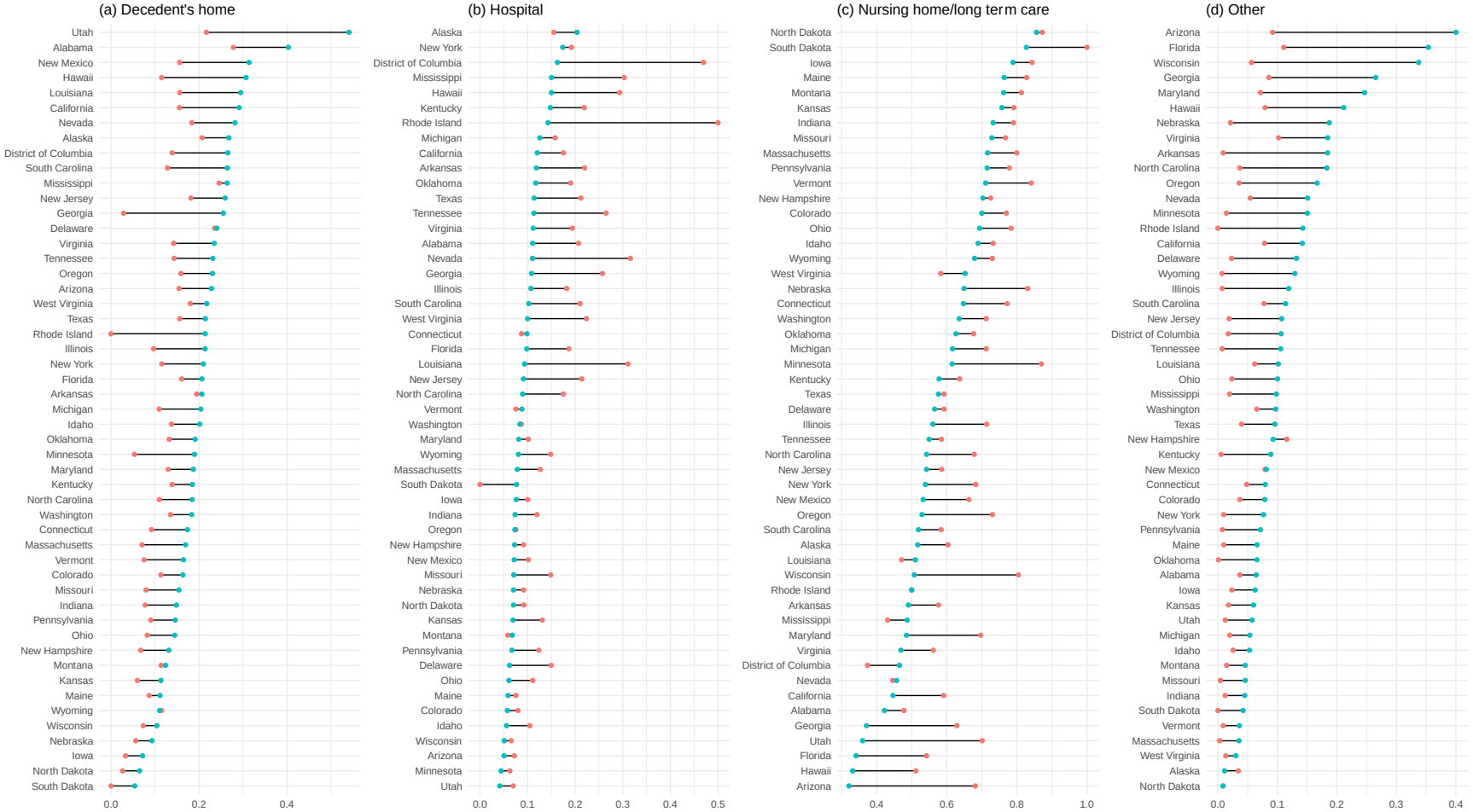

Figure 16 Changes in the percentage of decedents who died at different places in each state between 2000 and 2014: (a) Decedent's home; (b) Hospital; (c) Nursing home/long-term care; (d) Other. Red dots represent the year 2000 and blue dots represent the year 2014.

5.3.3 Associations between place of death and state level factors

The panel data regression results showing the associations between state-level factors and place of death resulting from a dementia-related disease are presented in Table 9. 7 states (Alaska, Georgia, South Dakota, North Dakota, Rhode Island, Vermont and Wyoming) and District of Columbia were excluded from the analysis due to small number problem. The independent variables explained 61%, 47%, 42% of the variation in home death, hospital death and nursing home/long-term care death, respectively. To examine the possible multicollinearity among independent variables, a pooled panel data analysis was carried out. The variation inflation factors (VIF) of all independent variables were less than 5, indicating a low degree of multicollinearity between independent variables.

The results showed that socio-demographic structure of dementia decedents was associated with deaths at different places. The percentage of decedents who were 85 years and older and who were married were positively associated with the percentage of home deaths; while the percentage of decedents who were non-Hispanic white and who obtained high school or less education were negatively associated with the percentage of home deaths. The percentage of female decedents was positively associated with the percentage of home deaths, but the association was not statistically significant. Percentage of decedents who were aged 85 years and older and percentage of decedents who were female were negatively associated with hospital death; while percentage of decedents who had high school or less education was positively associated with hospital death. The percentage of decedents who were aged 85 years and older and percentage of

decedents who were married were negatively associated with nursing home/long-term care death while percentage of decedents who were female, who were non-Hispanic white, and who had high school or less education were positively associated with nursing home/long-term care death.

Care facility resources also appeared to be associated with place of death among dementia patients. Specifically, the number of hospital beds per 1000 population was positively associated with hospital deaths. There was not a significant relationship between hospital bed availability with either home or nursing home/long-term care deaths. The number of nursing home beds per 1000 older adults was negatively associated with home deaths and positively associated with nursing home/long-term care deaths. However, the effect size of nursing home bed availability on home and nursing home/long-term care death were both minimal.

Public financing of care, especially Medicare and Medicaid, significantly impacts where dementia patients die. From the panel regression results, Medicare reimbursement rate on home health agency (HHA) was positively associated with home death and negatively with hospital death; however, there was not a significant relationship with nursing home/long-term care death. Medicare reimbursement rate on hospital and skilled nursing facility (HSNF) was not significantly associated with either of three outcomes. Medicaid expenditure rate on institutional long-term services and supports (LTSS) was negatively associated with home deaths and positively associated with nursing home/long-term care deaths but not hospital deaths. In the meantime, Medicaid expenditure rate on home and community-based services (HCBS) was negatively

associated with nursing home/long-term deaths and positively associated with home and hospital deaths.

Table 9 Associations between state socio-demographic characteristics and health care resources and place of death of the decedents whose underlying cause of death was a dementia-related disease (N=43).

Variables	Decedent's home		Hospital		Nursing home / long term care	
	β	(SE)	β	(SE)	β	(SE)
Socio-demographic structure						
% of decedents who were aged 85 years and older	0.51	(0.36)	2.30***	(-0.42)	-0.06	(0.47)
% of decedents who were female	0.78	(0.50)	-1.83**	(0.60)	0.78	(0.66)
% of decedents who were non-Hispanic White	-2.20***	(0.47)	0.63	(0.56)	2.20***	(0.62
% of decedents who were married	1.84***	(0.55)	-1.09	(0.65)	-1.40	(0.72)
% of decedents who had high school or less education	-1.85***	(0.40)	2.15***	(0.47)	2.00***	(0.52)
Care facility resources						
# of hospital beds per 1000 population	-0.06	(0.05)	0.25***	(0.06)	-0.07	(0.06)
# of nursing home beds per 1000 older adults	-0.02***	(0.00)	0.00	(0.00)	0.02***	(0.00)
Public care financing						
Medicare reimbursement rate on home health agencies (HHA) in 1000 dollars	0.02	(0.07)	-0.44***	(0.08)	0.23*	(0.09)
Medicare reimbursement rate on hospital and skilled nursing facilities (HSNF) in 1000 dollars	0.01	(0.02)	0.01	(0.02)	-0.04	(0.03)
Medicaid expenditure on institutional long term services and supports (LTSS) per older adults in 1000 dollars	-0.12***	(0.03)	-0.06	(0.03)	0.17***	(0.04)
Medicaid expenditure on home and community-based services (HCBS) per older adults in 1000 dollars	0.09***	(0.03)	0.05	(0.03)	-0.15***	(0.03)
Number of observations	645		645		645	
Number of groups	43		43		43	
F-statistics	111.1		49.8		58.6	
p-value	<0.01		<0.01		<0.01	
Adj. R-Squared	0.64		0.43		0.48	

Note: Alaska, District of Columbia, Georgia, South Dakota, North Dakota, Rhode Island, Vermont and Wyoming were excluded from analyses due to small numbers of death.

*** $p<0.001$, ** $p<0.01$, * $p<0.05$

5.4 Discussion

This study empirically assessed changes over time in place of death among U.S. older adults who reported dementia as the underlying cause of death between 2000 and 2014. Nationally, there was a trend that older adults who died from dementia were increasingly more likely to die at their homes, instead of institutional settings such as hospitals and nursing home/long-term care facilities. The shares of deaths at the two institutional settings had both dwindled, although their combination still makes up the majority. The share of death occurred at places other than the three mentioned above also increased during the study period, partly due to the increasing use of hospice facilities.

Socio-demographic features played a role in the place of death of decedents from dementia, as shown in Table 9. Numerous studies have shown higher utilization of nursing homes and other institutional LTC services among Whites compared with racial and ethnic minorities (Murtaugh et al., 1990; Pan et al., 1998; Wallace et al., 1998; Cagney and Agree, 1999; Borrayo et al., 2002; Cai and Temkin-Greener, 2015). Race and ethnicity represent life-long socioeconomic status that can contribute to differential patterns of end-of-life care, of which value is a decisive factor (Gruneir et al., 2007). The percentage of decedents who were married was positively associated with home deaths, demonstrating the significant role of social support in avoiding institutional placement. The percentage of decedents who had high school or less education showed a positive relationship with institutional deaths and a negative relationship with home deaths. This may be because that education attainment, on average a quality indicator of life-long socioeconomic status, increases access to information, power and resource, and subsequently gives patients and their families latitude to make end-of-life care decisions

that are more in line with their preferences. Interestingly, the relationship between education and institutional/home death appeared to be in the opposite direction to the one between race/ethnicity and institutional/home death. It points to the complexity of race and ethnicity as social constructs with a range of social meanings that may influence where dementia patients choose to die. For example, they are also related to the access to long-term care/end-of-life care services (Falcone and Broyles, 1994; Baicker et al., 2004; Davitt and Kaye, 2010) and the cultural norms and attitudes towards them (e.g. spirituality, family structure, language barriers, mistrust of the systems) (Cagney and Agree, 1999; Hopp and Duffy, 2000; Sylvia et al., 2004; Johnson et al., 2008).

One of the aims of this study was to relate changes in place of death of older adults who died from dementia to the state provisions of care facilities and finance resources. Results showed that the availability of care facility resources was directly associated with deaths at that facility. Larger state capacity to provide nursing home beds increased the probability of dying in nursing home/long-term care settings; so was the case for hospital beds and dying in hospitals. It is advisable that by regulating care facility resources supplies, states can shift place of death of dementia patients from institutional settings to homes and communities to better accommodate patient preference. In fact, states have been implementing various policies to control the provider supply for long-term care. One of the major strategies is through the certificate-of-need (CON) programs. In 1974, the National Health Planning and Resources Development Act (P.L. 93-641) prescribed that states must have structures involving submission of proposals and gaining the approval of certificate-of-need regulators before starting any capital projects including establishing new health care facilities and providing new services (Harrington

et al., 2004; Cauchi and Noble, 2018). Although the federal government did not reauthorize the national CON requirements in 1987, many states elected to continue their CON programs, especially for long-term care services, under state legislative authority (Harrington et al., 2004), despite that empirical research found little to no effects of CON laws on containing heath care cost. Some states additionally introduced moratoria programs to strengthen their regulation on provider supply. Between 1985 and 2002, the number of states operating CON and/or moratoria for nursing homes and home health agencies decreased, but the majority of states have kept nursing home bed CON/moratoria regulations (Harrington et al., 2004). As of 2016, 35 states and the District of Columbia maintain some form of CON program, 12 states have discontinued their CON programs and 3 states have variations (Cauchi and Noble, 2018). The facilities and services regulated by CON laws vary widely from state to state; however, current CON laws are more regulatory towards long-term care and outpatient facilities (Burt and Williams, 2012). Current status of CON laws and whether certain facilities/services are regulated were presented in Table 10. (For more information on current state CON laws, see http://www.ncsl.org/documents/health/CON_State_List.pdf). Partly due to these regulatory policies, the nursing home beds availability had steadily decreased across all states, potentially contributing to the reduced probability of nursing home/long-term care deaths. Meanwhile, the availability of hospital beds also appeared to be more limited over time in most states.

Table 10 State Certificate of Need (CON) laws and facilities regulated.

State	Has CON law as of 2016?	facility regulated		
		nursing home (beds)	hospital (beds)	home health agencies
Alabama	yes	yes	yes	yes
Alaska	yes	yes	yes	no
Arizona	no	no	no	no
Arkansas	yes	yes	no	yes
California	no	no	no	no
Colorado	no	no	no	no
Connecticut	yes	yes	yes	no
Delaware	yes	yes	yes	no
District of Columbia	yes	yes	yes	yes
Florida	yes	yes	yes	no
Georgia	yes	yes	yes	yes
Hawaii	yes	yes	yes	yes
Idaho	no	no	no	no
Illinois	yes	yes	yes	no
Indiana	no	no	no	no
Iowa	yes	yes	yes	no
Kansas	no	no	no	no
Kentucky	yes	yes	yes	yes
Louisiana	yes	yes	no	yes
Maine	yes	yes	yes	no
Maryland	yes	no	yes	yes
Massachusetts	yes	yes	yes	no
Michigan	yes	yes	yes	no
Minnesota	no	yes	yes	no
Mississippi	yes	yes	yes	yes
Missouri	yes	yes	yes	no
Montana	yes	yes	yes	yes
Nebraska	yes	yes	no	no
Nevada	yes	yes	yes	yes
New Hampshire	no	no	no	no
New Jersey	yes	yes	yes	yes
New Mexico	no	no	no	no
New York	yes	yes	yes	yes
North Carolina	yes	yes	yes	yes
North Dakota	no	no	no	no
Ohio	yes	yes	no	no
Oklahoma	yes	yes	no	no
Oregon	yes	yes	yes	no
Pennsylvania	no	no	no	no
Rhode Island	yes	yes	yes	yes
South Carolina	yes	yes	yes	no
South Dakota	no	no	no	no
Tennessee	yes	yes	yes	yes
Texas	no	no	no	no
Utah	no	no	no	no
Vermont	yes	yes	yes	yes
Virginia	yes	yes	yes	no
Washington	yes	yes	yes	no
West Virginia	yes	no	yes	yes
Wisconsin	no	no	no	no
Wyoming	no	no	no	no

Note:

1. Minnesota ended its CON programs in 1984 but started to implement a similar process called "public interest review" in 2004 to require proposal for constructing new hospital or hospital bed expansions. It also allows for exceptions to the moratorium on nursing homes.

2. New Hampshire ended its CON program in 2016.

3. Wisconsin maintains an approval process for nursing homes.

Long-term care is expensive. Care for patients with dementia is much more costly than for patients with other diseases (Kelley et al., 2017). Also, costs of care delivered at institutional settings are significantly higher than care at home (Wübker et al., 2015; Alzheimer's Association, 2018). Federal and state investments in public insurance programs such as Medicare and Medicaid can significantly impact patient's purchase power of end-of-life care at different settings and can consequently influence their place of death. Results showed that states with more generous Medicaid expenditure on institutional LTSS also had increased probability of nursing home/long-term care deaths and decreased probability of home deaths. States with higher investments in institutional LTSS may provide an incentive for care facilities such as nursing homes to keep providing services to patients instead of transferring them to hospitals (Intrator and Mor, 2004; Gruneir et al., 2007; Intrator et al., 2007). Also, nursing facilities in states with higher Medicaid nursing home reimbursement rates were more likely to hire nurse practitioners and physician assistants (Intrator et al., 2005). Better quality of care due to improved staffing may propel patients and their relatives to make the decision to enter nursing facilities and stay. As for HCBS, increased Medicaid expenditure was associated with higher rates of home deaths and lower rates of nursing home/long-term care deaths. Reasonably, dementia patients with better support at home and in the community would be better equipped to avoid institutional placement. There was a symmetrical relationship between institutional LTSS spending/dying at nursing home/long-term care and HCBS spending/dying at home. Medicaid expenditure, however, was not significantly associated with the rates of hospital deaths.

On the other hand, state Medicare spending had limited impact on place of death among dementia patients. Results showed that more generous Medicare reimbursement rate on HHA was negatively associated with the rates of hospital deaths; however, it was associated with increased rates of nursing home/long-term care deaths and surprisingly did not significantly increase rates of home deaths. Medicare covers home health care for persons who are homebound and in need of part-time nursing care or therapy services (Feder et al., 2000). Medicare expenditure on HSNF was not associated with differentials in place of death. This may be because Medicare is not designed to pay for long-term care. Medicare only pays for skilled nursing facilities for up to 100 days following a hospital stay of at least 3 consecutive days (postacute care) and offers hospice care benefits at the end of life (Feder et al., 2000; Eskildsen and Price, 2009; Ng et al., 2010). For most dementia patients who usually live a much longer period of time, Medicare is not the primary source of finance for long-term care.

The changing landscape of place of death of dementia patients from institutional settings to homes and communities can be situated in the broad ageing, and particularly "ageing in place", policy framework (Vasunilashorn et al., 2012; Wiles et al., 2012). "Ageing in place," defined as "the ability to live in one's own home and community safely, independently, and comfortably, regardless of age, income, or ability level" (Centers for Disease Control and Prevention, 2009), has been increasingly favored by health policy makers, health professionals, and older persons and their relatives. Different from other cross-sectional studies, this study used fixed-effects panel models to examine how changes in state factors (e.g. sociodemographic structure of decedents, care facility resources and public care financing) were associated with the changes in place of death of

dementia patients over time. The results demonstrated the importance of both sociodemographic and structural factors in determining where dementia patients die.

This study has several limitations, too. First, several states had very small numbers of dementia deaths across different places. Those states were excluded from the panel data analysis due to the potential biases that could be introduced to parametric estimates. The relationships found between place of death and state factors may not be generalized to those less populated states. Where dementia patients die in those rural states and how it is related to sociodemographic features, access to care facilities, and state financial supports may warrant special attention. Second, this study examined the relationships between state care financing, specifically Medicare reimbursements on HHA and HSNF and Medicaid expenditure on institutional LTSS and HCBS, and place of death among dementia patients. However, how much of those expenditures was directed towards older adult dementia patients is not clear. To better inform policies designed to face the challenge of providing quality end-of-life care for an increasing number of dementia patients, federal and state agencies need to create a data taxonomy that is more reflective of service use and spending of this sub-population. Additionally, the care finance factors in this study were focused on public expenditures. Other market characteristics such as out-of-pocket spending and financing through private long-term care insurance were not examined. These factors might also have had a large impact on where dementia patients die because they make up a significant portion of long-term care payment (Kaye et al., 2010). One of the goals of the National Alzheimer's Project Act (NAPA), which was signed into law by President Barack Obama in 2011, is to improve the ability of federal agencies to collect data on dementia-related monetary costs of

individuals and public programs (U.S. Department of Health and Human Services, 2012; Hurd et al., 2013). As the quality of data on the care financing incurred by dementia improves, we will be able to better understand the relationships between federal and state investments in dementia care and place of death of dementia patients. And lastly, transition between places of care for dementia patients at the end of their lives is not uncommon (Aneshensel et al., 2000; Klinkenberg et al., 2005; Teno et al., 2013). It is entirely possible that a dementia patient received end-of-life care at home or nursing home but was transferred to a hospital during episodes of acute complications of dementia and died there. The lack of data on the possible transitions of dementia patients between different settings of care could obscure the relationships between place of death and state factors found in this study.

5.5 Conclusion

The place of death is a function of the decedent's preference, health status at the end of life, familial circumstance, and access to options. Overwhelmingly, people with dementia and their relatives prefer home death for the patients. However, the majority of U.S. older adults who died from dementia (>75% in 2014) still died elsewhere (e.g. nursing home/long-term care, hospital, other). While over time the gap has been narrowing, there is still a large discrepancy between patient's preferred place of death and actualized one. The results of this study suggest that, to help more dementia patients to die at home, states may continue to use a combination of policies aiming at restricting institutional end-of-life care resources and investing in home and community-based services. It should be noted that, although dying at home may be pivotal to many

dementia patients, it is only one of many aspects of a good death. To ensure quality end-of-life care, other aspects of patient needs (e.g. physical, social, psychological, and spiritual) also need to be respected. As the utilization of home and community-based services continues to grow, Federal and state health agencies need to evaluate and monitor the quality of HCBS to ensure that quality of end-of-life care at home and in the community for people with dementia is not compromised.

CHAPTER 6: CONCLUSIONS

6.1 Summary of results

This dissertation examined that socio-spatial disparities in dementia mortality in the United States. Using national death certificate data and a retrospective space-time scan statistic, the first study detected spatiotemporal dementia mortality clusters based on small area units. The most likely high-risk clusters were found in the Ohio River Valley and Carolinas region, the Northwest, central California, and east Texas; while the most likely low-risk clusters were located in the Northeast and Florida. Temporal information of those clusters showed a reduction in relative risk in mortality in most of the highly likely cluster areas. Despite of the etiological difference in dementia between men and women, the study found highly similar spatial and temporal patterns in clusters by sex, with a few noticeable differences. This study provided evidence of small area variations in dementia mortality risk in both space and time in the U.S.

The second study examined "place effects" on differential individual dementia mortality risk using a multilevel framework. Results showed that while the overall "place effects" were small, certain environmental factors-area socioeconomic deprivation and $PM_{2.5}$ concentration, in particular-were significantly associated with individual dementia mortality risk. The relationship between area socioeconomic deprivation and dementia mortality risk was nonlinear; however, the detrimental effects of $PM_{2.5}$ concentration on dementia mortality risk showed a dose-response manner, with higher levels of $PM_{2.5}$ concentration associated with higher risk of dementia mortality. The relationship between area social integration and individual dementia mortality risk was non-significant, especially in the models adjusted for individual-level sociodemographic variables.

Although no interactive effects between contextual and individual-level variables were found in the full model, the effects of environmental variables on individual dementia mortality risk differed by age group in stratified analysis.

The third study assessed the changing landscape of place of death of decedents from dementia in the U.S. between 2000 and 2014. Results showed that there was a persistent shift from deaths at institutional settings (hospitals, nursing home/long-term care) to deaths at home and other places. However, there were wide interstate variations in such change. The disparities in place of death of decedents from dementia were examined by sociodemographic characteristics. Older age, being female, being non-Hispanic White, being non-married and having less education were associated with higher risk of death at nursing home/long-term care facilities in both 2000 and 2014. In addition to sociodemographic factors, state health care inputs were also significantly associated with where dementia patients died. Specifically, better availability of care facility resources at one setting (e.g. hospital beds, nursing home beds) was associated with higher rates of deaths at that setting. More generous Medicaid spending on institutional LTSS was associated with higher rates of deaths at nursing home/long-term care facilities; while more generous Medicaid spending on HCBS was associated with higher rates of home deaths. Medicaid expenditures on institutional LTSS and HCBS were not significantly associated with deaths at hospitals, but Medicare reimbursement rate on HHA was negatively associated with deaths at hospitals.

6.2 Future directions

Future work on the socio-spatial disparities in dementia mortality may be focusing on two aspects: first, this dissertation uses *county* as the spatial unit to measure contextual variables. Although it is the finest geography at which all death certificates are geocoded, such large resolution may limit the usefulness of the findings since the three environmental factors-area socioeconomic deprivation, area social integration and $PM_{2.5}$ concentration-can vary widely within counties. Future research should examine the effects of these environmental factor on dementia mortality risk using data at finer resolutions when available. Also, results from cross-sectional studies may not be very useful for inferring causality. Future research needs to incorporate the life-course approach in which environmental exposure is measured throughout different stages of one's life. Such approach not only can provide stronger evidence to support the causal relationship between environmental exposure and differential dementia mortality risk, but also offers the potential to identify critical stages of life when environmental exposure may have the most significant impacts.

Second, the study of place of death of decedents from dementia assessed the interstates variations in the distribution of deaths at different places and how state structural factors may contribute to the changing landscape. As more and more decedents from dementia die at home, the overall trend and socio-spatial disparities in the quality of end-of-life care at such setting warrant further investigation. It may help transform national and local policies aiming at "deinstitutionalize" end-of-life care for dementia patients from cost-oriented to quality (or value)-oriented. Moreover, the social and spatial processes (operating at both individual and group levels) leading to differential individual

decisions on place of death remain under-explored. Future research will need to engage persons with dementia (and their caregivers) at the micro scale to better understand the resources and barriers of ageing and death in place. Qualitative research methods such as participant observation, focus groups and in-depth interviews may be used to explore the nuances and complexities in the social and spatial relations between dementia patients and their places of end-of-life care and death.

REFERENCES

Agüero-Torres H, Fratiglioni L, Guo Z, Viitanen M, Winblad B. Prognostic Factors in Very Old Demented Adults: A Seven-Year Follow-Up From a Population-Based Survey in Stockholm. J Am Geriatr Soc 1998;46:444–52.

Ailshire J, Karraker A, Clarke P. Neighborhood social stressors, fine particulate matter air pollution, and cognitive function among older U.S. adults. Soc Sci Med 2017;172:56–63.

Ailshire JA, Clarke P. Fine Particulate Matter Air Pollution and Cognitive Function Among U . S . Older Adults. Journals Gerontol Ser B Psychol Sci Soc Sci 2014;70:322–8.

Ailshire JA, Crimmins EM. Fine particulate matter air pollution and cognitive function among older US adults. Am J Epidemiol 2014;180:359–66.

Alzheimer's Association. 2018 Alzheimer' s disease facts and figures. 2018.

Amieva H, Stoykova R, Matharan F, Helmer C, Antonucci TC, Dartigues JF. What aspects of social network are protective for dementia? Not the quantity but the quality of social interactions is protective up to 15 years later. Psychosom Med 2010;72:905–11.

Amin R, Burns JJ. Clusters of adolescent and young adult thyroid cancer in Florida counties. Biomed Res Int 2014;2014.

Aneshensel CS, Pearlin LI, Levy-Storms L, Schuler RH. The Transition From Home to Nursing Home Mortality Among People With Dementia. Journals Gerontol Ser B Psychol Sci Soc Sci 2000;55:S152–62.

Araya R, Dunstan F, Playle R, Thomas H, Palmer S, Lewis G. Perceptions of social capital and the built environment and mental health. Soc Sci Med 2006;62:3072–83.

Arslantaş D, Ozbabalik D, Metintaş S, Ozkan S, Kalyoncu C, Ozdemir G, et al. Prevalence of dementia and associated risk factors in Middle Anatolia, Turkey. J Clin Neurosci 2009;16:1455–9.

Azad NA, Al Bugami M, Loy-English I. Gender differences in dementia risk factors. Gend Med 2007;4:120–9.

Azage M, Kumie A, Worku A, Bagtzoglou AC. Childhood Diarrhea Exhibits Spatiotemporal Variation in Northwest Ethiopia: A SaTScan Spatial Statistical Analysis. PLoS One 2015;10:1–18.

Azzimondi G, D'Alessandro R, Pandolfo G, Feruglio FS. Comparative Study of the Prevalence of Dementia in Two Sicilian Communities with Different Psychosocial Backgrounds. Neuroepidemiology 1998;17:199–209.

Badrakalimuthu V, Barclay S. Do people with dementia die at their preferred location of death? A systematic literature review and narrative synthesis. Age Ageing 2014;43:13–9.

Baicker K, Chandra A, Skinner JS, Wennberg JE. Who You Are And Where You Live: How Race And Geography Affect The Treatment Of Medicare Beneficiaries. Health Aff 2004;23:VAR-33-VAR-44.

Bambra C, Robertson S, Kasim A, Smith J, Cairns-Nagi JM, Copeland A, et al. Healthy

land? An examination of the area-level association between brownfield land and morbidity and mortality in England. Environ Plan A 2014;46:433–54.

Barberger-Gateau P, Raffaitin C, Letenneur L, Berr C, Tzourio C, Dartigues JF, et al. Dietary patterns and risk of dementia: The Three-City cohort study. Neurology 2007;69:1921–30.

Barnes LL, Wilson RS, Bienias JL, Schneider JA, Evans DA, Bennett DA. Sex differences in the clinical manifestations of Alzheimer disease pathology. Arch Gen Psychiatry 2005;62:685–91.

Bassuk SS, Glass TA, Berkman LF. Social engagement and incident cognitive decline in community -- dwelling elderly persons. Ann Intern Med 1999a;131:165–73.

Bassuk SS, Glass TA, Berkman LF. Social Disengagement and Incident Cognitive Decline in Community-Dwelling Elderly Persons. Ann Intern Med 1999b;131:165.

Bates D, Maechler M, Bolker B, Walker S. lme4: Linear mixed-effects models using Eigen and S4. R Packag Version 2014;1:1–23.

Bekris L, Yu C. Review article: genetics of Alzheimer disease. J Geriatr Psychiatry Neurol 2010;23:213–27.

Berkman LF, Glass T, Brissette I, Seeman TE. From social integration to health: Durkheim in the new millennium. Soc Sci Med 2000;51:843–57.

Bermejo-Pareja F, Benito-León J, Vega S. Incidence and subtypes of dementia in three elderly populations of central Spain. J Neurol Sci 2008;264:63–72.

Beyer KMM, Comstock S, Seagren R. Disease maps as context for community mapping: A methodological approach for linking confidential health information with local geographical knowledge for community health research. J Community Health 2010;35:635–44.

Bickel H, Cooper B. Incidence and relative risk of dementia in an urban elderly population: findings of a prospective field study. Psychol Med 1994;24:179–92.

Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P. Risk of dementia in diabetes mellitus: a systematic review. Lancet Neurol 2006;5:64–74.

Blakey K, Feltbower RG, James PW, Libby G, Stiller C, Norman P, et al. Socio-economic patterning in early mortality of patients aged 0–49 years diagnosed with primary bone cancer in Great Britain, 1985–2008. Cancer Epidemiol 2018;53:49–55.

Blane D. Social determinants of health--socioeconomic status, social class, and ethnicity. Am J Public Health 1995;85:903–5.

Borrayo EA, Salmon JR, Polivka L, Dunlop BD. Utilization Across the Continuum of Long-Term Care Services. Gerontologist 2002;42:603–12.

Boscoe FP, McLaughlin C, Schymura MJ, Kielb CL. Visualization of the spatial scan statistic using nested circles. Health Place 2003;9:273–7.

Braveman PA, Cubbin C, Egerter S, Chideya S, Marchi KS, Metzler M, et al. Socioeconomic Status in Health Research: one size does not fit all. Jama 2005;294:2879–88.

Braveman PA, Egerter S, Williams DR. The social determinants of health: Coming of age. Annu Rev Public Health 2011;32:381–98.

Brehaut JC, Raina P, Lindsay J. Does cognitive status modify the relationship between education and mortality? Evidence from the Canadian Study of Health and Aging. Int Psychogeriatr 2004;16:75–91.

Bruandet A, Richard F, Bombois S, Maurage CA, Masse I, Amouyel P, et al. Cognitive decline and survival in Alzheimer's disease according to education level. Dement Geriatr Cogn Disord 2008;25:74–80.

Burt J, Williams K. Certificate of Need (CON) Law Series Part II of IV : The Current State of CON Programs Across the Country. Heal Cap Top 2012;5:1–3.

Cacciottolo M, Wang X, Driscoll I, Woodward N, Saffari A, Reyes J, et al. Particulate air pollutants, APOE alleles and their contributions to cognitive impairment in older women and to amyloidogenesis in experimental models. Transl Psychiatry 2017;7:e1022.

Cagney KA, Agree EM. Racial differences in skilled nursing care and home health use: The mediating effects of family structure and social class. Journals Gerontol - Ser B Psychol Sci Soc Sci 1999;54:223–36.

Cai X, Temkin-Greener H. Nursing Home Admissions Among Medicaid HCBS Enrollees. Med Care 2015;53:566–73.

Calderón-Garcidueñas L, Solt AC, Henríquez-Roldán C, Torres-Jardón R, Nuse B, Herritt L, et al. Long-term air pollution exposure is associated with neuroinflammation, an altered innate immune response, disruption of the blood-brain barrier, ultrafine particulate deposition, and accumulation of amyloid β-42 and α-synuclein in children and young adult. Toxicol Pathol 2008;36:289–310.

Carter CL, Resnick EM, Mallampalli M, Kalbarczyk A. Sex and Gender Differences in Alzheimer's Disease: Recommendations for Future Research. J Women's Heal 2012;21:1018–23.

Cauchi R, Noble A. CON-CERTIFICATE OF NEED STATE LAWS. Natl Conf State Legis 2018. http://www.ncsl.org/research/health/con-certificate-of-need-state-laws.aspx (accessed January 10, 2019).

Centers for Disease Control and Prevention. Healthy Places Terminology 2009. https://www.cdc.gov/healthyplaces/terminology.htm (accessed February 15, 2019).

Chen H, Kwong JC, Copes R, Hystad P, van Donkelaar A, Tu K, et al. Exposure to ambient air pollution and the incidence of dementia: A population-based cohort study. Environ Int 2017;108:271–7.

Chen J, Roth RE, Naito AT, Lengerich EJ, MacEachren AM. Geovisual analytics to enhance spatial scan statistic interpretation: an analysis of U.S. cervical cancer mortality. Int J Health Geogr 2008;7:57.

Chen R, Hu Z, Wei L, Wilson K. Socioeconomic status and survival among older adults with dementia and depression. Br J Psychiatry 2014;204:436–40.

Chêne G, Beiser A, Au R, Preis SR, Wolf PA, Dufouil C, et al. Gender and incidence of

dementia in the Framingham Heart Study from mid-adult life. Alzheimer's Dement 2015;11:310–20.

Clarke PJ, Weuve J, Barnes L, Evans DA, Mendes de Leon CF. Cognitive decline and the neighborhood environment. Ann Epidemiol 2015;25:849–54.

Cockerham WC, Hamby BW, Oates GR. The Social Determinants of Chronic Disease. Am J Prev Med 2017;52:S5–12.

Connolly A, Gaehl E, Martin H, Morris J, Purandare N. Underdiagnosis of dementia in primary care: Variations in the observed prevalence and comparisons to the expected prevalence. Aging Ment Heal 2011;15:978–84.

Cramm JM, Van Dijk HM, Nieboer AP. The importance of neighborhood social cohesion and social capital for the well being of older adults in the community. Gerontologist 2013;53:142–50.

Crooks VC, Lubben J, Petitti DB, Little D, Chiu V. Social network, cognitive function, and dementia incidence among elderly women. Am J Public Health 2008;98:1221–7.

Cukierman T, Gerstein HC, Williamson JD. Cognitive decline and dementia in diabetes - Systematic overview of prospective observational studies. Diabetologia 2005;48:2460–9.

Davitt JK, Kaye LW. Racial/ethnic disparities in access to medicare home health care: The disparate impact of policy. J Gerontol Soc Work 2010;53:591–612.

Dejardin O, Jones AP, Rachet B, Morris E, Bouvier V, Jooste V, et al. The influence of geographical access to health care and material deprivation on colorectal cancer survival: Evidence from France and England. Health Place 2014;30:36–44.

Deliens L, Cohen J, Hewitt JA, Wilson DM, Houttekier D. The Preferred Place of Last Days: Results of a Representative Population-Based Public Survey. J Palliat Med 2013;16:502–8.

Duron E, Hanon O. Hypertension, cognitive decline and dementia. Arch Cardiovasc Dis 2008;101:181–9.

Escobar Pinzon LC, Claus M, Perrar KM, Zepf KI, Letzel S, Weber M. Dying with dementia: symptom burden, quality of care, and place of death. Dtsch Aerzteblatt Online 2013;110:195–202.

Eskildsen M, Price T. Nursing home care in the USA. Geriatr Gerontol Int 2009;9:1–6.

Falagas ME, Vardakas KZ, Vergidis PI. Under-diagnosis of common chronic diseases: Prevalence and impact on human health. Int J Clin Pract 2007;61:1569–79.

Falcone D, Broyles R. Access to Long-Term Care: Race as a Barrier. J Health Polit Policy Law 1994;19:583–95.

Feder J, Komisar HL, Niefeld M. Long-Term Care In The United States: An Overview. Health Aff 2000;19:40–56.

Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, et al. Global prevalence of dementia: a Delphi consensus study. Lancet 2005;366:2112–7.

Figueroa R, Steenland K, MacNeil JR, Levey AI, Vega IE. Geographical differences in

the occurrence of Alzheimer's disease mortality: United States versus Puerto Rico. Am J Alzheimers Dis Other Demen 2008;23:462–9.

Fischer S, Min SJ, Cervantes L, Kutner J. Where do you want to spend your last days of life? Low concordance between preferred and actual site of death among hospitalized adults. J Hosp Med 2013;8:178–83.

Forest W, Aucincloss AH, Diez-roux A V, Mujahid MS, Shen M, Bertoni AG, et al. Neighborhood Resources for Physical Activity and Healthy Foods and Incidence of Type 2 Diabetes Mellitus. Arch Intern Med 2009;169:1698–704.

Forget H, Lacroix A, Somma M, Cohen H. Cognitive decline in patients with Cushing's syndrome. J Int Neuropsychol Soc 2000;6:20–9.

Fratiglioni L, Guo Z, Viitanen M, Winblad B. Mortality from Dementia in Advanced Age : A 5-Year Follow-Up Study of Incident Dementia Cases. J Clin Epidemiol 1999;52:737–43.

Fratiglioni L, Wang HX, Ericsson K, Maytan M, Winblad B. Influence of social network on occurrence of dementia: A community-based longitudinal study. Lancet 2000;355:1315–9.

Frecker M. Dementia in Newfoundland: identification of a geographical isolate? J Epidemiol Community Health 1991;45:307–11.

Freels S, Nyenhuis DL, Gorelick PB. Predictors of survival in African American patients with AD, VaD, or stroke without dementia. Neurology 2002;59:1146–53.

Fuhrer R, Dufouil C, Dartigues JF. Exploring sex differences in the relationship between depressive symptoms and dementia incidence: Prospective results from the PAQUID study. J Am Geriatr Soc 2003;51:1055–63.

Fukuda Y, Umezaki M, Nakamura K, Takano T. Variations in societal characteristics of spatial dsease clusters: Examples of colon, lung and breast cancer in Japan. Int J Health Geogr 2005;4:16.

Ganguli M, Rodriguez EG. Reporting of dementia on death certificates: a community study. J Am Geriatr Soc 1999;47:842–9.

Gao S, Hendrie HC, Hall KS, Hui S. The relationships between age, sex, and the incidence of dementia and Alzheimer disease: a meta-analysis. Arch Gen Psychiatry 1998;55:809–15.

Gaudart J, Poudiougou B, Ranque S, Doumbo O. Oblique decision trees for spatial pattern detection: optimal algorithm and application to malaria risk. BMC Med Res Methodol 2005;5:22.

Geerlings MI, Deeg DJ, Penninx BW, Schmand B, Jonker C, Bouter LM, et al. Cognitive reserve and mortality in dementia: the role of cognition, functional ability and depression. Psychol Med 1999;29:1219–26.

Geerlings MI, Deeg DJH, Schmand B, Lindeboom J, Jonker C. Increased Risk Of Mortality In Alzheimers-Disease Patients With Higher Education - a Replication Study. Neurology 1997;49:798–802.

Gillum RF, Obisesan TO. Differences in Mortality Associated with Dementia in US Blacks and Whites. J Am Geriatr Soc 2011;59:1823–8.

Gillum RF, Yorrick R, Obisesan TO. Population Surveillance of Dementia Mortality. Int J Environ Res Public Health 2011;8:1244–57.

Glass TA, Bandeen-Roche K, McAtee M, Bolla K, Todd AC, Schwartz BS. Neighborhood Psychosocial Hazards and the Association of Cumulative LeadDose With Cognitive Function in Older Adults. Am J Epidemiol 2009;169:683–92.

Gruneir A, Mor V, Weitzen S, Truchil R, Teno J, Roy J. Where People Die: A Multilevel Approach to Understanding Influences on Site of Death in America. Med Care Res Rev 2007;64:351–78.

Gu Y, Scarmeas N. Dietary Patterns in Alzheimers Disease and Cognitive Aging. Curr Alzheimer Res 2011;8:510–9.

Haining RP. Spatial data analysis: theory and practice. 2003.

Harrington C, Anzaldo S, Burdin A, Kitchener M, Miller N. Trends in state certificate of need and moratoria programs for long term care providers. J Health Soc Policy 2004;19:31–58.

Hebert LE, Scherr PA, Bienias JL, Bennett DA, Evans DA. Alzheimer disease in the US population: prevalence estimates using the 2000 census. Arch Neurol 2003;60:1119–22.

Hebert LE, Weuve J, Scherr P a., Evans D a. Alzheimer disease in the United States (2010-2050) estimated using the 2010 census. Neurology 2013;80:1778–83.

Helmer C, Damon D, Letenneur L, Fabrigoule C, Barberger-Gateau P, Lafont S, et al. Marital status and risk of Alzheimer's disease A French population-based cohort study. Neurology 1999;53:1953–8.

Helmer C, Joly P, Letenneur L, Commenges D, Dartigues JF. Mortality with dementia: Results from a French prospective community-based cohort. Am J Epidemiol 2001;154:642–8.

Henry J Kaiser Family Foundation F. State Health Facts: Hospital Beds per 1,000 Population by Ownership Type n.d. https://www.kff.org/other/state-indicator/beds-by-ownership/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D (accessed January 10, 2019).

Henry KA, Niu X, Boscoe FP. Geographic disparities in colorectal cancer survival. Int J Health Geogr 2009;8:48.

Hopp FP, Duffy SA. Racial Variations in End-of-Life Care. J Am Geriatr Soc 2000;48:658–63.

Houttekier D, Cohen J, Bilsen J, Addington-Hall J, Onwuteaka-Philipsen BD, Deliens L. Place of death of older persons with dementia. A study in five European countries. J Am Geriatr Soc 2010;58:751–6.

Hsu CE, Jacobson H, Mas FS. Evaluating the disparity of female breast cancer mortality among racial groups - a spatiotemporal analysis. Int J Health Geogr 2004;3:4.

Hurd MD, Martorell P, Delavande A, Mullen KJ, Langa KM. Monetary costs of dementia

in the United States. N Engl J Med 2013;368:1326–34.

Huss A, Spoerri A, Egger M, Röösli M. Residence near power lines and mortality from neurodegenerative diseases: Longitudinal study of the Swiss population. Am J Epidemiol 2009;169:167–75.

Intrator O, Feng Z, Mor V, Gifford D, Bourbonniere M, Zinn J. The employment of nurse practitioners and physician assistants in U.S. nursing homes. Gerontologist 2005;45:486–95.

Intrator O, Grabowski DC, Zinn J, Schleinitz M, Feng Z, Miller S, et al. Hospitalization of nursing home residents: The effects of states' medicaid payment and bed-hold policies. Health Serv Res 2007;42:1651–71.

Intrator O, Mor V. Effect of State Medicaid Reimbursement Rates on Hospitalizations from Nursing Homes. J Am Geriatr Soc 2004;52:393–8.

Islam MK, Merlo J, Kawachi I, Lindström M, Gerdtham U-G. Social capital and health: Does egalitarianism matter? A literature review. Int J Equity Health 2006;5:3.

James BD, Bennett DA. Causes and Patterns of Dementia: An Update in the Era of Redefining Alzheimer's Disease. Annu Rev Public Health 2019;40:1–20.

James BD, Leurgans SE, Hebert LE, Scherr P a, Yaffe K, Bennett D a. Contribution of Alzheimer disease to mortality in the United States. Neurology 2014;82:1045–50.

Jean H, Emard J-FF, Thouez J-PP, Houde L, Robitaille Y, Mathieu J, et al. Alzheimer's disease: Preliminary study of spatial distribution at birth place. Soc Sci Med 1996;42:871–8.

Jia J, Wang F, Wei C, Zhou A, Jia X, Li F, et al. The prevalence of dementia in urban and rural areas of China. Alzheimer's Dement 2013;10:1–9.

Johnson KS, Kuchibhatla M, Tulsky JA. What explains racial differences in the use of advance directives and attitudes toward hospice care? J Am Geriatr Soc 2008;56:1953–8.

Jones SG, Kulldorff M. Influence of Spatial Resolution on Space-Time Disease Cluster Detection. PLoS One 2012;7:e48036.

Kaye HS, Harrington C, Laplante MP. Long-term care: Who gets it, who provides it, who pays, and how much? Health Aff 2010;29:11–21.

Kelley AS, Mcgarry K, Gorges R, Skinner JS. The Burden of Health Care Costs in the Last 5 Years of Life. Ann Intern Med 2017;163:729–36.

Kennelly SP, Lawlor BA, Kenny RA. Blood pressure and dementia - a comprehensive review. Ther Adv Neurol Disord 2009;2:241–60.

Klinkenberg M, Visser G, van Groenou MI, van der Wal G, Deeg DJ, Willems DL. The last 3 months of life: care, transitions and the place of death of older people. Heal Soc Care Community 2005;13:420–30.

De Kloet ER, Oitzl MS, Joëls M. Stress and cognition: Are corticosteroids good or bad guys? Trends Neurosci 1999;22:422–6.

Krieger N. Theories for social epidemiology in the 21st century: an ecosocial perspective.

Int J Epidemiol 2001;30:668–77.

Krieger N. Epidemiology and Social Sciences : Towards a Critical Reengagement in the 21st Century. Epidemiol Rev 2000;22:155–63.

Krieger N. Epidemiology and the web of causation: Has anyone seen the spider? Soc Sci Med 1994;39:887–903.

Kuiper JS, Zuidersma M, Oude Voshaar RC, Zuidema SU, van den Heuvel ER, Stolk RP, et al. Social relationships and risk of dementia: A systematic review and meta-analysis of longitudinal cohort studies. Ageing Res Rev 2015;22:39–57.

Kulldorff M. SaTScan User Guide. 2006.

Kulldorff M. Prospective time periodic geographical disease surveillance using a scan statistic. J R Stat Soc Ser a-Statistics Soc 2001;164:61–72.

Kulldorff M. A spatial scan statistic. Commun Stat - Theory Methods 1997;26:1481–96.

Kulldorff M, Athas WF, Feuer EJ, Miller BA, Key CR. Evaluating cluster alarms: A space-time scan statistic and brain cancer in Los Alamos, New Mexico. Am J Public Health 1998;88:1377–80.

Kulldorff M, Feuer EJ, Miller BA, Freedman LS. Breast cancer clusters in the northeast United States: a geographic analysis. Am J Epidemiol 1997;146:161–70.

Kulldorff M, Heffernan R, Hartman J, Assunçao R, Mostashari F. A space-time permutation scan statistic for disease outbreak detection. PLoS Med 2005;2:0216–24.

Kulldorff M, Tango T, Park PJ. Power comparisons for disease clustering tests. Comput Stat Data Anal 2003;42:665–84.

Landfield P, Blalock E, Chen K, Porter N. A new glucocorticoid hypothesis of brain aging: implications for Alzheimer's disease. Curr Alzheimer Res 2007;4:205–12.

Lane MJ, Davis DR, Cornman CB, Macera CA, Sanderson M. Location of death as an indicator of end-of-life costs for the person with dementia. Am J Alzheimers Dis Other Demen 1998;13:208–10.

Lapane KL, Gambassi G, Landi F, Sgadari A, Mor V, Bernabei R. Gender differences in predictors of mortality in nursing home residents with AD. Neurology 2001;56:650–4.

Law MR, Morris JK. Why is mortality higher in poorer areas and in more northern areas of England and Wales? J Epidemiol Community Health 1998;52:344–52.

Lefebvre A, Bertrand X, Vanhems P, Lucet JC, Chavanet P, Astruc K, et al. Detection of temporal clusters of healthcare-associated infections or colonizations with Pseudomonas aeruginosa in two hospitals: Comparison of SaTScan and WHONET software packages. PLoS One 2015;10:1–14.

Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D, et al. Dementia prevention, intervention, and care. Lancet 2017.

Llibre Rodriguez JJ, Ferri CP, Acosta D, Guerra M, Huang Y, Jacob KS, et al. Prevalence of dementia in Latin America, India, and China: a population-based cross-sectional survey. Lancet 2008;372:464–74.

Lupien SJ, McEwen BS, Gunnar MR, Heim C. Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nat Rev Neurosci 2009;10:434–45.

Macintyre S, Ellaway A, Cummins S. Place effects on health: how can we conceptualise, operationalise and measure them? Soc Sci Med 2002;55:125–39.

Manjourides J, Suh H, Tallon LA, Pun VC, Salhi C. Cognitive impacts of ambient air pollution in the National Social Health and Aging Project (NSHAP) cohort. Environ Int 2017;104:102–9.

Marmot M. Social determinants of health inequalities. Lancet 2005;365:1099–104.

Marmot M, Wilkinson R. Social determinants of health. 2007.

Masuchi Y. The place of death among people with dementia in Finland – The change from 1998 to 2013. 2013.

Masuchi Y, Jylhä M, Raitanen J, Aaltonen M. Changes in place of death among people with dementia in Finland between 1998 and 2013: A register study. Alzheimer's Dement Diagnosis, Assess Dis Monit 2018;10:86–93.

Matthews F, Brayne C, Medical Research Council Cognitive Function and Ageing Study Investigators. The incidence of dementia in England and Wales: Findings from the five identical sites of the MRC CFA study. PLoS Med 2005;2:e193.

Matthews KA, Xu W, Gaglioti AH, Holt JB, Croft JB, Mack D, et al. Racial and ethnic estimates of Alzheimer ' s disease and related dementias in the United States (2015 – 2060) in adults aged 65 years. Alzheimer's Dement 2019;15:17–24.

McEwen B. Re-examination of the glucocorticoid hypothesis of stress and aging. Prog Brain Res 1992;93:365–83.

McEwen BS, Tucker P. Critical biological pathways for chronic psychosocial stress and research opportunities to advance the consideration of stress in chemical risk assessment. Am J Public Health 2011;101:131–9.

Meeussen K, Van Den Block L, Echteld M, Boffin N, Bilsen J, Van Casteren V, et al. Older people dying with dementia: A nationwide study. Int Psychogeriatrics 2012;24:1581–91.

Mehta KM, Yaffe K, Perez-Stable EJ, Stewart A, Barnes D, Kurland BF, et al. Race/ethnic differences in AD survival in US Alzheimer's Disease Centers. Neurology 2008;70:1163–70.

Menec VH, Shooshtari S, Nowicki S, Fournier S. Does the relationship between neighborhood socioeconomic status and health outcomes persist into very old age? A population-based study. J Aging Health 2010;22:27–47.

Meng X, D'Arcy C. Education and dementia in the context of the cognitive reserve hypothesis: A systematic review with meta-analyses and qualitative analyses. PLoS One 2012;7:e38268.

Messer LC, Laraia BA, Kaufman JS, Eyster J, Holzman C, Culhane J, et al. The development of a standardized neighborhood deprivation index. J Urban Heal 2006;83:1041–62.

Middleton LE, Yaffe K. Promising strategies for the prevention of dementia. Arch Neurol 2009;66:1210–5.

Mielke MM, Vemuri P, Rocca WA. Clinical epidemiology of Alzheimer's disease: Assessing sex and gender differences. Clin Epidemiol 2014;6:37–48.

Miniño AM, Arias E, Kochanek KD, Murphy SL, Smith BL. Deaths: final data for 2000. Natl Vital Stat Reports 2002;50:1–119.

Mitchell SL, Teno JM, Miller SC, Mor V. A National Study of the Location of Death for Older Persons with Dementia. J Am Geriatr Soc 2005;53:299–305.

Morenoff JD, Sampson R, Raudenbush SW. Neighborhood inequality, collective efficacy, and the spatial dynamics of urban violence. Criminology 2001;39:517–58.

Morgan K, Clarke D. To what extent is dementia underreported on British death certificates? Int J Geriatr Psychiatry 1995;10:987–90.

Mujahid MS, Roux VD, Morenoff JD, Raghunathan TE, Cooper RS, Ni H, et al. Neighborhood characteristics and hypertension. Epidemiology 2008;19:590–8.

Murphy S, Xu J, Kochanek K. Deaths: Final Data for 2013. Natl Vital Stat 2016.

Murphy SL, Xu J, Kochanek KD, Curtin SC, Arias E. Death: Final Data for 2015. Natl Vital Stat Reports 2017;66:1–75.

Murray AT, Grubesic TH, Wei R. Spatially significant cluster detection. Spat Stat 2014;10:103–16.

Murtaugh CM, Kemper P, Spillman BC. The risk of nursing home use in later life. Med Care 1990;28:952–62.

Nagai M, Hoshide S, Kario K. Hypertension and dementia. Am J Hypertens 2010;23:116–24.

Nash DT, Fillit H. Cardiovascular Disease Risk Factors and Cognitive Impairment. Am J Cardiol 2006;97:1262–5.

NCHS. Health, United States, 2016 - Individual Charts and Tables: Spreadsheet, PDF, and PowerPoint files. Table 092: Nursing homes, beds, residents, and occupancy rates, by state: United States, selected years 1995–2015 2018. https://www.cdc.gov/nchs/hus/contents2016.htm#092 (accessed January 10, 2019).

NCHS. Multiple Cause of Death files n.d.

Ng T, Harrington C, Kitchener M. Medicare and Medicaid in long-term care. Health Aff 2010;29:22–8.

Nkhoma ET, Ed Hsu C, Hunt VI, Harris AM. Detecting spatiotemporal clusters of accidental poisoning mortality among Texas counties, U.S., 1980 - 2001. Int J Health Geogr 2004;3:25.

Noale M, Limongi F, Zambon S, Crepaldi G, Maggi S. Incidence of dementia: evidence for an effect modification by gender. The ILSA Study. Int Psychogeriatrics 2013;25:1867–76.

Oei NYL, Everaerd WTAM, Elzinga BM, Van Well S, Bermond B. Psychosocial stress

impairs working memory at high loads: An association with cortisol levels and memory retrieval. Stress 2006;9:133–41.

Ogunniyi A, Baiyewu O, Gureje O, Hall KS, Unverzagt F, Siu SH, et al. Epidemiology of dementia in Nigeria: results from the Indianapolis-Ibadan study. Eur J Neurol 2000;7:485–90.

Ogunniyi A, Hall KS, Gureje O, Baiyewu O, Gao S, Unverzagt FW, et al. Risk factors for incident Alzheimer's disease in African Americans and Yoruba. Metab Brain Dis 2006;21:235–40.

Olichney JM, Hofstetter CR, Galasko D, Thal LJ, Katzman R. Death certificate reporting of dementia and mortality in an Alzheimer's disease research center cohort. J Am Geriatr Soc 1995;43:890–3.

Oudin A, Forsberg B, Adolfsson AN, Lind N, Modig L, Nordin M, et al. Traffic-related air pollution and dementia incidence in Northern Sweden: A longitudinal study. Environ Health Perspect 2016;124:306–12.

Ouvrard C, Meillon C, Dartigues J-F, Ávila-Funes JA, Amieva H, Carr D. Do Individual and Geographical Deprivation Have the Same Impact on the Risk of Dementia? A 25-Year Follow-up Study. Journals Gerontol Ser B 2017;00:1–10.

Ozdenerol E, Williams BL, Kang SY, Magsumbol MS. Comparison of spatial scan statistic and spatial filtering in estimating low birth weight clusters. Int J Health Geogr 2005;4:19.

Pan SM, Yang JT, Chen CC. The predictors of long-term care service utilization among older Americans. Kaohsiung J Med Sci 1998;14:226–33.

Paradise M, Cooper C, Livingston G. Systematic review of the effect of education on survival in Alzheimer's disease. Int Psychogeriatr 2009;21:25–32.

Pavlik VN, Doody RS, Massman PJ, Chan W. Influence of premorbid IQ and education on progression of Alzheimer's disease. Dement Geriatr Cogn Disord 2006;22:367–77.

Perron M, Veillette S, Emard J. Aspects of Social Epidemiology in the Study of Alzheimer's Disease in Saguenay (Quebec)/IMAGE Project. Can J Aging/La Rev Can Du Vieil 1993;12:382–98.

Pickett KE, Pearl M. Multilevel analyses of neighbourhood socioeconomic context and health outcomes: a critical review. J Epidemiol Community Health 2001;55:111–22.

Plante GE. Vascular response to stress in health and disease. Metabolism 2002;51:25–30.

Plassman BL, Langa KM, Fisher GG, Heeringa SG, Weir DR, Ofstedal MB, et al. Prevalence of dementia in the United States: The aging, demographics, and memory study. Neuroepidemiology 2007;29:125–32.

Power MC, Adar SD, Yanosky JD, Weuve J. Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: A systematic review of epidemiologic research. Neurotoxicology 2016;56:235–53.

Power MC, Lamichhane AP, Liao D, Xu X, Jack CR, Gottesman RF, et al. The Association of Long-Term Exposure to Particulate Matter Air Pollution with Brain MRI

Findings: The ARIC Study. Environ Health Perspect 2018;126:027009.

Power MC, Weisskopf MG, Alexeeff SE, Coull BA, Spiro A, Schwartz J. Traffic-Related Air Pollution and Cognitive Function in a Cohort of Older Men. Environ Health Perspect 2011;119:682–7.

Prates MO, Kulldorff M, Assunção RM. Relative risk estimates from spatial and space-time scan statistics: Are they biased? Stat Med 2014;33:2634–44.

Prince M, Acosta D, Ferri CP, Guerra M, Huang Y, Rodriguez JJL, et al. Dementia incidence and mortality in middle-income countries, and associations with indicators of cognitive reserve: A 10/66 Dementia Research Group population-based cohort study. Lancet 2012;380:50–8.

Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. Alzheimer's Dement 2013;9:63–75.

Prince M, Cullen M, Mann A. Risk factors for Alzheimer's disease and dementia: a case-control study based on the MRC elderly hypertension trial. Neurology 1994;44:97–104.

Qiu C, Bäckman L, Winblad B. The influence of education on clinically diagnosed dementia incidence and mortality data from the Kungsholmen Project. Arch Neurol 2001;58:2034–9.

R Development Core Team. R: A language and environment for statistical computing 2014.

Ranft U, Schikowski T, Sugiri D, Krutmann J, Krämer U. Long-term exposure to traffic-related particulate matter impairs cognitive function in the elderly. Environ Res 2009;109:1004–11.

Raudenbush SW, Bryk AS. Hierarchical linear models: Applications and data analysis methods. 2002.

Regidor E. Social determinants of health: a veil that hides socioeconomic position and its relation with health. J Epidemiol Community Health 2006;60:896–901.

Remes O, Wainwright N, Surtees P, Lafortune L, Khaw K-T, Brayne C. Sex differences in the association between area deprivation and generalised anxiety disorder: British population study. BMJ Open 2017;7:e013590.

Reyniers T, Deliens L, Pasman HR, Morin L, Addington-Hall J, Frova L, et al. International variation in place of death of older people who died from dementia in 14 European and non-European countries. J Am Med Dir Assoc 2015;16:165–71.

Robinson WS. Ecological correlations and the behavior of individuals. Am Sociol Rev 1950;15:351–7.

Romero JP, Benito-León J, Louis ED, Bermejo-Pareja F. Under reporting of dementia deaths on death certificates: A systematic review of population-based cohort studies. J Alzheimer's Dis 2014;41:213–21.

Rosso AL, Flatt JD, Carlson MC, Lovasi GS, Rosano C, Brown AF, et al. Neighborhood socioeconomic status and cognitive function in late life. Am J Epidemiol 2016;183:1088–97.

Rupasingha A, Goetz SJ, Freshwater D. The production of social capital in US counties. J Socio Econ 2006;35:83–101.

Russ TC, Batty GD, Hearnshaw GF, Fenton C, Starr JM. Geographical variation in dementia: systematic review with meta-analysis. Int J Epidemiol 2012;41:1012–32.

Russ TC, Stamatakis E, Hamer M, Starr JM, Kivimäki M, Batty GD. Socioeconomic status as a risk factor for dementia death: Individual participant meta-analysis of 86 508 men and women from the UK. Br J Psychiatry 2013;203:10–7.

Salinas-Rodríguez A, Fernández-Niño JA, Manrique-Espinoza B, Moreno-Banda GL, Sosa-Ortiz AL, Qian Z (Min), et al. Exposure to ambient PM2.5concentrations and cognitive function among older Mexican adults. Environ Int 2018;117:1–9.

Sapolsky RM. Glucocorticoids, stress, and their adverse neurological effects: Relevance to aging. Exp Gerontol 1999;34:721–32.

Schrijvers EMC, Verhaaren BFJ, Koudstaal PJ, Hofman A, Ikram MA, Breteler MMB. Is dementia incidence declining? Trends in dementia incidence since 1990 in the Rotterdam Study. Neurology 2012;78:1456–63.

Scribner RA, Simonsen NR, Leonardi C. The Social Determinants of Health Core: Taking a Place-Based Approach. Am J Prev Med 2017;52:S13–9.

Shah R. The role of nutrition and diet in Alzheimer disease: A systematic review. J Am Med Dir Assoc 2013;14:398–402.

Sharp ES, Gatz M. Relationship between education and dementia: An updated systematic review. Alzheimer Dis Assoc Disord 2011;25:289–304.

Sharp SI, Aarsland D, Day S, Sønnesyn H, Ballard C. Hypertension is a potential risk factor for vascular dementia: Systematic review. Int J Geriatr Psychiatry 2011;26:661–9.

Sheehan TJ, DeChello LM. A space-time analysis of the proportion of late stage breast cancer in Massachusetts, 1988 to 1997. Int J Health Geogr 2005;4:15.

Sheffield KM, Peek MK. Neighborhood context and cognitive decline in older mexican americans: Results from the hispanic established populations for epidemiologic studies of the elderly. Am J Epidemiol 2009;169:1092–101.

Sherman RL, Henry KA, Tannenbaum SL, Feaster DJ, Kobetz E, Lee DJ. Applying Spatial Analysis Tools in Public Health: An Example Using SaTScan to Detect Geographic Targets for Colorectal Cancer Screening Interventions. Prev Chronic Dis 2014;11:E41.

Sisco SM, Marsiske M. Neighborhood Influences on Late Life Cognition in the ACTIVE Study. J Aging Res 2012;2012:1–11.

Sleeman KE, Ho YK, Verne J, Gao W, Higginson IJ. Reversal of English trend towards hospital death in dementia: a population-based study of place of death and associated individual and regional factors, 2001–2010. BMC Neurol 2014;14:59.

Sommerlad A, Ruegger J, Singh-Manoux A, Lewis G, Livingston G. Marriage and risk of dementia: systematic review and meta-analysis of observational studies. J Neurol Neurosurg Psychiatry 2017:jnnp-2017.

Sörman DE, Rönnlund M, Sundström A, Adolfsson R, Nilsson LG. Social relationships and risk of dementia: A population-based study. Int Psychogeriatrics 2015;27:1391–9.

Spruill TM. Chronic psychosocial stress and hypertension. Curr Hypertens Rep 2010;12:10–6.

Srinivasan V, Braidy N, Chan EKW, Xu Y-H, Chan DKY. Genetic and environmental factors in vascular dementia: an update of blood brain barrier dysfunction. Clin Exp Pharmacol Physiol 2016;43:515–21.

Steenland K, MacNeil J, Vega I, Levey A. Recent trends in Alzheimer disease mortality in the United States, 1999 to 2004. Alzheimer Dis Assoc Disord 2009;23:165–70.

Stern Y, Tang MX, Denaro J, Mayeux R. Increased risk of mortality in Alzheimer's disease patients with more advanced educational and occupational attainment. Ann Neurol 1995;37:590–5.

Sudakin DL, Horowitz Z, Giffin S. Regional Variation in the Incidence of Symptomatic Pesticide Exposures: Applications of Geographic Information Systems. J Toxicol Clin Toxicol 2002;40:767–73.

Sundström A, Westerlund O, Kotyrlo E. Marital status and risk of dementia: A nationwide population-based prospective study from Sweden. BMJ Open 2016;6:1–7.

Sylvia E, Born W, Greiner KA, Butler J, Ahluwalia JS. Knowledge, Attitudes, and Beliefs about End-of-life Care among Inner-City African Americans and Latinos. J Palliat Med 2004;7:247–56.

Taylor SE, Repetti RL, Seeman T. HEALTH PSYCHOLOGY: What is an Unhealthy Environment and How Does It Get Under the Skin? Annu Rev Psychol 1997;48:411–47.

Teno JM, Clarridge BR, Casey V, Welch LC, Wetle T, Shield R, et al. Family Perspectives on End-of-Life Care at the Last Place of Care. J Am Med Assoc 2004;291:88–93.

Teno JM, Gozalo PL, Bynum JPW, Leland NE, Miller SC, Morden NE, et al. Change in end-of-life care for medicare beneficiaries: Site of death, place of care, and health care transitions in 2000, 2005, and 2009. JAMA - J Am Med Assoc 2013;309:470–7.

Thygesen LC, Ersbøll AK. When the entire population is the sample: strengths and limitations in register-based epidemiology. Eur J Epidemiol 2014;29:551–8.

Tinetti ME, McAvay GJ, Murphy TE, Gross CP, Lin H, Allore HG. Contribution of individual diseases to death in older adults with multiple diseases. J Am Geriatr Soc 2012;60:1448–56.

Townsend P, Phillimore P, Beattie A. Health and deprivation: inequality and the North. 1988.

U.S. Census Bureau. Annual Estimates of the Civilian Population by Single Year of Age and Sex for the United States and States: April 1, 2010 to July 1, 2017. 2018. https://www.census.gov/data/datasets/2017/demo/popest/state-detail.html (accessed January 10, 2019).

U.S. Census Bureau. 2017 National Population Projections Tables 2017.

https://www.census.gov/data/tables/2017/demo/popproj/2017-summary-tables.html (accessed February 18, 2019).

U.S. Census Bureau. TIGER/Line® Shapefiles and TIGER/Line® Files 2012a. https://www.census.gov/geo/maps-data/data/tiger-line.html (accessed March 15, 2017).

U.S. Census Bureau. Intercensal Estimates of the Resident Population by Five-Year Age Groups, Sex, Race and Hispanic Origin for States and the United States: April 1, 2000 to July 1, 2010. 2012b. https://www.census.gov/data/datasets/time-series/demo/popest/intercensal-2000-2010-state.html (accessed January 10, 2019).

U.S. Census Bureau. 2006-2010 American Community Survey 5-Year Estimates 2011:http://factfinder.census.gov.

U.S. Department of Health and Human Services. National Plan to Address Alzheimer's Disease 2012. https://aspe.hhs.gov/pdf-document/national-plan-address-alzheimers-disease (accessed February 16, 2019).

Underwood E. The polluted brain. Science 2017;355:342–5.

Uphoff EP, Pickett KE, Cabieses B, Small N, Wright J. A systematic review of the relationships between social capital and socioeconomic inequalities in health: a contribution to understanding the psychosocial pathway of health inequalities. Int J Equity Health 2013;12:54.

Vasunilashorn S, Steinman BA, Liebig PS, Pynoos J. Aging in place: Evolution of a research topic whose time has come. J Aging Res 2012;2012.

Vincent GK, Velkoff VA. The Next Four Decades: The Older Population in the United States: 2010 to 2050. 2010.

Volicer L, Hurley AC, Blasi Z V. Characteristics of dementia end-of-life care across care settings. Am J Hosp Palliat Med 2003;20:191–200.

van de Vorst IE, Koek HL, Stein CE, Bots ML, Vaartjes I. Socioeconomic Disparities and Mortality After a Diagnosis of Dementia: Results From a Nationwide Registry Linkage Study. Am J Epidemiol 2016;184:219–26.

Wallace SP, Levy-Storms L, Kington RS, Andersen RM. The Persistence of Race and Ethnicity in the use of Long-Term Care. Journals Gerontol Ser B Psychol Sci Soc Sci 1998;53B:S104–12.

Waller LA, Carlin BP. Disease Mapping. 2010.

Wang H-X, Karp A, Winblad B, Fratiglioni L. Late-Life Engagement in Social and Leisure Activities Is Associated with a Decreased Risk of Dementia: A Longitudinal Study from the Kungsholmen Project. Am J Epidemiol 2002;155:1081–7.

Weisent J, Rohrbach B, Dunn JR, Odoi A. Detection of high risk campylobacteriosis clusters at three geographic levels. Geospat Health 2011;6:65–76.

Wen H, Zhang Z, Huang J, Duan L, Wang Q. Mortality of dementia and its major subtypes in urban and rural communities of Beijing. Biomed Environ Sci 2011;24:483–90.

Wen M, Cagney KA, Christakis NA. Effect of specific aspects of community social

environment on the mortality of individuals diagnosed with serious illness. Soc Sci Med 2005;61:1119–34.

Weuve J, Hebert LE, Scherr PA, Evans DA. Deaths in the United States among persons with Alzheimer's disease (2010-2050). Alzheimer's Dement 2014;10:e40–6.

Weuve J, Puett RCR, Schwartz J, Yanosky JD, Laden F, Grodstein F. Exposure to particulate air pollution and cognitive decline in older women. Arch Intern Med 2012;172:219–27.

Wilding S, Martin D, Moon G, Wilding S. Place and preference effects on the association between mental health and internal migration within Great Britain. Health Place 2018;52:180–7.

Wiles JL, Leibing A, Guberman N, Reeve J, Allen RES. The Meaning of "Aging in Place" to Older People. Gerontologist 2012;52:357–66.

Wilker EH, Preis SR, Beiser AS, Wolf PA, Au R, Kloog I, et al. Long-Term Exposure to Fine Particulate Matter, Residential Proximity to Major Roads and Measures of Brain Structure. Stroke 2015;46:1161–6.

Winkleby M a., Jatulis DE, Frank E, Fortmann SP. Socioeconomic status and health: How education, income, and occupation contribute to risk factors for cardiovascular disease. Am J Public Health 1992;82:816–20.

World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. 1992.

Wörn J, Ellwardt L, Aartsen M, Huisman M. Cognitive functioning among Dutch older adults: Do neighborhood socioeconomic status and urbanity matter? Soc Sci Med 2017;187:29–38.

Wright AA, Keating NL, Balboni TA, Matulonis UA, Block SD, Prigerson HG. Place of death: Correlations with quality of life of patients with cancer and predictors of bereaved caregivers' mental health. J Clin Oncol 2010;28:4457–64.

Wu Y, Prina AM, Brayne C. The association between community environment and cognitive function: a systematic review. Soc Psychiatry Psychiatr Epidemiol 2015a;50:351–62.

Wu Y, Prina AM, Jones AP, Barnes LE, Matthews FE, Brayne C. Community environment, cognitive impairment and dementia in later life: results from the Cognitive Function and Ageing Study. Age Ageing 2015b;44:1005–11.

Wu YC, Lin YC, Yu HL, Chen JH, Chen TF, Sun Y, et al. Association between air pollutants and dementia risk in the elderly. Alzheimer's Dement Diagnosis, Assess Dis Monit 2015;1:220–8.

Wübker A, Zwakhalen SMG, Challis D, Suhonen R, Karlsson S, Zabalegui A, et al. Costs of care for people with dementia just before and after nursing home placement: primary data from eight European countries. Eur J Heal Econ 2015;16:689–707.

Xu W, Wu C. Detecting spatiotemporal clusters of dementia mortality in the United States, 2000–2010. Spat Spatiotemporal Epidemiol 2018;27:11–20.

Yip PK, Shyu YI, Liu SI, Lee JY, Jan PL, Yang CT, et al. The Multi disciplinary Project of Dementia Study in Northern Taiwan (DSNT): Background and Methodology. Acta Neurol Taiwan 1997;6:210–6.

Zeki Al Hazzouri A, Haan MN, Osypuk T, Abdou C, Hinton L, Aiello AE. Neighborhood socioeconomic context and cognitive decline among older mexican Americans: Results from the sacramento area latino study on aging. Am J Epidemiol 2011;174:423–31.

Zeng Y, Gu D, Purser J, Hoenig H, Christakis N. Associations of environmental factors with elderly health and mortality in china. Am J Public Health 2010;100:298–305.

Zhang ZX, Zahner GEPP, Román GC, Liu XH, Wu CB, Hong Z, et al. Socio-demographic variation of dementia subtypes in China: Methodology and results of a prevalence study in Beijing, Chengdu, Shanghai, and Xian. Neuroepidemiology 2006;27:177–87.

Zunzunegui M-V, Alvarado BE, Del Ser T, Otero A. Social networks, social integration, and social engagement determine cognitive decline in community-dwelling Spanish older adults. J Gerontol B Psychol Sci Soc Sci 2003;58:S93–100.

CURRICULUM VITAE

EDUCATION

Ph.D. (2019 expected). Geography, University of Wisconsin Milwaukee, Milwaukee, Wisconsin, USA
Dissertation: Social-spatial disparities in dementia mortality in the United States
Committee: Dr. Changshan Wu (chair), Dr. Kirsten Beyer, Dr. Woonsup Choi, Dr. Alison Donnelly, Dr. Kevin Matthews

M.S. 2014. Geography, University of Wisconsin Milwaukee, Milwaukee, Wisconsin, USA

B.E. (with honor). 2007. Land Resource Management, Wuhan University, China

RESEARCH INTERESTS

Health and medical geography
Social and environmental determinants of chronic disease
Socio-spatial inequalities in health and health care access
Human/environment interactions
GIS in public health

PUBLICATIONS

Peer-reviewed journal articles

Wei Xu, Changshan Wu. 2018. Detecting spatiotemporal clusters of dementia mortality in the United States, 2000-2010. *Spatial and spatio-temporal epidemiology* 27:11-20.

Kevin A. Matthews, **Wei Xu**, Anne H. Gaglioti, James B. Holt, Janet B. Croft, Dominic Mack, Lisa C. McGuire. 2018. Racial and ethnic estimates of Alzheimer's disease and related dementias in the United States (2015–2060) in adults aged ≥ 65 years. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association. (in press)*

- Press mention:
    - Forbes, *New Research Says Alzheimer's And Other Dementias Will Hit Minorities Hardest In Coming Years.* https://www.forbes.com/sites/robinseatonjefferson/2018/09/25/new-research-says-alzheimers-and-other-dementias-will-hit-minorities-hardest-in-coming-years/#31a1322741db
    - USA Today, *CDC: Alzheimer's disease, dementia cases to double by 2060* https://www.usatoday.com/story/news/nation-now/2018/09/21/cases-alzheimers-dementia-double-2060-

cdc/1377453002/?fbclid=IwAR0mK4AZbkPR6tAljoODwWhQ-01JkDqOlpA41T3Kr6ig_qLWV02RB8Q9pvE

Publications in progress

Sima Namin, Yuhong Zhou, **Wei Xu**, Kirsten Beyer. 2019. The Legacy of the Home Owner's Loan Corporation and the Political Ecology of Urban Trees and Air Pollution in the United States. *Health & Place*. (under review)

Wei Xu, Changshan Wu. 2019. Assessment of changes in the place of death of older adults who died from dementia in the United States, 2000-2014. *Applied Geography*. (ready for submission)

Wei Xu, Kirsten Beyer. 2019. Individual socio-demographic attributes, area socio-physical environments and dementia mortality risk: A multilevel logistic regression analysis. *International Journal of Environmental Research and Public Health. (*ready for submission*)*

Wei Xu, Changshan Wu. 2019. Creating county dementia mortality profile for end-of-life care planning: a decision tree approach. (in preparation)

Hung Chak Ho, Chengbin Deng, **Wei Xu**. 2019. Local community characteristics and cancer and all-cause mortality: a spatial structural equation modeling approach. (in preparation)

PRESENTATIONS

Academic conferences

Presented

2018. Area social deprivation, social capital and individual dementia mortality risk in US older adults: a population-based study. 2018 AAG Annual Meeting, New Orleans, LA, April 10 – 14, 2018

2017. Detecting spatiotemporal clusters of dementia mortality in the United States, 2000-2010. 2017 AAG Annual Meeting, Boston, MA, April 5 – 9, 2017

2016. Social deprivation, Rurality and Mortality of Alzheimer's Disease and Related Dementia in the Contiguous United States. 2016 AAG Annual Meeting, San Francisco, CA, March 29 – April 2, 2016

2015. The geography of mortality attributed to Alzheimer's disease and its association with socioeconomic context in the contiguous United States, 2000 -2010. The 16th International Medical Geography Symposium, Vancouver, BC, Canada, July 5 – 10, 2015

2014. Developing Population Grid with Demographic Trait: An Example for Milwaukee County, Wisconsin. 2014 AAG Annual Meeting, Tampa, FL, April 8-12, 2014

Chaired

2017. Geospatial Health Research Symposium: Geographies of Ageing. 2017 AAG Annual Meeting, Boston, MA, April 5 – 9, 2017

Invited lectures, presentations, & workshops

2018. Dan Siercks, Stephen Appel, **Wei Xu**. *GIS and High Performance Computing*. UWM Libraries Digital Humanities Lab, University of Wisconsin Milwaukee

EXTERNAL GRANTS

2017. Socio-spatial disparities in dementia mortality in the United States: a multilevel analysis. Emerging Directions for Addressing Health Disparities in Alzheimer's Disease (R03). National Institutes of Health (NIH). (under review)

2017. Socio-spatial Disparities in Dementia Mortality in the United States, Doctoral Dissertation Research Improvement grant, National Science Foundation (NSF) (Not funded)

SERVICES

2015-2018. President. GIS Club, University of Wisconsin Milwaukee

- Organized the Humanitarian OpenStreetMap team and collaborative mapping sessions
- Organized professional workshops such as photogrammetry, high performance computing
- Organized collaboration with Groundwork Milwaukee to survey local business district developments

2016-2017. Project assistant. Undergraduate Program Committee, Department of Geography, University of Wisconsin Milwaukee

- Student major/minor advising
- Facilitated the evaluation of undergraduate programs

2012-2015. Treasurer. Student Chapter of the American Society for Photogrammetry and Remote Sensing (ASPRS), University of Wisconsin Milwaukee

2013. Graduate Student Representative. Department of Geography, University of Wisconsin Milwaukee

2012-2013. Project assistant. Public Relations Committee, Department of Geography, University of Wisconsin Milwaukee

RESEARCH EXPERIENCE

2018. Student worker. Project: Racism, Residential Racial Segregation, and Breast Cancer Survival Disparities among Black, Hispanic and non-Hispanic White Women (NIH R01). Medical College of Wisconsin. Supervised by Dr. Kirsten Beyer.

2018. Student worker. Project: Breast and Lung Cancer Disparities in Wisconsin: Trends and Patterns. Medical College of Wisconsin. Supervised by Dr. Kirsten Beyer.

2014. Research assistant. Project: Spatial and Longitudinal Patterns in County Age-Specific Net Migration in the United States 1950-2010. Department of Geography, University of Wisconsin Milwaukee. Supervised by Dr. Zengwang Xu

TEACHING EXPERIENCE

2012-2018. Teaching Assistant, Department of Geography, University of Wisconsin Milwaukee

- GEOG625, labs for Intermediate Geographic Information Science
- GEOG525, labs for Geographic Information Science
- GEOG547, labs for Spatial Analysis
- GEOG405, labs for Cartography
- GEOG215, labs for Introduction to Geographic Information Science (both in person and online)
- GEOG114, discussion for The Geography of Race in the U.S.
- GEOG110, discussion for The World: Peoples and Regions

2016, 2018. Guest lecture. Department of Geography, University of Wisconsin Milwaukee

- GEOG 247: Quantitative Analysis in Geography

HONORS AND AWARDS

2018. Distinguished Dissertation Fellowship. Graduate School. University of Wisconsin Milwaukee

2015-2018. Mary Jo Read Graduate Fellowship, Department of Geography, University of Wisconsin Milwaukee

2014-2019. Mary Jo Read Travel Award, Department of Geography, University of Wisconsin Milwaukee

2017. Outstanding Graduate Student Service Award, Department of Geography, University of Wisconsin Milwaukee

2015. Chancellor's Graduate Student Award, University of Wisconsin Milwaukee

2015. Second place, Student GIS Project Competition, GIS Council, University of Wisconsin Milwaukee

2015. Health and Medical Geography Special Group (HMGSG) Travel Award, American Association of Geographers (AAG)

2006-2007. Undergraduate scholarship (second tier), School of Resources and Environmental Sciences, Wuhan University, China

AFFLIATIONS

2012 – present. Association of American Geographers (AAG), member

Specialty groups:

- Health and Medical Geography
- Geographic Information Science & System
- Spatial Analysis & Modeling
- Population

2018 – present. Wisconsin Land Information Association, member.

2015 – present. International Society of Urban Health (ISUH), member

2015 – present. The International Association of Chinese Professionals in Geographical Information Sciences (CPGIS), member

PROFESSIONAL TRAINING AND SKILLS

Computer skills

GIS & Remote sensing: *ArcGIS Desktop Suite, ArcGIS Online, QGIS, GeoDa, ERDAS*

Statistics: SPSS, Stata, SaTScan

Programming: R, RStudio, Python

Language skills

Fluent in English and Chinese

REFERENCES

Dr. Changshan Wu

Professor, Department of Geography, University of Wisconsin Milwaukee

Address: Bolton 482, 3210 N. Maryland Ave, Milwaukee WI 53201

Email: cswu@uwm.edu

Dr. Kirsten Beyer

Associate professor, Institute for Health and Society, Division of Epidemiology, Medical College of Wisconsin

Address: 8701 Watertown Plank Rd, Milwaukee, WI 53226

Email: kbeyer@mcw.edu

Dr. Alison Donnelly

Associate professor, Department of Geography, University of Wisconsin Milwaukee

Address: Bolton 426, 3210 N. Maryland Ave, Milwaukee WI 53201

Email: donnela@uwm.edu