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LIFESTYLE BEHAVIORS AND COGNITIVE STATUS IN A COMMUNITY

SAMPLE OF OLDER ADULTS

by

Heeyoung Smith

A thesis submitted in partial fulfillment of the requirement for the degree

of

MASTER OF SCIENCE

in

Family, Consumer, and Human Development

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2011

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ABSTRACT

Lifestyle Behaviors and Cognitive Status in a Community Sample of Older Adults

by

Heeyoung Smith, Master of Science

Utah State University, 2011

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Lifestyle behaviors have been associated with better cognitive status and reduced risk of dementia. However, only individual or combinations of a few lifestyle behaviors have been studied. The present study examines the association between lifestyle behaviors and cognitive status in older adults including six lifestyle behaviors: cognitive activities, social activities, physical activities, religious involvement, diet, and alcohol consumption.

The study population is a sample of 1,216 community-dwelling men and women age 65 years and older from Cache County, Utah. The present study is conducted using the extant data from the Cache County Study on Memory Health and Aging (CCSMHA), a prospective longitudinal study, which has been ongoing since 1995 with its focus on Alzheimer's disease and other forms of dementia. Data related to lifestyle behaviors, cognitive status, and dementia diagnosis in the third study wave were analyzed for the purpose of the present study. Three lifestyle patterns were identified based on the six lifestyle behaviors: the least engaged, the moderately engaged secular, and the most engaged religious. The most engaged religious pattern represented a healthy lifestyle on all lifestyle domains with exception to almost no use of alcohol. The moderately engaged secular pattern represented a moderately healthy lifestyle on all domains with least engagement in religious behavior. The least engaged pattern showed an unhealthy lifestyle on all domains with moderate engagement in religious behavior. The results showed that participants in the least engaged had a lower cognitive status and higher rate of being diagnosed with cognitive impairment or dementia compared to those with other two lifestyle patterns.

The findings suggest that engaging in healthy lifestyle behaviors in later life might protect from or delay loss of cognitive ability and dementia risk.

(129 pages)

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Heeyoung Smith

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CHAPTER I

PROBLEM STATEMENT

Public Health Significance of Dementia

The older population is growing rapidly as life expectancy increases. Currently people 65 years old are expected to live an average of 18.7 more years in the United States. Moreover, the growth of the older population will be accelerated in 2011 as the "baby boomers" (people born between 1946 and 1964) start turning age 65. The number of people aged 65 and over is expected to nearly double between 2006 (37 million) and 2030 (71.5 million; Federal Interagency Forum on Aging-Related Statistics, 2008).

Population projections estimate corresponding increases in the numbers of people who will suffer from Alzheimer's disease (AD) or other forms of dementia because the risk is higher with increasing age (van der Flier & Scheltens, 2005). In the U.S., it was estimated that approximately 3.4 million people aged 70 and older had dementia in 2007 (Plassman et al., 2007). If the current trend continues, the number of Americans with AD alone will rise from 5.1 million today to 7.7 million by 2030 and somewhere between 11 and 16 million by 2050 (Alzheimer's Association, 2009). At the global level, 26.6 million cases of AD were identified in 2006 and the number is expected to grow to 107.8 million by 2050 (Brookmeyer, Johnson, Ziegler-Graham, & Arrighi, 2007). The annual AD incidence rate is expected to increase from 454,000 today to 959,000 in 2050 in the United Sates alone (Hebert, Beckett, Scherr, & Evans, 2001).

The burdens associated with dementia are tremendous on the affected individual, relatives, and society. According to the Alzheimer's Association, 87% of caregivers are

relatives of the individual with AD; 60% are women; and 14% are aged 65 and older. Caregivers of an individual with dementia are exposed to emotional stress as well as health problems (Mausbach, Patterson, Rabinowitz, Grant, & Schulz, 2007) and financial dilemmas (Alzheimer's Association, 2009). The estimated costs of formal care for dementia patients in the U.S. averaged \$27,672 per patient per year. The indirect costs, such as lost wages, averaged \$10,400 to \$34,517 per patient per year (Rice et al., 2001). Now more than ever, an effort to reduce dementia risk and delay timing of severe symptoms is critical.

Some individuals with cognitive impairment are not diagnosed with dementia but are still considered at high risk of dementia or AD, these people are often labeled by diagnostic categories such as "mild cognitive impairment," "subsyndromal Alzheimer's disease, "cognitive impairment, not dementia," and "age-associated cognitive decline." Annual conversion rates of approximately 9.4% (Tuokko et al., 2003) and 14.3% (Tschanz et al., 2006) from "cognitive impairment, not dementia" to dementia were reported in two large epidemiological studies. More studies are needed to examine, not only risk and protective factors for dementia, but also for this intermediate state of cognitive impairment that does not yet meet dementia criteria, to better understand factors that prevent or delay onset of dementia.

The known risk factors for dementia include old age, carrying one or more Apolipoprotein E (APOE) ɛ4 alleles, family history of AD, vascular disease, and lower education (Miech et al., 2002; Pope, Shue, & Beck, 2003). Although science offers no solution at this time to avoid the effects of genetic factors connected to AD or dementia,

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it is important, and within our power, to seek a better understanding of environmental factors, especially those that are modifiable such as lifestyle behaviors.

There is evidence in the literature that a number of lifestyle behaviors are associated with dementia risk. Lifestyle behaviors are actions that are performed over a long period of time such as being involved with cognitive activities (e.g., reading, writing), participating in social activities (e.g., social clubs, groups, organizations), exercising regularly, eating a healthy diet, or use of alcohol or tobacco. Frequent participation in leisure activities including activities in the cognitive (Scarmeas, Levy, Tang, Manly, & Stern, 2001; Verghese et al., 2003; Wang, Karp, Winblad, & Fratiglioni, 2002; Wilson, Bennett, et al., 2002) and social domains (Scarmeas et al., 2001; Wang, Karp, et al., 2002) have been associated with reduced risk of dementia. Frequent participation in physical activities (Laurin, Verreault, Lindsay, MacPherson, & Rockwood, 2001; Lindsay et al., 2002), church attendance (Hill, Burdette, Angel, & Angel, 2006; Reyes-Ortiz et al., 2008), healthy diet (Barberger-Gareau et al., 2007; Scarmeas, Stern, Tang, Mayeux, & Luchsinger, 2006), low to moderate alcohol consumption (Anstey, Mack, & Cherbuin, 2009; Peters, Peters, Warner, Beckett, & Bulpitt, 2008), and not smoking (Anstey, von Sanden, Salim, & O'Kearney, 2007) have also been associated with reduced risk of dementia. Among these lifestyle behaviors, activities that are predominantly cognitive have been consistently associated with reduced risk for dementia and cognitive decline. Studies demonstrate how lifestyle behaviors affect cognitive health in varied combinations. However few studies have attempted to examine the wide array of lifestyle behaviors considered in the present study. Examining the effects of all the lifestyle behaviors collectively on dementia risk is needed. In

addition, an effort to find discernable patterns in lifestyle behaviors will aid in the identification of subpopulations that can then be studied for different dementia risks and ultimately, to provide more information for clinical implications in dementia prevention.

Theoretical Perspective

Cognitive reserve is "the ability to optimize or maximize performance through differential recruitment of brain networks" (Stern, 2002, p. 451). A person who has more cognitive reserve is able to use brain networks more efficiently. Also, a person with higher cognitive reserve is better able to use alternative brain networks or cognitive strategies when a normal network is damaged.

Higher education or occupational attainment (Stern, 2002) and engagement in leisure activities (Newson & Kemps, 2005; Scarmeas & Stern, 2003) have been associated with increased cognitive reserve. The perspective of cognitive reserve implies that engagement in an active and healthy lifestyle in later life increases reserve that will help sustain cognitive function and slow the rate of decline.

The perspective of cognitive reserve suggests that late-life leisure activities and behaviors might stimulate cognition and increase reserve (or skills), thus helping to perform everyday life efficiently and to preserve cognitive health over a longer period, even under the influence of dementia pathology.

Purpose of the Research

The purpose of the present study was to examine the association between lifestyle behaviors and dementia in a sample of 1,216 people age 65 years and older who are residents of Cache County, Utah. The lifestyle behaviors that were examined in this study include cognitive activities, social interaction, physical activities, religious involvement, diet, and alcohol consumption. The present study hypothesized that there exists a finite set of distinct patterns of lifestyle behaviors that is related to late-life cognitive health, particularly dementia. For example, people might be (1) physically, socially active, and have a healthy diet but not cognitively active, (2) cognitively and religiously active but not physically or socially active and have an unhealthy diet, (3) active in all domains and eat in a healthy way, and so forth. If distinct lifestyle patterns were identified, these could then be compared to determine relative risk for dementia. Results could be of great potential clinical benefit in efforts to target subpopulations at greatest risk for dementia due to their collective patterns of lifestyle behaviors.

Summary

The prevalence and incidence of dementia are major public health concerns. The impact of dementia on society and families, both economically and psychologically, is substantial. Although there are immutable risk factors for dementia such as APOE genotype, age, and gender, it is important to focus on modifiable lifestyle behaviors such as cognitive activities, physical activities, and diet. The association between lifestyle behaviors and dementia risk has been studied typically on the basis of a single aspect, or a combination of two to three aspects. There have been no studies that have examined the association between the arrays of lifestyle behaviors and dementia proposed for the present study. If there exist significant cumulative effects across the range of lifestyle behaviors taken singly or

in small subsets, such knowledge would be important but totally missed via the piecemeal approach thus far taken in extant literature.

The present study examined the association between six lifestyle behaviors and both current cognitive and dementia status, including: cognitive activity, social interaction, physical activity, religious involvement, diet, and alcohol consumption. This was accomplished through use of extant data available from the Cache County (Utah) Study on Memory Health and Aging, an epidemiological study of dementia and risk and protective factors, in a sample of over 5,000 older adults, spanning 1995-2007. There are two components to this thesis project. The first was to determine the existence of lifestyle typologies, or patterns of lifestyle behaviors, and the second was to determine whether the various typologies are associated with different average levels of cognitive status and differential risk for dementia.

CHAPTER II

REVIEW OF LITERATURE

This chapter provides first, a brief review of the public health significance of dementia. This is followed by an explanation of the "cognitive reserve hypothesis," which is a theoretical perspective of lifestyle behaviors and late life cognitive health. Next, a review is provided of studies that examined the association between individual lifestyle behaviors and cognitive function or risk of dementia in older adults. Finally, studies that analyzed lifestyle behaviors with Latent Class Analysis are summarized, with a summary of the current state of knowledge on this topic.

Dementia is a syndrome characterized by progressive deterioration of cognitive functions. Common neuropsychiatric symptoms of dementia include apathy, agitation, and depression. Alzheimer's disease (AD) is the most common form of dementia in older adults (about 60%; Breitner et al., 1999), followed by vascular dementia (about 20%; Breitner et al., 1999). AD is a neurodegenerative disorder that is assumed to be caused by neuritic plaques and neurofibrillary tangles accumulating in the brain (van der Flier & Scheltens, 2005). AD is preceded by a long phase of progressive cognitive decline that leads to symptoms such as memory loss, impaired judgment, and decreased ability to conduct everyday activities (Hodges, 2006; Pope et al., 2003). Vascular dementia (VaD) is thought to be caused by different types of vascular pathology in the brain such as large vessel and small vessel disease. Other frequent causes of dementia include frontotemporal lobar degeneration (see Appendix A) and dementia with Lewy bodies (see Appendix A, van der Flier & Scheltens, 2005). The known risk factors for cognitive decline and AD include old age, carrying APOE genotype with one or more ɛ4 alleles, family history of AD, vascular disease, lower education (Pope et al., 2003), and gender (Breitner et al., 1999; Fratiglioni, Winblad, & von Strauss, 2007).

Prevalence and Incidence of Dementia

In epidemiology, the prevalence of a disease is defined as the total number of cases of the disease in the population at a specific point in time, or the proportion of the population that has disease. Incidence is a measure of the risk of developing new cases of the disease within a specified period of time (van der Flier & Scheltens, 2005). Prevalence of dementia in European studies ranged between 5% and 10% among those aged 65 and older and doubles every 4 years up to 30% at age 80 (Ritchie & Lovestone, 2002). Dementia prevalence in developing countries was lower ranging approximately between 2% and 5% in those aged 65 and older (Haan & Wallace, 2004). The incidence rate of dementia in persons aged 65 and older (per 1,000 person years, see Appendix A) has been estimated to be between 13.3 and 25.48 in North-American cohort studies, and between12.5 and 35 in European studies (Haan & Wallace, 2004).

A recent estimate of the national prevalence of dementia was 3,407,000 (95% CI 2,793,000 - 4,021,000) in the U.S. in a representative sample (n = 856, age ≥ 70 ; Plassman et al., 2007). The proportion of "All dementia" showed that 68.5% was female and 83.4% was non-Hispanic White in the sample. Estimated national prevalence of "All dementia" increases with age: 4.97% (95% CI 2.61-7.32) among persons aged 71-79 years; 24.19% (95% CI 19.28-29.11) among persons aged 80-89 years; 37.36% among persons aged 90 years and older. AD accounted for about 69.9% of all dementia and VaD accounted for 17.4%. Other types of dementia such as "dementia, undetermined etiology," Parkinson's dementia, normal-pressure hydrocephalus, frontal lobe dementia, alcohol dementia, traumatic brain injury, and Lewy body dementia accounted for 12.7%. Dementia risk increased with age (OR 1.17; 95% CI 1.13-1.22 for one year increase) and the presence of at least one APOE ε 4 allele (OR 2.56; 95% CI 1.71-3.82), and decreased with higher education (OR 0.91; 95% CI 0.87-0.96 for one year increase in education; Plassman et al., 2007).

Cognitive Impairment with No Dementia

Late-life cognitive impairment has drawn attention in dementia studies for its prevalence and its clinical importance in identifying individuals at enhanced risk of dementia, thereby facilitating the development of interventions that may delay or perhaps even prevent onset of dementia to those at greatest risk.

The concept "cognitive impairment with no dementia" (CIND), that was introduced by the Canadian Study of Health and Aging (Graham et al., 1997), is the broadest category of late-life mild cognitive disorders that included mild cognitive impairment (MCI; Petersen et al., 1999). MCI is an amnestic state that is transitional between normal cognitive function and dementia (Petersen et al., 1999). CIND includes other criteria of cognitive impairment that could be originated from delirium, long-term alcohol and other drug use, depression, and other psychiatric illness whereas MCI has its focus specifically on memory impairment (Tuokko et al., 2003).

The prevalence of CIND in the Cache County Study, which combined prodromal AD and other cognitive syndromes similar to the criteria of CIND used in the Canadian

Study, was 6.74% (Tschanz et al., 2006). The Canadian Study reported prevalence of CIND as 16.8% (Graham et al., 1997). Annual conversion rates to dementia from CIND were 14.3% in the Cache County Study and 9.4% in the Canadian Study (Tschanz et al., 2006; Tuokko et al., 2003).

Theoretical Perspective

The concept of reserve (or brain reserve) was proposed by Katzman (1993) and further developed by Stern and colleagues (Scarmeas, Zarahn, Anderson, Habeck, et al., 2003; Stern, 2002) to account for the individual differences between clinical expression and the degree of brain pathology. *Brain reserve* concerns size of the brain and neuronal count whereas *cognitive reserve* proposed by Stern (2002, 2009) is derived from utility of brain networks, for example, use of different regions of the brain (Stern, 2009). The perspective of cognitive reserve is employed in this thesis to explain the relationship between lifestyle behaviors and risk of dementia or cognitive function.

Cognitive reserve (CR) is "the ability to optimize or maximize performance through differential recruitment of brain networks" (Stern, 2002, p. 451). Individuals with more CR are able to utilize brain networks more efficiently in the face of cognitive decline that is related to older age. Moreover, individuals with more CR are able to use alternative brain networks or cognitive strategies when the normal network is damaged, for example, by AD pathology (compensation; Stern, 2002). CR is accumulated by life experiences such as education, occupational attainment, and leisure activities (Stern, 2009). Leisure activities considered in CR are common activities that contain cognitive, social, and physical components such as reading newspapers, playing cards or other games, going to theaters or movies, going for walking or rides, taking part in sports, dancing or exercise, visit or being visited by friends or relatives or neighbors, and so forth (Scarmeas, Zarahn, Anderson, Habeck, et al., 2003).

It is assumed that the critical threshold of brain pathology that will be manifest in clinically detectable change in cognitive abilities varies by individuals. In other words, in the case of AD, individuals are at the different degree of AD pathology when they are diagnosed as cognitively impaired. The assumption is that cognitive aging or AD pathology has a different effect in each individual because individuals differ in how they cope with cognitive decline or brain damage caused by AD.

This assumption has been supported by neuroimaging studies. A study using positron emission tomographic (PET) measuring amyloid plaques (index of AD pathology) reveal the impact of higher education. Roe et al. (2008) found that people who did not have plaques in their brains did not show dementia symptoms clinically, however, among those who did show plaques in their brains, the severity of dementia symptoms was related to how much education they had completed. A study using resting regional cerebral blood flow (rCBF) found an inverse relationship between lower rCBF (more AD pathology) and increased education, occupation, or leisure activities (Scarmeas, Zarahn, Anderson, Habeck, et al., 2003) suggesting that individuals with more CR (increased leisure activities) tolerate more AD pathology.

In the case of AD, the perspective of CR posits that individuals with more CR can tolerate a larger lesion of brain pathology for a longer time than an individual with less CR before reaching the threshold of functional impairment as described in Figure 1. For that reason, individuals with more CR have more AD pathology at the point dementia is



AD Neuropathology

Figure 1. Theoretical illustration of showing progression of AD pathology in two individuals with high and low cognitive reserve. The point of inflection is where memory begins to be affected by AD pathology. Adopted from "Cognitive reserve," by Y. Stern, 2009, *Neuropsychologia*, 47, p. 2017.

diagnosed. Individuals with more CR maintain higher cognitive function but once clinical symptoms of AD become apparent, their cognitive ability tends to decline more rapidly. The rapid cognitive decline and functional loss in the presence of severe AD pathology may result in higher probability of death. With all the above assumptions, clinical symptoms of dementia would appear later and the rate of incident dementia would be lower in individuals with more CR (Stern, 2009).

The perspective of CR may provide explanations for the relationships between lifestyle behaviors and cognitive function or dementia status. Engagement in leisure activities later in life may increase CR in older adults and consequently it is associated with lower incidence of dementia and higher cognitive function. In other words, individuals who engage in healthy lifestyle behaviors can maintain higher cognitive function and, in the case of dementia, they can tolerate the pathology of dementia for a longer period of time until they experience clinical manifestation of dementia thus showing lower rate of dementia diagnosis.

Lifestyle Behaviors and Late-life Cognitive Health

Cognitive status (or cognitive function), indicate a global cognitive ability that is measured by widely used cognitive tests such as Modified Mini-mental State (3MS) Examination (Teng & Chui, 1987) as in the present study. Examination of cognitive status is the first step of dementia diagnosis as it is an important indicator of possible dementia. Given that cognitive status is closely related to dementia diagnosis, studies that examined the association between lifestyle behaviors and cognitive status, cognitive decline, or any type of dementia as outcomes were of interest in the present study and thus were reviewed together.

Studies reporting findings relating each of six lifestyle behavior and cognitive function or dementia risk were reviewed in this section. Review of studies in cognitive, social, and physical activities are combined because these activities are usually grouped in studies. Studies in religious behavior, diet, and alcohol consumption are reviewed in order. Methodological differences, measurement differences, and considered confounders in research are also summarized. In addition, studies that used Latent Class Analysis were briefly reviewed.

Cognitive, Social, and Physical Activities

Studies have been finding the benefits of engagement in cognitive, social, and physical activities on cognitive function or decreased risk of dementia. The majority of these studies examined cognitive, social, and physical activities together in a study under the title of "leisure activities" rather than examining activities representing a single dimension such as social dimension only.

Studies of leisure activities showed benefits of engaging in activities in all cognitive, social, and physical domains whereas some studies found no association of certain domains (e.g., physical activities). For example, in a sample of 776 people followed for 6 years, Karp et al. (2006) found that higher mental, physical, and social component sum score based on 29 leisure activities were associated with reduced risk of dementia (29% -39%) adjusting for age, gender, education, comorbidity (see Appendix A), cognitive function, depressive symptoms, and functional status. Moreover, higher scores in all three components or two or more components were the most beneficial (47% reduced risk). The component scores were rated by the researchers and also older adults giving scores (0 = none, 1 = low, 2 = moderate, 3 = high) by mental, social, and physical component for each of the 29 activities allowing overlap of activities. Sums of each component score was dichotomized at the median.

Other studies found beneficial effects of leisure activities that are predominantly cognitive and social but beneficial effects of physical activities remained unclear. Wang, Karp, et al. (2002) examined the relationships between engagement in mental, social, productive, physical, and recreational activities, and risk for incident dementia in a sample of 1,375 people followed for over 6 years. Examples of mental activities included

reading books or newspapers, writing, studying, working crossword puzzles, painting, or drawing; physical activities included swimming, walking, or gymnastics; social activities included attending the theater, concerts, or art exhibitions, traveling, playing cards or games, or participating in social groups or a pension organization. Productive activities included gardening, housekeeping, volunteering, and working for pay after retirement. Recreational activities included watching television or listening to the radio. The authors found that persons who engaged in mental, social, and productive activities had 42% to 46% reduced risk for dementia when frequency of participation was daily, compared to less often than daily. The effects of physical and recreational activities were not significant. The results were adjusted for age, gender, education, comorbidity, cognitive function, depressive symptoms, and functional status. The findings were stable even after adjusting for APOE genotype and social network.

Verghese et al. (2003) conducted a 5-year follow-up study of 469 people and found that cognitive activities (n = 6), but not physical activities (n = 11) were associated with reduced risk of dementia, AD, and better cognitive test scores, especially episodic memory (see Appendix A). They reported approximately 7% reduced risk of dementia, AD, or any type of dementia with the measure of continuous activity variable (1 point for 1 activity per week) but the reduced risk increased to 63% when they changed the activity measure to tertiles (upper tertile versus lower two tertiles). The effects were stable after controlling for baseline cognitive status (in addition to important covariates) and even after excluding subjects with possible preclinical dementia. In terms of individual activity, reading, playing board games, playing musical instruments, and dancing were good predictors of above outcomes. A similar study in a sample of 1,772 people aged 65 years and older found that the number of activities participated in a month among13 leisure activities reduced the risk for dementia by 11% when it was treated as a continuous variable and 38% reduced risk when it was dichotomized at the median (Scarmeas et al., 2001). When the activities were grouped into intellectual (reading newspapers or magazines, playing cards or games or bingo, and going to classes), physical (walking for pleasure or going for an excursion and physical conditioning), and social (visiting or being visited by friends or relatives, going out to movies or restaurants or clubs or centers, doing voluntary community work, and going to church or synagogue) continuous variables, the intellectual activities were associated with the lowest risk of dementia (24%) followed by physical activities (20%) and social activities (15%). The individual activities that were strongly associated with reduced risk for dementia were reading magazines or newspapers, visiting friends or relatives, going out to movies or restaurants, and walking for pleasure or going for an excursion (27%-51% reduced risk) suggesting that activities of different components, not only mental or intellectual, may be associated with dementia risk.

Wilson, Bennett, et al. (2002) found that cognitively stimulating activities, but not weekly hours of physical activity, was associated with reduced risk of AD in a 4-year follow-up study of 842 people. In a composite measure of 7 cognitive activities (e.g., viewing television, reading a newspaper, and playing games like cards and crosswords), a one-point increase in cognitive activity score was associated with a 64% reduction in risk of incident AD controlling for demographics, APOE genotype, depressive symptoms, comorbidity, and perceived prestige of lifetime occupations. The same measure of cognitive activity was associated with decreased risk of AD in a sample of 801 older Catholic nuns, priests, and brothers 4.5 years later (33% reduced risk; Wilson, Mendes de Leon, et al., 2002).

The inconsistency of the effect of physical activities may stem from the fact that many leisure activities have cognitive, social, and physical components (Verghese et al., 2003). Yet, there are other studies with evidence that physical activity is associated with reduced risk for dementia or cognitive function. Two nationally representative studies found beneficial effects of physical activities (Laurin et al., 2001; Podewils et al., 2005). In the Canadian Study of Health and Aging, Laurin et al. (2001) conducted a 5-year follow-up study of 4,615 people and reported that high levels of physical activity were associated with reduced risk of cognitive impairment (CIND), AD, and dementia of any type (42%, 50% and 37% reduced risk, respectively) compared with no activity. A high level of physical activity was defined as an exercise engaged in three or more times per week at intensity greater than walking whereas a moderate level was at intensity equal to walking, and the rest was a low level of physical activity. When the above association was analyzed by gender, the association was only significant for women with outcomes of cognitive impairment (CIND), cognitive loss, and AD after adjustment for demographics and family history of dementia.

In the Cardiovascular Health Study of 3,375 people with over 5-year follow-up period, the highest quartile of physical energy expenditure had 15% reduced risk of dementia compared to those in the lowest quartile. Participants engaged in four or more activities had a 49% reduced risk of dementia compared to those engaged in 0-1 activity, but only among APOE e4 allele non-carriers when stratified by APOE genotype. The study adjusted for demographics, APOE genotype, functional status, social support, and

the baseline 3MS score (Podewils et al., 2005). Another population-based study with a sample of 1,146 found self-reported high exercise level was associated with 61% reduced risk of decline on Mini-Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975) during 2 years after adjusting for demographics and self-reported health (Lytle, Bilt, Pandav, Dodge, & Ganguli, 2004).

There are studies that found cross-sectional associations between the level of leisure activities and cognitive function (Bielak, Hughes, Small, & Dixon, 2007; Newson & Kemps, 2005). Bielak and colleagues found a significant cross-sectional but a weak longitudinal relationship between leisure activities in a sample of 530 people during a 6year follow-up. Especially, activities with predominant cognitive component (novel information processing, see Appendix A) were associated with all components of cognitive speed (i.e., simple- and choice-reaction time, lexical- and semantic-decision). Cognitive speed is a computer-based task to measure participant's reaction time on stimuli that was based on signals, words, and sentences (Bielak et al., 2007).

Newson and Kemps (2005) found a generally active lifestyle based on activities such as household maintenance (e.g., gardening, car maintenance), domestic chores (e.g., washing dishes, preparing a main meal), social activities (e.g., participating in outdoor recreation or sports, participating at a club) were associated with higher levels of current cognitive function and slower cognitive decline over 6 years in a sample of 755 participants. The cross-sectional effects were stronger on cognitive tests (i.e., speed of processing, picture naming, incidental recall, verbal fluency; total variance accounted by activity 5%-14%) than the longitudinal effects on cognitive change (i.e., speed of processing, picture naming, incidental recall; total variance accounted by activity 0.6%-4%).

In summary, there is evidence that cognitive, social, and physical activities are beneficial to cognitive health in later life. While some activities may involve but a single component, many activities span cognitive, social, and physical dimensions. However, the findings from the previous studies in leisure activities suggest that cognitively stimulating activities have greater benefit on cognitive function and reducing risk of dementia.

Religious Behavior

Several studies reported an association between religious involvement and cognitive function (Hill et al., 2006; Reyes-Ortiz et al., 2008; Van Ness & Kasl, 2003) indicating that engagement in religious behavior may benefit cognitive health in older adults. A large population-based longitudinal study found an inverse association between religious attendance and cognitive dysfunction in older adults (Van Ness & Kasl, 2003). In a sample of 2,812 people who attended religious services once a week or more, compared to those who attended religious services less than once a week, showed less cognitive dysfunction 3 years later (36% reduced risk), but not 6 years later, after adjustment for significant factors such as social engagement, functional disability, comorbidity, and baseline cognitive function. Religious identity, based on how deeply the person is religious and how the religion is a source of strength and comfort, had no significant association. The non-significant association at the 6-year follow up was explained by the higher death rate among participants who reported infrequent religious

attendance and among those with cognitive dysfunction at baseline. The authors argued that because the inverse relationship remained significant (3 years later) after social engagement was controlled, it might indicate that religious attendance may be a unique predictor of cognition (Van Ness & Kasl, 2003).

Building upon these findings, two longitudinal studies with the same sample of 3,050 Mexican Americans aged 65 and older have found protective effect of religious attendance on cognitive change during 2, 5, 7, and 11 years of follow-up. In the 7-year follow-up study, the effects of monthly, weekly, and more than weekly religious attendance on cognitive decline remained significant but attenuated (36%, 24%, and 29%, respectively) when significant factors such as baseline cognitive function, functional disability, sensory impairment, and advanced age were taken into account. This indicated that a significant portion of the association between religious attendance and cognitive decline may be explained by these factors. Smoking, drinking, and depression did not change the effects (Hill et al., 2006). In the 11-year follow-up study, infrequent church attendees (never or almost never, several times a year, or once/twice a month) had a greater cognitive decline compared to frequent church attendees (almost every week or more than once a week). The difference was greater especially among individuals with depression indicating that frequent church attendance may mediate the association between depressive symptoms and cognitive decline (Reyes-Ortiz et al., 2008).

Kaufman, Anaki, Binns, and Freedman (2007) found significant associations between higher levels of perceived spirituality and private religious practices, and slower rate of cognitive decline in 70 participants with AD over 3 years. These two variables accounted for 17% of the total variance of cognitive decline after controlling for baseline level of cognition, age, gender, and education. Other religious behaviors such as how people assess themselves as being religious, religious attendance, or religious belief or experience had no significant effects on cognitive decline. Although not examined, they suggested that the associations might be related to health outcomes that spirituality and religiosity may affect health outcomes such as lower rates of depression, higher compliance with treatment, less health-risk taking behaviors (e.g., smoking, drinking), healthier lifestyles (e.g., healthy diets), enhanced of social ties and enhanced cognitive stimulation (Kaufman et al., 2007).

Diet

Studies suggest that a healthy diet may be beneficial for late life cognition (Barberger-Gareau et al., 2007; Kang, Asherio, & Grodstein, 2005; Morris, Evans, Tangney, Bienias, & Wilson, 2006; Scarmeas et al., 2006; Wengreen et al., 2010). Kang and colleagues found that participants who reported high vegetable consumption experienced less cognitive decline over 2 years compared to those with low vegetable consumption in a sample of 15,080 female older adults. However, fruit consumption was not significantly related to rate of cognitive decline (Kang et al., 2005). Similar patterns were found in a sample of 3,718 participants, aged 65 years and older. Compared with the rate of cognitive decline among participants in the lowest quintile of vegetable intake, participants in the fourth quintile showed slower decline by 40% and by 38% among participants in the fifth quintile after adjusting for age, gender, and education. No significant association between fruit consumption and cognitive decline was found (Morris et al., 2006). Another study found that daily fruit and vegetable consumption was associated with a decreased risk of all cause dementia (28% reduced risk; Barberger-Gareau et al., 2007). Weekly fish consumption was associated with a reduced risk of AD (35% reduced risk) and dementia of any type, but only among APOE ε4 non-carriers (Barberger-Gareau et al., 2007).

The Mediterranean diet was associated with incident AD approximately 4 years later in a sample of 2,258 older adults (Scarmeas et al., 2006). The Mediterranean diet (MeDi) is characterized by a high intake of vegetables, legumes, fruits, cereals, and unsaturated fatty acids; low intake of saturated fatty acids; a moderately high intake of fish; a low-to-moderate intake of dairy products; a low intake of meat and poultry; a regular but moderate intake of ethanol (generally wine during meals). Compared with participants in the lowest tertile, those in the middle MeDi tertile had 15% reduced risk of AD and 40% reduced risk of AD among those in the highest tertile (Scarmeas et al., 2006).

In the Cache County Study, a population-based cohort study with a sample of 5,092 older adults aged 65 and older, Wengreen et al. (2010) found that both higher Dietary Approaches to Stop Hypertension (DASH) and Mediterranean scores were associated with higher 3MS cognitive test scores at baseline and lower decline over 11 years. Participants in the highest quintile of the DASH diet adherence score had 0.92 points higher 3MS cognitive test scores than those in the lowest quintile ($p \le 0.001$). Similarly, participants in the highest quintile of the Mediterranean adherent score had 1.08 higher 3MS scores than those in the lowest quintile ($p \le 0.001$). Participants in the highest quintile of the Mediterranean adherent score had eline, respectively, compared to those in the lowest quintile after 11 years of follow-up.

The magnitude of difference was greater especially for the 4-component score that was based on the adherence to whole grains, low-fat dairy, vegetables, and nuts. Compared to participants in the lowest quintile, those in the highest quintile of the 4-component score showed 1.75 points greater baseline score ($p \le 0.001$) and 1.62 points lower decline over 11 years of follow-up (Wengreen et al., 2010). Although the findings are limited to this study, it suggests that adherence to these types of healthy diets may protect older adults from cognitive decline.

Alcohol Consumption

The findings from studies relating alcohol consumption to rate of cognitive decline or dementia risk are mixed. A meta-analysis based on 23 studies examined the association between alcohol consumption and incident dementia and/or cognitive decline in older adults. The studies included 20 epidemiological cohort and 3 retrospective matched case-control studies based on a cohort, with most studies having longer than 5 years of follow-up. Although studies varied in the definition of optimal alcohol consumption and type, small amounts of alcohol consumption were protective for dementia (37% reduce risk) and AD (43% reduced risk), but not for vascular dementia or cognitive decline (Peters et al., 2008).

Another study that conducted a systematic review including 15 prospective studies with 2 to 8 years of follow-up showed a similar pattern. Compared with nondrinkers, light to moderate drinkers had 25% to 28% reduced risk for any type of dementia. When drinkers and non-drinkers were compared, drinkers had a 34% reduced risk of AD and a 47% reduced risk of any type of dementia, but not for cognitive decline (Anstey et al., 2009).

Ganguli, Vander Bilt, Saxton, Shen, and Dodge (2005) reported that minimal and moderate drinking, compared to no drinking, were associated with less cognitive decline in a representative cohort of 1,277 persons aged 65 and older, over an average of a 7-year follow-up period. In this study, compared to quitters (excluding abstainers), minimal drinking had a 74% reduced risk for average annual decline on MMSE, 84% for learning, 76% for memory, and 66% for naming. Moderate drinking had a 93% reduced risk of average annual decline on MMSE and had a 96% reduced risk on Trailmaking. The effect of heavy drinking could not be examined due to small numbers of participants in this group. When separately analyzed, much of the difference in cognitive decline was explained when current drinkers were compared to quitters, rather than lifelong abstainers. Abstainers were more likely women (86.6% versus 62.8%, p < 0.001) and less likely to have ever smoked (14.5% versus 48.5%, p < 0.001) compared to quitters, but these two groups were not significantly different in age, education, depression, number of prescription drugs, or self-reported history of conditions in which alcohol use might have been medically restricted. The authors explained that quitters might quit because of perceived cognitive difficulties, alternatively, quitting might remove a previous benefit of alcohol thus hastening cognitive decline.

Mehlig et al. (2008) argued that wine, but not other types of alcoholic beverages, is associated with reduced risk for incidence of dementia over 34 years in a sample of 1,462 women. Wine consumption was protective for dementia (44% reduced risk) whereas consumption of liquor increased the risk by 16%. The findings suggested that ingredients other than ethanol might contribute to a beneficial effect of alcohol on dementia risk, such as flavonoids found in products derived from grapes (e.g., grape juice, wine). Flavonoids, as reported in a meta-analysis of randomized controlled trials, are associated with significant improvements in executive function (see Appendix A) and memory, and in some studies, also with increases in general cognition and processing speed (Macready et al., 2009).

Suggested possible mechanisms for the association between low to moderate drinking and less cognitive decline or reduced risk of dementia were through the benefits to cardiovascular and cerebrovascular functioning (Anstey et al., 2009; Ganguli et al., 2005); or through underlying adverse effects of heavy drinking and potential beneficial effects of light to moderate drinking (Ganguli et al., 2005).

Differences in Sample Composition of Published Studies

Studies reviewed on the effects of leisure activities on cognitive function and dementia were population-based longitudinal studies and several studies with large samples of volunteers. The sample size ranged from 469 to 15,080 people, except for one study of religious behavior with a clinic base sample of 70 people (Kaufman et al., 2007). Age of the participants were mostly 65 years old and older at the beginning of the study; two studies had participants 75 years old and older; one study of religious behavior with a clinic base sample from 49 to 94 years old. A study that examined effects of vegetable and fruit consumption on cognitive decline (Kang et al., 2005) and a study that examined effects of alcohol consumption on dementia (Mehlig et

al., 2008) only had female participants. Follow-up years of studies ranged from 2 to 7 years.

Differences in Measurements Used in Published Studies

Measurement of leisure activities varied by study (e.g., number or type of activities). Because leisure activities contain more than one component, some studies categorized them into cognitive (or mental), social, and physical activities whereas some studies divide them into different categories such as productive activities (e.g., Wang, Karp, et al., 2002), or novel- or passive-information processing (Bielak et al., 2007). A study was unique in using mental, social, and physical component scores for each of 29 leisure activities allowing overlap of activities. The component scores were rated by three researchers and 13 older adults who did not participate in the study (Karp et al., 2006). Few studies used a composite score of activities (Scarmeas et al., 2001; Wilson, Bennett, et al., 2002) whereas most other studies used a categorical measure based on frequency of engagement. A study that used both continuous (number of activity per week) and categorical measure (highest tertile versus lowest tertile) found different effect sizes of leisure activities on dementia (7% versus 63% reduced risk; Verghese et al., 2003).

Cognitive function (or cognitive status) is measured with the global cognitive tests such as MMSE and 3MS in many studies. Some studies used measures of distinct dimensions of cognition. For example, a study used cognitive speed that measured a participant's reaction time on stimuli that was based on signals, words, and sentences (i.e., simple- and choice-reaction time, lexical- and semantic-decision; Bielak et al., 2007).
Other studies used various cognitive tests to test abilities such as speed of processing, picture naming, incidental recall, and verbal fluency (Newson & Kemps, 2005); or learning, memory, visuospatial, fluency, Trailmaking, and naming (Ganguli et al., 2005).

Considered Confounders

All studies adjusted for age, gender, and education. Most studies adjusted for comorbidity, functional status, depressive symptoms, and baseline cognitive ability. APOE genotype and family history of dementia were adjusted for in some studies. Adjustment for social network (Wang, Karp, et al., 2002) or depressive symptoms (Karp et al., 2006) in addition to the above key variables marginally changed the association of activities and dementia. One study related education, occupation, and cognitive activities to AD and reported that when cognitive activities were entered into the model in addition to education and occupation, the beneficial effects of these two variables disappeared (Wilson, Bennett, et al., 2002). Social engagement measured by items such as marital status, living arrangement, participation in social, political, or community groups was adjusted for in a study that examined the relationship between religious attendance and cognitive decline (Van Ness & Kasl, 2003).

Use of Latent Class Analysis and Finding Lifestyle Patterns

Latent class analysis (LCA; Goodman, 1974, 2002) has been widely applied in psychiatry in identifying subtypes of disorders (Leoutsakos, Zandi, Bandeen-Roche, & Lyketsos, 2010). In the Cache County Study, LCA was used to classify neuropsychiatric symptoms in individuals with AD (Lyketsos et al., 2001). LCA was used to find patterns of neuropsychiatric symptoms based on informant reports using the Neuropsychiatric Inventory. The three patterns found in this study (i.e., symptoms related with cognition, emotions, and psychosis) could contribute to treatment implications (Lyketsos et al., 2001).

Latent class analysis has also been used to study patterns of health and lifestyle behaviors (de Vries et al., 2008; Ingledew, Hardy, & Cooper, 1995; Laska, Pasch, Lust, Sroty, & Ehlinger, 2009), dietary (Patterson, Dayton, & Graubard, 2002), smoking behaviors (Rose et al., 2007), and alcohol consumption (Smith & Shevlin, 2008). The Dutch SMILE cohort study with a sample of 9,449 people with the mean age of 51.11 years identified three clusters of people: healthy, unhealthy, and poor nutrition typologies, via analysis of five health behaviors: non-smoking, alcohol use, fruit consumption, vegetable consumption, and physical exercise (de Vries et al., 2008). Ingledew et al. (1995) derived two latent classes of health behavior: healthy versus more mixed behaviors based on eating, exercising, alcohol, smoking behaviors using the latent class analysis. Different classes of health risk behaviors between female and male college students were identified (Laska et al., 2009). For example, (1) poor lifestyle, yet low-risk behaviors, (2) high risk, (3) moderate lifestyle, few risk behaviors, and (4) health conscious classes were clustered for females based on diet, physical activity, substance use, sexual behavior, stress, and sleep.

These studies that have successfully employed LCA have demonstrated its merits as an analytic tool that can aid in the identification of distinct lifestyle behavior pattern subgroups, or typologies. Thus, the present study also used this technique, but applied it for the first time to a wider array of lifestyle dimensions, with the objective of identification of typologies that have differential risk for dementia.

Summary

In summary, the findings are sometimes mixed as to what specific type of activity, religious behavior, or food component was a significant predictor of all cause dementia (any type of dementia), or cognitive function. However, there is substantial evidence that lifestyle behaviors considered in the present study: cognitive activities, social interaction, physical activities, religious involvement, diet, and alcohol consumption are associated with cognitive function and/or risk of dementia in older adults. Typically, these studies examined one or more of the various lifestyle behaviors as separate variables. Additionally, there were a small number of studies that identified patterns in lifestyle behaviors. Such patterns, or typologies, aggregate across an array of behaviors and as such, may be useful in examining the kind of lifestyle patterns that are either beneficial or that impose added risk for adverse cognitive health in late life.

Objectives and Hypotheses

The present study investigated cross-sectional relationships between lifestyle behaviors and cognitive function among older adults using extant data from the Cache County Study on Memory Health and Aging (CCSMHA), a large epidemiological study. The present study hypothesized that healthy lifestyle behaviors are associated with higher levels of cognitive status and lower rates of dementia. The list of hypotheses is as follows: *Hypothesis 1*: There are distinct patterns that exist across the six dimensions of lifestyle behaviors defining subgroups such as an active lifestyle, engaged lifestyle, and an unhealthy lifestyle.

Hypothesis 2: Participants in less engaged or less active subgroups of lifestyle behaviors have significantly lower cognitive function test scores compared to participants in more active or more engaged subgroups of lifestyle behaviors.

Hypothesis 3: In terms of discrete clinical endpoints for dementia, participants in less engaged or less active subgroups of lifestyle behaviors have a higher probability of being diagnosed with the "cognitive impairment with no dementia" or "dementia" compared to participants in more active or more engaged subgroups of lifestyle behaviors. (*Alternative Hypothesis for Hypothesis #2 and #3, in the event that Hypothesis #1 is not supported*).

Hypothesis 4: If distinct lifestyle patterns (subgroups) are not identified, each lifestyle behavior is used as a predictor of cognitive function and clinical dementia subgroup, singly rather than combined. Higher level of engagement in each healthy lifestyle behavior is associated with higher cognitive function and lower probability of being diagnosed with the "cognitive impairment with no dementia" or "dementia," compared to participants with lower level of engagement.

CHAPTER III

METHODS

The purpose of this study is to investigate the relationship between lifestyle behaviors and incident dementia among older adults. The present study was based on the extant data from the Cache County Study on Memory Health and Aging (CCSMHA). Descriptions of study design, subjects, measurement, and analysis plan are provided in this section.

Study Design

The Cache County Study on Memory Health and Aging (CCSMHA) is a longitudinal, population-based epidemiological study focused on Alzheimer's disease and other forms of dementia. Five thousand and ninety-two participants were enrolled in the study among 5,677 eligible Cache County residents in Utah who were 65 years or older as of January 1, 1995 (Breitner et al., 1999). A baseline interview was conducted between 1995 and 1996 and three follow-up interviews ("waves") were conducted in three to four year intervals over a period of 10 years. At each of these four waves, a multi-stage dementia ascertainment protocol was employed to identify prevalent (first wave) and incident (Wave 2-4) cases of dementia. Lifetime exposures of a wide array of health-related variables were measured at baseline, and interval exposures were measured at each incidence wave.

Subjects

The original sampling frame for the CCSMHA was a Health Care Financing Administration list of Medicare beneficiaries who were aged 65 and older on January 1, 1995 and permanent residents of Cache County, Utah. The baseline sample included 5,092 participants reflecting a 90% participation rate, reducing non-responder bias (Norton, Breitner, Welsh, & Wyse, 1994). Because it was not until the study's third wave that the interview protocol was expanded to include a broad array of lifestyle behaviors, the present study began with measurement of the exposure variables at Wave 3, then examined their cross-sectional effect on cognitive status and the rate of dementia in Wave 3. Appendix B displays the progression of subjects from the baseline interview through the three study waves.

The sample considered here consists of 1,216 participants who completed Wave 3 screening interview and clinical assessment (CA). The sample included participants who had a positive cognitive screening result (n = 547), or were part of a designated subsample (n = 664), a panel of participants who were randomly selected by age, gender, and APOE genotype regardless of their prior results on cognitive screening (Breitner et al., 1999). Appendix C provides a detailed explanation of how and why the designated subsample was selected. Appendix D provides a comparison of the designated subsample (who were more representative of the full surviving cohort than the cognitive screen positive participants) and the individuals who completed the screening visit but who were not selected for the CA. The purpose of these comparisons is to demonstrate

the extent of generalizability of the final sample of Wave 3 CA participants used in the present study.

Procedures

At each study wave, participants were interviewed by a trained interviewer using a structured interview format. Interviewers received ongoing training during the period of fieldwork and their quality of interview was scrutinized by field supervisor review of a randomly chosen 10% of the audio recorded interviews. Interview books were also checked by quality assurance monitors and the interviewers were requested to correct all errors and clarify ambiguities.

First, a letter of introduction with the administrator's signature of the Health Care Financing Administration was mailed to the participants. The letter explained the legitimacy of the study and that the participation in the study would have no effect on their Medicare benefits. This was followed by the study's own introductory letter presenting the details associated with the study and an upcoming visit from an interviewer. The interviewer visited the participant 1 to 4 weeks later. For those agreeing to participate, an informed consent was obtained prior to conducting the interview. Following the informed consent procedure, the interviewer administered a brief cognitive test, an interview designed to assess risk factors related to depression and dementia, and collected buccal scrapings (see Appendix A) for APOE genotyping. The three follow-up interviews were similar in their procedures with the exception that buccal DNA samples were not collected. Participants screening positive for possible dementia were selected, along with a panel of "designated subsample" (see Appendix C) for clinical evaluation, from which dementia diagnoses were rendered. In addition to the baseline interview, a mail-in questionnaire containing psychosocial factors (e.g., social support and religious behavior) was given to the participants in Wave 2-4 (this occurred at the CA in Wave 3; Breitner et al., 1999; Franklin, 2005).

All procedures of the CCSMHA were approved by the Institutional Review Boards of the Duke University Medical Center, the Johns Hopkins University School of Public Health, and Utah State University, and written informed consent was obtained at each interview.

Measurement

Lifestyle behavior patterns were derived using data from the Wave 3 screening interview and the clinical assessment. By study design, participants who scored below 91 (out of 100) points on the education and sensory/motor-adjusted 3MS test or who were rated greater than 3.27 on the Informant Questionnaire for Cognitive Decline in the Elderly (IQCODE, Jorm & Jacomb, 1989) were considered to be "screen positive" for possible dementia. These individuals, along with a panel of designated subsample, and all persons aged 85 years or older, were selected for the clinical assessment for further examination (Breitner et al., 1999). Dementia ascertainment and measurement of the six lifestyle behavior domains to be examined were operationalized as follows.

Dementia Ascertainment

Cognitive screening. Participants received cognitive screening using a revision of 3MS, modified for application in epidemiologic studies (Tschanz et al., 2002). The

3MS is a screening test for dementia which assesses orientation, attention, memory, language, praxis, and the ability to follow simple commands (Teng & Chui, 1987). Scores range from 0 to 100 and higher scores indicate better performance. Test-retest reliability of 0.78 over 3 years and internal consistency 0.91 were reported (Bassuk & Murphy, 2003). The 3MS used in this study is the modified version in which recall of personal demographic information was modified to the recall of current and past prominent politicians because of the difficulty of verifying the reported personal demographics. Other minor changes included shortening the time allotted for the verbal fluency item. Good sensitivity was demonstrated for detecting dementia in the Utah population (Tschanz et al., 2002). The 3MS score was adjusted for the participant's sensory deficits so that participants who had sensory difficulties could have equal mean scores (Breitner et al., 1999).

Proxy screening. The IQCODE was administered for participants who could not complete 3MS; those with 3MS score below 60; those who scored below 15 out of 20 orientation questions early in the interview; and those whose information was judged as not reliable. The IQCODE scores ranged from 0 (no impairment) to 5 (extreme impairment; Breitner et al., 1999).

Clinical assessment. Participants who scored lower than 91 out of 100 points on the 3MS or higher than 3.27 on the IQCODE, or those who were 85 years or older were recommended to undergo clinical assessment (CA) along with designated subsample. The CA was conducted by a research nurse and psychometrician at the participant's residence. The nurse recorded a narrative history of cognitive symptoms, a medical history, and current medications. The nurse then conducted a standardized blood pressure measurement and a standardized neurologic examination on the participant using a brief protocol (Breitner et al., 1995). The nurse also interviewed the informant using the Neuropsychiatric Inventory (Cummings et al., 1994) and the Dementia Severity Rating Scale (Clark & Exbank, 1996) to assess the participant's cognitive and functional impairment. The psychometrician administered a 1-hour battery of neuropsychological tests. A brief examination of mental status, insight, hand praxis, and gait was recorded in a 7-minute videotape segment (Breitner et al., 1999).

Initial diagnostic conferences. The CA results were reviewed at initial diagnostic conferences that included a neuropsychologist, a board-certified geriatric psychiatrist, the examining nurse, and technician. Dementia was diagnosed using the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R; American Psychiatric Association, 1987) and other forms of dementia such as Alzheimer's disease (AD) and vascular dementia (VaD) were also diagnosed in these conferences. Participants were assigned into one of the seven categories as follows: probable AD, possible AD, dementia of unknown etiology, demented-not AD, mild/ambiguous, or other (Breitner et al., 1999).

Follow-up laboratory testing and neuroimaging. Participants whose initial classification was probable AD, dementia of unknown etiology, or non-AD dementia were requested to receive follow-up laboratory testing and neuroimaging. Tests included complete blood count, routine chemistries (CHEM-20), serumB₁₂, folate, thyroid function tests, and urinalysis, and standardized brain MRIs or CTs (Breitner et al., 1999).

Physician examinations. Five physicians visited and examined the demented participants at their residence. These physicians who were blind to the results of the

nurse's neurologic examinations and the initial working diagnoses repeated the neurologic examination and tested participants with the 3MS. They also reviewed the clinical history and the Neuropsychiatric Inventory with the informants (Breitner et al., 1999).

Final clinical diagnoses. Final clinical diagnoses were made at consensus conferences after reviewing all information. The conferees (six to eight members) included two neuropsychologists, two to three geriatric psychiatrists, a neuroscientist, and a neurologist. Along with dementia diagnoses, a diagnosis of "prodromal AD" was made for individuals with VaD or other cognitive disorders including individuals with progressive mild/ambiguous cognitive syndromes (Breitner et al., 1999). Dementia cases for the present study came from those so diagnosed in Wave 3 as well as those who completed Wave 3 CA (18-month follow-up). The follow-up CA was designed to confirm diagnoses from the initial clinical evaluation over time. Dementia diagnosis was categorized into three levels for the present study: Non-case, cognitive impairment with no dementia, and dementia.

Lifestyle Behaviors

Cognitive activities. Engagement in cognitively stimulating activities was measured with the 11-item activity questionnaire including reading the newspaper, talking about issues, playing cards or games, balancing a checkbook, doing crossword puzzles, taking courses or classes, reading books, writing a journal, drawing or painting, looking at art, and going to plays or concerts (see Appendix E). These activities were selected because some of them were thought to be related to *novel information* processing (Bielak et al., 2007; Carlson et al., 2008; Hultsch, Hertzog, Small, & Dixon, 1999) or that most of them were rated as having high *mental components* compared to social or physical components (Karp et al., 2006). Karp et al. reported high inter-rater consistency of .90 (Cronbach's α) for grading of three components of mental, social, and physical components in 29 activities (includes 9 activities used in this measure). Cronbach's α for mental component was .89. The three components were highly correlated, particularly for the correlation between mental and social components (Pearson's r = .76; Karp et al., 2006).

Participants were asked to report the frequency of the activity on a 6-point scale (from 1 = never or less than once a month to 6 = everyday). The scores of the 11 items were summed up to create composite score ranging from 11 to 66. As dichotomous variables were used in LCA to create a dichotomous variable indicating "high" versus "low to moderate" cognitive activity group, the total score was split into upper tertile versus lower two tertiles.

Social interaction. Social interaction was measured with the 4-item self-report questionnaire asking the frequency of social contact and time spent in social settings such as volunteering, clubs, or other organizations. Three items were extracted from the Social Interaction Subscale in the Duke Social Support Index (DSSI; Koenig et al., 1993) and an item concerning volunteer work was included. The wordings of the questions included: How often do you attend meetings of social clubs, groups, or organizations such as bridge clubs, book clubs, hospital, volunteer, gardening clubs, Rotary club, Kiwanis, VFW, and so forth; How often do you talk on the telephone with family, friends, or neighbors; How often do you get together with family, friends, or neighbors; How often in the past year have you spent time doing volunteer work (see Appendix E). The frequency of participation was rated on a 6-point Likert scale with responses: Never or less than once a month, once a month, two to three times a month, once a week, a few times a week, and every day.

The scores of the four items were summed to create a composite score ranging from 4-24. To create a dichotomous variable indicating "high" versus "low to moderate" social interaction, the total score was split into upper tertile versus lower two tertiles.

Physical activities. Physical activities were measured with a questionnaire asking about the following activities in the past 12 months: walking for exercise, heavy housework, garden or yard work, using an exercise machine, calisthenics or lifting weights, and moderate to vigorous exercise. Participants were asked the frequency of each activity and average hours or minutes spent each time on an activity (see Appendix E).

These activities had a mixture of low, moderate, and heavy intensity but mostly represented moderate to heavy intensity when compared to the measures of other studies (Mazzeo & Tanaka, 2001; Stewart et al., 2001). It was not appropriate to apply standard measures such as a metabolic equivalent value (MET, Ainsworth et al., 1993; Stewart et al., 2001) because different intensity of activities was combined in one item. Instead, total hours spent per week doing above activities were calculated. Wilson et al. (2002) reported using the measure of weekly hours produced similar results as compared to the measure of energy expenditure in examining the association between physical activities and AD.

Physical activity score was dichotomized into "high" versus "low to moderate" activity by recoding the total hours spent per week doing above activities into upper tertile versus lower two tertiles. This made the cut point of "7 hours or more per week" versus "less than 7 hours per week" spent on physical activities.

Religious involvement. Religious involvement was measured with a modified form of the Religious Background and Behavior (RBB) questionnaire (Connors, Tonigan, & Miller, 1996). The original RBB includes 13 items. The first item asks to indicate the descriptor of the participant among atheist, agnostic, unsure, spiritual, and religious. The next six items ask the frequency of engaging in the following behaviors during the past year on an 8-point Likert scale: thought about God, prayed, meditated, attended worship services, read/studied scriptures/holy writings, and had direct experiences of God. The last six items ask the frequency of participation in these six domains in lifetime. High test-retest reliability of .94, internal consistency of .60, and convergent validity of .50 between RBB and religious attendance were established (Connors et al., 1996).

The RBB questionnaire used in the present study consisted of an initial item: the participant's religious belief on the spectrum (1-5) of atheist, unsure, and religious. The other six items (i.e., participation in thinking of God, praying, meditating, attending worship service, reading scripture/holy writings, and having direct experiences with God) were measured on a 5-Likert scale with responses: never, less than once a month, once or twice a month, once a week, or more than once a week (see Appendix E). Religious involvement was computed as the sum of the raw scores of the items (ranging from 7-35), and then dichotomized into "high" versus "low to moderate" via a split into upper two

tertiles versus lower tertile. This made the cut point of "once a week or more often" versus "once or twice a month or less often."

Diet. Diet was measured by using a 142-item food frequency questionnaire (FFQ) which was validated and applied in several previous studies (Munger, Folsom, Kushi, Kaye, & Sellers, 1992; Willett et al., 1985, 1988). Validity studies for food frequency commonly use the approach to examining the concordance of food frequency responses and multiple food records over a period as a measure of "usual diet" (Thompson & Byers, 1994). Correlations in the range of .40 to .70 have been reported between food frequency questionnaires and food records (Thompson & Byers, 1994). The reproducibility (reliability) ranging from .50 to .70 has been reported for food frequency questionnaires over periods of 1 to 10 years (Willett, 1998).

Participants were asked how often they consumed a variety of food listed during the past year on a 9-point scale ranging from 1 = never or less than once a month to 9 = more than six times per day. The Dietary Approaches to Stop Hypertension (DASH) diet score was obtained by assigning scores to eight food/nutrient components. The eight components included a high intake of fruits, vegetables, low-fat dairy products, nuts and legumes, and whole grains; and a low intake of sodium, sweets and sweetened beverages, and red and processed meat (Wengreen et al., 2010).

The DASH diet is recommended as a balanced eating pattern within energy needs in the current Dietary Guidelines for Americans (United States Department of Health & Human Services, 2005). The food components represent food groups targeted in the DASH diet (Vogt et al., 1999). Quintile cut-offs were used to assign participants a food component score ranging from 1 to 5. A score of 5 was given to those in the highest quintile and a score of 1 was given to those in the lowest quintile. Sweets and sweetened beverages, sodium, and red and processed meat were reverse scored. The quintiles were dichotomized into "healthy diet" for the top two quintiles and "less healthy diet" for the bottom three quintiles.

Alcohol consumption. Alcohol consumption was measured on the items included in the FFQ asking the type of alcohol (regular/light beer, red/white wine, or liquor) by serving frequency on a 9-point scale, ranging from 1 = never, or less than once a month to 9 = more than six times per day. One serving of beer was equivalent to 12 oz (12.8g of alcohol), one serving of wine was equivalent to 4 oz (11g of alcohol), and one liquor serving was equivalent 1.5 oz (14 g of alcohol). Based on the literature that low to moderate alcohol consumption is protective against cognitive decline or dementia (Anstey et al., 2009; Ganguli et al., 2005; Peters et al., 2008), participants were assigned into "low to moderate drinkers," if they consumed 1g to 30g a day, and "non-drinkers or heavy drinkers," if they consumed never or less than 1g per month or more than 30g a day. The non-drinkers and the heavy drinkers were combined together because only 0.2% (n = 2) of in the sample consumed more than 30g a day and low to moderate drinking is found to be protective against dementia based on the findings in the literature.

Covariates

Age, gender, education, APOE genotype, functional status, and comorbidity were examined as covariates. These variables are known to be significant predictors of incident dementia and which are almost universally adjusted for when dementia studies report effects of any given risk or protective factor. Age at wave 3 and years of education

were used as measures of age and education. APOE genotype was divided into APOE E4 carrier versus ɛ4 non-carrier. A participant was APOE ɛ4 carrier if the person had APOE allele combinations of $\varepsilon 2/\varepsilon 4$, $\varepsilon 3/\varepsilon 4$, and $\varepsilon 4/\varepsilon 4$, and APOE $\varepsilon 4$ non-carrier if the person had APOE allele combinations of $\varepsilon 2/\varepsilon 2$, $\varepsilon 2/\varepsilon 3$, and $\varepsilon 3/\varepsilon 3$. Comorbidity was operationalized as presence versus absence of any of the following medical conditions: hypertension, hypercholesterolemia, coronary bypass surgery, heart attack, coronary angioplasty, diabetes, Parkinson disease, stroke, severe head injury, and cancer. Functional status was measured by the 7-item Instrumental Activities of Daily Living (IADL; Fillenbaum, 1985). The question concerning "getting to places out of walking distance" was replaced with "traveling." Participants were asked if they need help doing the following activities: Traveling, shopping, preparing meals, using the telephone, doing housework, taking medicine, and handling money on a 3-point scale $(1 = \text{without help}, 2 = \text{with some help}, 1 = \text{with some help}, 2 = \text{with some hel$ 3 = unable to do without help). A continuous score was created combining the number of activities that the participant was able to do without any help which ranged from 0 to 7. The IADL score was reverse coded so a higher score indicated higher functional dependence.

Data Analysis

As the first step of analysis descriptive statistics on all studied variables are provided, including possible and actual range of points on all lifestyle behavior domain score, frequencies, and proportion into "high" versus "low to moderate" categories. Attrition analysis was conducted to test any significant differences on demographics and health factors between respondents and non-respondents of religious involvement because this variable had the lowest response rate (55.3%) due to using a mail-in questionnaire. One-way analysis of variance (ANOVA) was conducted to examine significant differences in mean level of age, education, and functional status between the latent classes. Tukey HSD post hoc paired comparisons were conducted to evaluate pairwise differences among the means with alpha at .05. A chi-square test was conducted to examine significant differences in frequencies of gender, APOE genotype, and comorbidity between latent classes.

To test Hypothesis #1, the six lifestyle variables were subjected to latent class analysis (LCA) to examine the structure underlying lifestyle behaviors in older adults. In LCA, the observed lifestyle variables are considered to be indicators of an unobserved variable (latent variable). The main assumption of the model is that the observed lifestyle variables are mutually independent within a latent class and the association between the observed variables is explained by the latent classes or the underlying lifestyle patterns (local independence; Goodman, 2002).

Usage of dichotomous input variables is more common for LCA than multinomial variables (Francis, 2008; Goodman, 2002). Two sets of probabilities were estimated for the unknown parameters of the underlying class structure: the probability of the individual belonging to each class and the probability of responding on" high" versus "low to moderate" engagement in a lifestyle behavior within the class (Magidson & Vermunt, 2004).

The optimal number of latent classes was selected taking into account balance between parsimony (smaller number of classes), model fit, and interpretability of the underlying lifestyle patterns (Chung, Flaherty, & Schafer, 2006). The likelihood-ratio chi-squared statistic (G^2) was used as a measure of model fit. Larger values indicate poorer model fit for the data. In addition to the likelihood-ratio chi-squared statistic (G^2), global goodness of fit measures of the Bayesian information criterion (BIC) and the Akaike information criterion (AIC) was used. These measures combine goodness of fit and parsimony by penalizing for sample size and model complexity (number of parameters). A model with lower values of BIC and AIC indicate better parsimony and model fit (Magidson & Vermunt, 2004). Pairwise deletion of missing cases was conducted in all analyses. Using pairwise deletion drops the respondent only on the variables that have missing values whereas listwise deletion excludes the entire record of the respondent if any single value is missing. Pairwise deletion maximally uses all available data and allows retaining 1,216 participants in LCA, but a weakness is that the contribution of religious involvement is coming from only 55.3% of the sample who returned the religious behavior questionnaire. LCA was conducted using SAS PROC LCA (Lanza, Collins, Lemmon, & Schafer, 2007).

To test Hypothesis #2, the best fitting model based on three latent classes was used to derive lifestyle patterns, placing individuals into classes by their highest membership probability. Assigned latent class from this model was then used as the key independent variable in a one-way ANOVA to predict 3MS cognitive test score in Wave 3 before and after adjustment for functional status, education, age, and APOE genotype.

To test Hypothesis #3, latent class membership was cross-tabulated with cognitive group (non-case, CIND, dementia) with a chi-square statistic computed to determine the degree of association between these two variables.

Hypothesis #4 was not tested because distinct lifestyle patterns were identified during LCA procedures.

CHAPTER IV

RESULTS

The present chapter provides results from all data analyses. First, descriptive statistics of the sample on all studied variables are provided. Second, results from latent class analysis (LCA) are provided to reveal presence of distinct subpopulations of individuals exhibiting different behavioral patterns. Third, the results are presented that provided a demographic comparison of the various LCA subgroups ("latent classes") using one-way ANOVA to compare mean age, education, and functional status between subgroups, and using chi-square tests to examine association between subgroups and categorical variables of gender, APOE genotype, and presence/absence of comorbid medical conditions. Finally, results of cross-sectional analyses comparing subgroups with cognitive outcomes are presented.

Descriptive Statistics

Table G1 (see Appendix G) presents descriptive statistics of the sample on demographics, lifestyle behavior variables, and other important variables. In the sample of 1,216 participants 45% were male (n = 547). Mean age at Wave 3 clinical assessment was 82.5 years old (SD = 5.52) and mean education was 13.64 years (SD = 2.94). APOE ϵ 4 carriers were 34.6% of the sample (n = 418). 64.1% (n = 780) of participants had at least one or more of the following medical conditions: hypertension, hypercholesterolemia, coronary bypass surgery, heart attack, coronary angioplasty, diabetes, Parkinson disease, stroke, severe head injury, and cancer. There was 5.5% of

the participants (n = 64) who consumed moderate amount of alcohol, 0.2% (n = 2) who were in heavy drinking level (> 30g/day, not presented) and 94.3% of the participants (n= 1,093) who consumed none or minimal amount of alcohol (< 1g/day, not presented). On average, people were involved in religious behaviors once a week. Bivariate correlations between lifestyle behaviors and covariates of age, gender, education, APOE genotype, IADL, and comorbidity ranged from .08 to .39 (Pearson's r, p < 0.5, see Appendix H).

Attrition Analysis

The lowest response rate was shown in religious involvement (55.3%) which was an additional mail-in questionnaire in the Wave 3 clinical assessment. It had 672 respondents and 544 non-respondents. Attrition analysis was conducted to examine any differences between these two groups (Table I1 and Table I2 in Appendix I). Respondents and non-respondents were statistically significantly different on gender, functional status, age, education, and 3MS cognitive test score. On average, nonrespondents were more likely to be female (61.2% versus 50%), to have higher functional dependence (M = 1.32, SD = 2.06; M = 0.94, SD = 1.78), and were approximately 2 years older (M = 83.60, SD = 5.54; M = 81.68, SD = 5.35), had 10 months less education (M = 13.20, SD = 2.82; M = 14.00, SD = 2.98), and scored 3 points lower on 3MS cognitive test (M = 86.44, SD = 9.72; M = 89.48, SD = 9.00). Among variables showing statistically significant differences, the magnitude of differences on gender, functional status, and cognitive test score were of a magnitude deemed to also be of practical significance. There were no significant differences on APOE genotype, comorbidity, depressive symptoms, or Body Mass Index.

Proportions of Proxy Report in Measures of Lifestyle Behaviors

Measures of lifestyle behaviors obtained through in-person interviews in Wave 3 (i.e., 4 item-cognitive activities, physical activities, diet, and alcohol consumption) had 0.3% to 4.7% of proxy report. A mail-in questionnaire in CA (i.e., 7-item cognitive activities, social interaction, and religious involvement) had 21.2% to 21.6% of proxy report (see Appendix F).

Presence of Distinct Latent Classes of Behaviors: Hypothesis 1

LCA of lifestyle behaviors was conducted with each variable dichotomized as described in Chapter 3 with the sample size of 1,216. The appropriate number of classes was determined considering balance between parsimony, model fit, and interpretability (Chung et al., 2006). Table 1 presents fit statistics for latent class models with 2, 3, and 4 classes. The 3-class solution had the lower AIC and BIC indicating good parsimony and model fit. The 2-class solution had slightly lower BIC but the likelihood ratio chi-square (G^2) was larger indicating poorer model fit. Increasing the number of classes to 4 increased both AIC and BIC indicating worse model fit. Considering interpretability, in the 2-class solution, conditional probabilities of behaviors for a given latent class were much closer between classes for some indicator variables making assignment of individuals to latent classes more uncertain. Thus, the model based on three classes was

Table 1

Number of	Degrees of				
classes	Log-likelihood	G^2	freedom	AIC	BIC
2	-3163.14	81.51	50	107.51	173.85
3	-3142.79	40.80	43	80.80	182.86
4	-3138.83	32.88	36	86.88	224.67

Fit Statistics of Latent Class Models

Note. *N* = 1,216.

selected for the best model fit that is parsimonious and had more straightforward interpretability.

In order to investigate the quality of classification, the means of posterior probabilities were calculated to see whether the likelihood of the average person belonging to a latent class is substantially high compared to the likelihood of the person belonging to the other latent classes. The mean of the highest posterior probability was .78 (SD = .15) whereas the mean of the second highest posterior probability was .22 (SD = .15) and the mean of the lowest posterior probability was .002 (SD = .015). The means of posterior probabilities showed that the average person is likely to be in the class with nearly 4 times higher probability compared with the likelihood of being in other classes. There was more than 50% of the sample whose top classification probability was 75% higher than the lowest classification probability.

Table 2 shows proportion of the sample in each class and probabilities of exhibiting the given lifestyle behavior, within each class, also depicted graphically in



Figure 2. Conditional probabilities for each of six lifestyle behaviors in each of three latent classes. (N = 1,216).

Figure 2. The results of LCA supported Hypothesis 1 that there are distinct patterns across the six dimensions of lifestyle behaviors.

The three classes were labeled according to the pattern of lifestyle behaviors, combined across all indicators. Participants in the "least engaged" class, which comprised 50% of the sample, were unlikely (< 28%) to report most behaviors, with the exception of religious involvement at moderate likelihood (42%). Participants in the "moderately engaged secular" class consisted of 4% of the sample. This group of people were very likely to report moderate alcohol consumption (99%), very unlikely to report religious involvement (4%), and moderately likely to report all other behaviors (18% - 45%). The "most engaged religious" class accounted 46% of the sample. Participants in this group showed very high religious engagement (93%), moderate to high engagement in all other lifestyle behaviors, except no alcohol consumption.

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Table 2

	Least engaged $(n = 671)$	Moderately engaged secular $(n = 59)$	Most engaged religious $(n = 486)$
Lifestyle behavior	ρ estimates (probability of having high level of the lifestyle behavior)	ρ estimates (probability of having high level of the lifestyle behavior)	ρ estimates (probability of having high level of the lifestyle behavior)
γ estimates (proportion of sample in the class)	.50	.04	.46
Cognitive activities	.06	.28	.44
Social interaction	.07	.18	.51
Physical activities	.25	.42	.39
Religious involvement	.42	.04	.93
Diet	.28	.45	.50
Alcohol consumption	.01	.99	.00

Latent Class Analyses of Lifestyle Behaviors

Note. G^2 (43, N = 1,216) = 40.80, p < .05.

Demographic Comparison of Three Latent Classes

Age, Education, and Functional Status

One-way ANOVA were conducted to test for significant differences in mean level of age, education, and functional status between the three classes. As shown in Table J1 least engaged class (M = 82.94, SD = 5.95) was significantly older than most engaged religious class (M = 82.06, SD = 4.93), F(2, 1,213) = 3.96, p = .02, $\eta^2 = .006$. However, the mean age difference was not practically significant. Mean age differences between least engaged class and moderately engaged secular class, and between moderately

engaged secular class (M = 81.97, SD = 4.76) and most engaged religious class were not significant. The Eta-squared shows that latent class does not explain age differences. The age differences between latent classes were not substantially different (Cohen's d0.02-0.18).

In terms of differences between latent classes on educational attainment, moderately engaged secular class had highest education (M = 15.49, SD = 2.92) followed by most engaged religious class (M = 14.03, SD = 2.88) then least engaged class (M =13.20, SD = 2.88). All mean education differences were statistically significant, F(2,1,212) = 24.58, p < .001, $\eta^2 = .039$. The Eta-squared shows that latent class account for small proportion of variance in education. The differences were substantial between the three classes (Cohen's d 0.50-0.79), especially, between least engaged class and moderately engaged secular class (Cohen's d = 0.79).

The least engaged class had significantly higher functional dependence (M = 1.50, SD = 2.21) than the other two classes: moderately engaged secular class (M = 0.25, SD = 0.96); most engaged religious class (M = 0.67, SD = 1.37), F(2, 1,207) = 34.69, p < .001, $\eta^2 = .054$. The Eta-square indicates that latent class accounted for a moderate proportion of variance in functional status. The differences were practically significant: Cohen's d = 0.73 for least engaged class and moderately engaged secular class; Cohen's d = 0.45 for least engaged class and most engaged religious class. There was no significant functional difference between moderately engaged secular class and most engaged religious class.

Gender, APOE Genotype, and Comorbidity

As can be seen by the frequencies and proportions cross tabulated in Table J2, the latent classes showed different gender distribution, χ^2 (2, N = 1,216) = 8.43, p = .015, Cramér's V = .083. There were 55% female participants in least engaged class, compared to 37.3% in moderately engaged secular class and 57.2% in most engaged religious class. Cramér's V indicates a small relationship between latent class and gender. Practical significance implications are that males are much more likely to belong to moderately engaged secular class than are females.

The latent classes had different rate of APOE genotype: χ^2 (2, *N* = 1,209) = 6.63, *p* = .036, Cramér's *V* = .074. The least engaged class had 37.7% of participants who carried APOE ε 4 allele, compared to 32.2% in moderately engaged secular class and 30.5% in most engaged religious class. Cramér's *V* indicates a small relationship between latent class and APOE genotype. Practical significance implications are that individuals who do not carry APOE ε 4 allele are more likely to belong to most engaged religious class than are individuals who do carry APOE ε 4 allele.

Interestingly, although there were differences in functional status between the three latent classes, there were no differences in presence of at least one comorbid medical condition: $\chi^2(2, N = 1,216) = 0.10, p = .949$, Cramér's V = 0.009.

Latent Class and Cognitive Status: Hypothesis 2

One-way ANOVA was conducted to test for significant differences in mean levels of cognitive function (3MS cognitive test score) on the three latent classes, with and without adjustment for functional status, education, age, and APOE genotype. The means and 95% CIs for 3MS cognitive test score as a function of class membership are shown in Table 3. There was a statistically significant effect of class membership on cognitive function at the p < .001 level for the three latent classes, F(2, 1, 188) = 41.43, p < .001, $\eta^2 = .07$. The Eta-squared indicates a moderate relationship between latent class and cognitive function. The difference remained significant after separate adjustment for functional status, education, age, and APOE genotype, and after simultaneous adjustment for all four covariates.

Tukey HSD post hoc test was conducted to evaluate pairwise differences among the unadjusted mean 3MS cognitive test score with alpha at .05. The mean score for least engaged class (M = 85.93, SD = 10.57) was significantly lower than the mean score for moderately engaged secular (M = 91.08, SD = 6.09) and most engaged religious (M =90.73, SD = 7.15). The differences between least engaged class and moderately engaged secular class (Cohen's d = 0.59), and least engaged class and most engaged religious class (Cohen's d = 0.53) were practically significant. There was no significant difference in mean score between moderately engaged secular and most engaged religious. After adjustment for the four covariates (i.e., functional status, education, age, and APOE genotype), the mean differences were significant only between least engaged class and most engaged religious class, F(2, 1, 184) = 14.77, p < .001, $\eta^2 = .02$. The results supported Hypothesis 2 that participants in less engaged class of lifestyle behaviors have lower cognitive test scores compared to participants in more engaged classes of lifestyle behaviors.

Table 3

		Latent classes			
		Moderately	Most engaged		
	Least engaged	engaged secular	religious		
Condition	<i>n</i> = 671	<i>n</i> = 59	<i>n</i> = 486	F	η^2
Unadjusted	85.93 _a	91.08 _b	90.73 _b	41.43***	.07
	[85.11, 86.74]	[89.50, 92.67]	[90.09, 91.36]		
Adjusted for	86.75 _a	89.19 _b	89.86 _b	20.46***	.03
functional	[86.12, 87.37]	[87.13, 91.26]	[89.14, 90.56]		
status					
Adjusted for	86.36 _a	89.60 _b	90.42 _b	29.87***	.05
education	[85.68, 87.04]	[87.34, 91.85]	[89.64, 91.20]		
Adjusted for	86.06 _a	90.90 _b	90.57 _b	38.14***	.06
age	[85.37, 86.75]	[88.61, 93.18]	[89.77, 91.37]		
Adjusted for	85.97 _a	91.09 _b	90.73 _b	40.36***	
APOE	[85.27, 86.68]	[88.76, 93.42]	[89.91, 91.54]		.06
genotype					
Adjusted for	87.08 _a	88.25 _{ab}	89.70 _b	14.77***	
all 4	[86.47, 87.69]	[86.23, 90.26]	[88.99, 90.40]		.02
covariates					

3MS Sensory Adjusted Cognitive Test Score by Latent Class

Note. N = 1,216. Numbers in brackets are 95% confidence intervals of the means. Means with differing subscripts within rows are significantly different at p < .05 in the Tukey honestly significant difference comparisons. ***p < .001.

Latent Class and Dementia: Hypothesis 3

A chi-square test was conducted relating latent classes to dementia diagnoses: non-case, CIND, and dementia in Wave 3 (see Table 4). There were differences in dementia diagnoses between classes, χ^2 (4, n = 1,211) = 65.20, p < .001, Cramér's V = .23. There were 23.5% of participants diagnosed with dementia in least engaged class, compared to 9.9% in most engaged religious and 5.2% in moderately engaged secular class. There were 40.1% of participants with cognitive impairment in least engaged class, compared to 34.9% in most engaged religious class and 30.5% in moderately engaged secular class. Cramér's *V* indicates a medium to large relationship between latent class and dementia diagnoses. Practical significance implications are that individuals diagnosed with dementia or cognitive impairment are much more likely to belong to the least engaged class than are non-cases. The results supported Hypothesis 3 that participants in less engaged class have a higher probability of being diagnosed with the CIND or dementia compared to participants in more engaged classes of lifestyle behaviors.

Summary

A best fitting model based on three latent classes was selected in LCA. Primary findings were that latent class was associated with cognitive function and being diagnosed with dementia or CIND in Wave 3. The association between latent class and cognitive function remained significant even after controlling for functional status, education, and age. Practically, differences were found between least engaged class and

Table 4

	Cognitive group			χ^2
Latent class	Non-case $n = 548$	$\frac{\text{CIND}}{n - 455}$	Dementia n = 208	df p-value Cramár's V
Least engaged	n = 348 n = 243	n = 455 n = 268	n = 208 n = 157	$\frac{\chi^2 = 65.20}{\chi^2 = 65.20}$
	(36.4)	(40.1)	(23.5)	df = 4 p < .001
Moderately	<i>n</i> = 38	<i>n</i> = 18	<i>n</i> = 3	V = .23
engaged secular	(64.4)	(30.5)	(5.1)	
Most engaged	<i>n</i> = 267	<i>n</i> = 169	<i>n</i> = 48	
religious	(55.2)	(34.9)	(9.9)	

Crosstabulation of Wave 3 Cognitive Group by Latent Class

Note. N = 1,216. Percentages appear in parentheses below group frequencies. CIND = cognitive impairment with no dementia.

moderately engaged secular class, and between least engaged class and most engaged religious class.

There were differences between latent class on age, gender, education, and APOE genotype. The differences were practical except for age. Bigger differences were found between least engaged class and moderately engaged secular class, or between least engaged class and most engaged religious class. No effect of latent class was found in the presence of at least one comorbid medical condition.

CHAPTER V DISCUSSION

Overview

The purpose of this study was to examine associations between lifestyle behaviors, especially, underlying lifestyle patterns across several behaviors, and late-life cognitive status. Six lifestyle behaviors: cognitive activities, social interaction, physical activities, religious involvement, diet, and alcohol consumption were considered.

The present study proposed three hypotheses as follows: (1) There are distinct patterns that exist across the six dimensions of lifestyle behaviors defining subgroups such as an active lifestyle, healthy lifestyle, and an unhealthy lifestyle, (2) Participants in less engaged subgroups of lifestyle behaviors have lower cognitive function test scores compared to participants in more engaged subgroups of lifestyle behaviors, and (3) Participants in less engaged or less active subgroups of lifestyle behaviors have a higher probability of being diagnosed with CIND or dementia compared to participants in more active or more engaged subgroups of lifestyle behaviors.

This section provides interpretation of the results for each hypothesis, theoretical interpretation, conclusions, limitations, and directions for future studies.

Lifestyle Patterns

The first hypothesis that tested existence of distinct patterns across the six dimensions of lifestyle behaviors was supported by the data. The LCA identified the best fitting model as one based on three classes, assigning each individual into one of the three latent classes by his/her lifestyle profile. The latent classes were labeled as the "least engaged," the "moderately engaged secular," and the "most engaged religious." Participants in the most engaged religious class were highly involved in religious behaviors and had the healthiest lifestyle among the three classes, as defined in this study, except that they did not consume any alcohol. Participants in the moderately engaged secular class were least likely to be involved in religious behaviors, had moderately healthy lifestyles, and consumed moderate amount of alcohol. Participants in the least engaged class were moderately involved in religious behaviors, had the least healthy lifestyle among classes, and consumed minimal alcohol.

There were similar studies that identified latent classes based on lifestyle behaviors, but no other research examined latent classes based on the six lifestyle behaviors that were used in this thesis. For example, the Dutch SMILE cohort study identified three classes: a healthy, an unhealthy, and a poor nutrition, based on five lifestyle behaviors of non-smoking, low to moderate alcohol use, fruit consumption, vegetable consumption, and physical exercise in a sample of 9,449 participation with their age older than 12 years (Mean age = 51.11 years; de Vries et al., 2008). The class characterized as the healthy class had high probabilities of adhering to the healthy (or norm) level of physical activity and alcohol consumption, and moderate probabilities of adhering to non-smoking, and vegetable and fruit consumption. The class characterized as the poor nutrition had low probabilities on physical activity, high probabilities on nonsmoking and low to moderate alcohol consumption, and low probabilities on vegetable and fruit consumption. And the unhealthy class had low probabilities on all five behaviors, with moderate probabilities on non-smoking and alcohol consumption. Ingledew et al. (1995) identified two latent classes (the healthy versus mixed behaviors) based on eating, exercising, alcohol, and smoking behaviors in a sample of 110 people with the mean age of 36.1 years. The healthy class engaged in all four aspects of healthy lifestyle and the mixed class tended to engage in the healthy lifestyle behaviors except for one or two unhealthy behaviors.

The characteristics of the most engaged class in the present study was similar to the healthy class of the above two studies and the least engaged class was similar to the unhealthy class of the Dutch SMILE cohort study. If the sample of the present study had higher drinking and smoking rates as in other populations, the patterns may have been more similar to the Dutch SMILE cohort study. However, it should be noted that the participants of the above two studies were younger and that the study of Ingledew et al. (1995) had a sample, which was limited to a group of nurses.

In the present study, latent classes did not show unique patterns by lifestyle domains except for religious involvement and alcohol consumption; rather, higher engagement in one domain (e.g., cognitive activities) was related to higher engagement in other domains (e.g., social interaction, physical activities, and diet). Unique characteristics were shown in religious involvement and alcohol consumption. The most engaged class was highly religious and did not consume alcohol, whereas the moderately engaged class was not so religious, consumed a moderate amount of alcohol, and had the smallest numbers of members (n = 59). This may have reflected the unique characteristic of the Utah population, with 90% of older adults in the Cache County cohort self-reporting to be members of The Church of Jesus Christ of Latter-day Saints (LDS) and whose use of alcohol (or tobacco) is proscribed by the Church (Norton et al., 2006). The

three distinct lifestyle patterns seem to well project the population of Cache County. However, a different latent class solution could have resulted had different cutpoints been applied when dichotomizing the six lifestyle variables.

The least engaged class, who had low probabilities on all healthy behaviors except moderate probability on religious involvement, were more functionally dependent compared with the other two classes. Although the association between latent class and cognitive status remained significant, adjustment for functional status lowered the effect size more than 50%, indicating that functional status might be associated with cognitive status. Possible relationships might be that participants who have more functional problems have difficulties in doing activities, participants have more functional problems because of low engagement in healthy behaviors, or lower cognitive status is associated with higher functional dependency.

A population-based longitudinal study of 2,581 people age 65 and older found that lower cognitive function and smoking were associated with higher functional dependence, and moderate alcohol consumption and exercise were associated with lower functional dependence (Wang, Belle, Kukull, & Larson, 2002). Based on these findings, low engagement in healthy lifestyle behaviors may be associated with higher functional dependence in the least engaged class. Longitudinal studies have found that cognitive decline is a risk factor for functional impairment (Agüero-Torres, Thomas, Winblad, & Fratiglioni, 2002; McGuire & Ajani, 2006). Lower MMSE scores were associated with increased dependence in IADL (Agüero-Torres et al., 2002). Because participants in the least engaged class had a higher rate of dementia and cognitive impairment, higher cognitive impairment might be associated with higher functional dependence in this class.
The least engaged class had fewer years of education compared with the other two classes. It would be reasonable to think that people with higher education would engage in more healthy behaviors such as cognitive activities. A Canadian study in a sample of 13,756 people 20 years old and older examined the associations between demographics and lifestyle behaviors and reported that a lower level of education was associated with higher odds of excessive drinking, and lower likelihood of engaging in regular physical activities (Qi, Phillips, & Hopman, 2006). Another study reported that people with higher education attainment engaged more in leisure-time physical activities in a sample of 4,437 people age 25 to 64 years old (Borodulin, Laatikainen, Lahti-Koski, & Lakka, 2008). Adjustment for education lowered the effect size more than 28% indicating that education might be associated with cognitive status. Higher levels of education are associated with higher cognitive function (Wilson et al., 2009) and a lower level of education is a known risk factor for dementia (Plassman et al., 2007). Higher rates of cognitive impairment and dementia may reflect a lower level of education in this class.

The APOE ε 4 allele, another known risk factor for cognitive decline and dementia, had higher prevalence in the least engaged class compared to participants in two other classes (37.7% versus 32.2% and 30.5%). It is difficult to find the evidence that carrying APOE ε 4 allele lowers engagement in lifestyle behaviors. A high rate of APOE ε 4 allele might be associated with a higher rate of dementia in the least engaged class. However, adjusting for APOE status did not change the association between latent class and cognitive function.

Lifestyle Pattern and Cognitive Status

The second hypothesis that participants in the less engaged class would have significantly lower cognitive test scores compared to participants in more engaged classes, was also supported. Participants in least engaged class scored significantly lower than the other two classes (85.93 versus 91.08 and 90.73). This association remained significant even after adjusting for functional status, education, age, and APOE genotype, indicating that there is a unique effect of lifestyle pattern on cognitive function.

Although there was no other research that studied latent class of lifestyle behaviors and cognitive function, there were studies that found stronger cross-sectional relationships rather than longitudinal relationships between engaged lifestyle (leisure activities) and better cognitive function when both cross-sectional and longitudinal associations were examined (Bielak et al., 2007; Newson & Kemps, 2005). Bielak et al. (2007) related composite scores of each aspect of leisure activities such as physical, social, and novel information processing to current and changes in cognitive speed using multiple regression. Novel information processing had the largest effect on current cognitive ability. Newson and Kemps also used composite score of all different aspects of general activities such as social, service (to others), domestic, and household maintenance to relate to current cognitive test scores and changes in the scores using the multiple regression. The significant cross-sectional relationship between engaged lifestyle and cognitive function in the present study is consistent with these findings; however, these studies included different activity items and did not include lifestyle aspects of religious, diet, or alcohol consumption.

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The least engaged class had significantly worse functional status (M = 18.92, SD = 3.47) than the other two classes (M = 20.71, SD = 1.13; M = 20.17, SD = 1.82). This suggests that functional dependence of participants in least engaged class could have limited their engagement in activities. Controlling for functional status reduced the effect of latent class on cognitive function. However, latent class still accounted for the mean differences in cognitive test score.

Lifestyle Pattern and Dementia

Results also supported the third hypothesis which stated that participants in the less engaged class would be more likely to carry CIND or dementia diagnosis, compared to participants in more engaged classes of lifestyle behaviors. The least engaged class had the highest probability of having CIND (40.1%) and dementia (23.5%) whereas moderately engaged secular class had the lowest probability of having CIND (30.5%) and dementia (5.1%). The most engaged religious class had the second highest probability having CIND (34.9%) and dementia (9.9%).

There was no research relating latent class of lifestyle behaviors and dementia, but there were studies that found associations between engaged lifestyles and reduced risk of dementia. Although the relationship in this thesis was cross-sectional, the results were consistent with the findings of longitudinal studies that found protective effects of engaging in cognitive, social, and physical activities (e.g., Karp et al., 2006; Scarmeas et al., 2001; Verghese et al., 2003), and the beneficial effects of being involved in religious behavior (Hill et al., 2006), low to moderate alcohol consumption, (Ganguli et al., 2005), and a healthy diet (Wengreen et al., 2010) on reduced risk of cognitive decline and dementia.

The finding that moderately engaged secular class had the lowest probability of CIND or dementia diagnosis can be explained by two points. More males were likely to be in this class (62.7% versus 42.8% and 45%) and because being a woman may be accompanied by a higher risk of dementia (Breitner et al., 1999; Fratiglioni et al., 2007), the relative risk of being diagnosed as CIND or dementia could have been lower in this class. Another point is that most participants in the moderately engaged secular class consumed low to moderate amounts of alcohol, whereas participants in other two classes consumed a minimal amount of alcohol. Based on the literature that moderate alcohol consumption is beneficial (Anstey et al., 2009; Ganguli et al., 2005; Peters et al., 2008), participants in the moderately engaged secular class may have had the least diagnosis of CIND and dementia. However, it should be noted that, with LCA, the variance explained by each lifestyle behavior cannot be compared as such in a multiple regression because the "membership" to a class (an underlying lifestyle pattern) itself is the predictor variable, and not the individual lifestyle variables nor the association between these variables (Goodman, 2002). Therefore, it may be inappropriate to make inferences such as moderate alcohol consumption in the moderately engaged secular class is associated with a lower rate of CIND or dementia.

An alternative explanation is also possible. Having dementia or CIND could have limited participants' ability or interest to engage in activities (cognitive, social, religious, physical) for participants in the least engaged class, particularly if the cognitive decline was antecedent to a reduction in engagement in these activities. Due to the crosssectional nature of the present study, the causal relationship cannot be explained in this study. However, longitudinal studies that examined with dementia cases removed in earlier waves to eliminate the effect of preclinical dementia reported that the association between leisure activities and dementia remained unchanged (Verghese et al., 2003; Wilson, Bennett, et al., 2002).

Cognitive Reserve

The perspective of cognitive reserve (CR) hypothesizes that there are individual differences in coping with brain damage and individuals with more CR can perform tasks better by efficiently utilizing brain networks. Individuals with more CR also can tolerate more brain pathology through the use of compensational brain networks (Stern, 2002, 2009). Life experience such as education, occupational attainment, and late-life leisure activities have been associated with increased CR (Scarmeas et al., 2001). Leisure activities examined in CR studies are common activities that contain cognitive, social, and physical components such as reading newspapers, playing cards or other games, going to theaters or movies, going for walks or rides, taking part in sports, dancing, or exercise, visiting or being visited by friends or relatives or neighbors (Scarmeas, Zarahn, Anderson, Habeck, et al., 2003).

The findings of the present study were consistent with the perspective of CR. Participants in the moderately engaged secular class and the most engaged religious class may have more CR, thus they had better cognitive function resulting in lower rates of CIND and dementia than the participants in the least engaged class. Studies of engagement in late-life leisure activities and cognitive function (e.g., Newson & Kemps, 2005; Hultsch et al., 1999) or dementia risk (e.g., Scarmeas et al., 2001; Wang, Karp, et al., 2002; Wilson, Bennett, et al., 2002) have been consistent with the perspective of CR.

The underlying neural mechanisms are not clear, but imaging studies and rodent studies have been providing some physiologic evidence for CR. It is hypothesized that individuals with more CR are able to use brain networks efficiently. In the case of AD, individuals with more CR are hypothesized to be able to utilize alternative brain networks or cognitive strategies when the normal brain networks are disrupted by AD pathology. And because individuals with higher CR can tolerate more AD pathology than individuals with lower CR, AD pathology is more severe in individuals with higher CR (Stern, 2002).

In an imaging study, resting regional cerebral blood flow (rCBF), an indirect index of cerebral changes in AD pathology (more AD pathology is associated with lower rCBF), had an inverse relationship with education, IQ, and leisure activity in individuals with AD controlling for clinical severity (Scarmeas, Zarahn, Anderson, Habeck, et al., 2003). Lower rCBF (more AD pathology) among AD patient with higher leisure activity supported the perspective that engaging in leisure activities increases CR and individuals with more CR tolerate more AD pathology. The association between leisure activity and rCBF remained significant after adjustment for education and IQ (Scarmeas, Zarahn, Anderson, Habeck, et al., 2003).

A study using positron emission tomographic (PET) images found that people with higher educational attainment showed better cognitive function in the presence of AD pathology than people with lower education (Roe et al., 2008). This suggests that clinical symptoms of AD are less severe among individuals with higher CR that was measured by educational attainment. Using functional magnetic resonance imaging (fMRI) to compare patterns in the brain activity in younger and older adults while performing cognitive tasks with different processing demands showed that younger participants used the same brain area for the tasks but older participants used other brain areas for the tasks (Scarmeas, Zarahn, Anderson, Hilton, et al., 2003). This could indicate that older adults may use different brain networks to compensate for age related cognitive changes. The findings suggested that there may be a neural basis in CR that can be measured by brain images (Stern, 2009).

Rodent studies have been consistent with the perspective of CR, finding that rodents housed in enriched cages with physical, social, and sensory stimuli showed increase in hippocampal neurogenesis (Olson, Eadie, Ernest, & Christie, 2006), and showed better cognitive performance compared with standard-housed rodents. Enriched experiences also prevented or reduced the cognitive and neurochemical deficits in the adult rats associated with nonhandling (Pham, Söderström, Windblad, & Mohammed, 1999) and mitigated cognitive deficits in mice under the influence of AD pathology (Jankowsky et al., 2005).

In summary, all the hypotheses of this thesis were fully supported by the findings, and were consistent the perspective of CR. Underlying mechanisms of lifestyle behaviors and cognitive outcomes are not clear, but imaging studies and rodent studies provide a physiologic basis of these relationships.

Limitations

In this study, only cross-sectional relationships were examined thus precluding the ability to more fully study the casual relationship of lifestyle patterns and cognitive function or risk of dementia.

Lifestyle variables were treated as binary (high versus low to moderate) to find clearly distinctive patterns in LCA. This may have resulted in decreased precision of the measures that originally had multiple categories. Trichotomous variables were also examined at the beginning of the LCA to avoid this issue but dichotomous variables produced better results in model fit and interpretability.

Chi-square test (as was used to compare latent classes with dementia group) can only show whether the two variables are independent. Because of the small number of participants in the moderately engaged secular class (n = 59), changing cell size by even one person can change the percentage sizably.

Income may be a potential confounding factor in the relationships of lifestyle patterns and cognitive outcomes. Income could not be included as a covariate because it was not measured.

Informant report was used in measuring lifestyle behaviors in cases where the information of the participant was judged as not reliable (0.3% -21.6%). There might be biases in differences between types of informants. For instance, the spouse may report different frequencies of doing the activities than the child of the participant. In addition, there might be possible social desirability in responses in both self-report and informant

report. They might report more frequent participation in leisure activities because it is socially desirable.

Selection bias may be a threat to internal validity. The sample used for this study was different from the entire Wave 3 population. The sample consists of participants who received clinical assessment and these participants had higher risk for cognitive impairment or dementia than those who did not receive clinical assessment. Because dementia diagnosis procedures are complicated and expensive, not all participants could receive clinical assessment; rather only those who had higher risk were selected. However, the sample also included a designated subsample (more than half the sample) that might have better represented the whole Wave 3 population.

Attrition bias may be a threat to internal validity. Non-response rate for religious involvement was 44.7%. Attrition analysis showed that non-respondents were more likely to be women, higher on functional dependence, and scored lower on cognitive tests. The response rate for this particular questionnaire was lower because no reminder was sent to avoid measurement burden.

The findings may be limited to the Utah population because the majority of the population is Caucasian and are members of the LDS Church. This highly religious population has extremely low drinking and smoking rates. The patterns of lifestyle behaviors and their relationships with dementia risk may be different in populations that have more diverse ethnicity and less religious involvement. The moderately engaged secular group may be very different in another population. This group in this population can be unique because they are likely to stay in this region by their choice in retirement

thus being more resilient compared to a similar group living elsewhere in an area in which they are not a minority.

On the other hand, the homogeneous sample of the present study may be an advantage. The effect of lifestyle patterns may be more detectable in this sample than in a heterogeneous sample. Also, the findings can have local implications in the aspect that human service workers do work with a local population. Moreover, the findings may extend to other segments of the U.S. with the majority of Caucasian residents with religious homogeneity.

Directions for Future Studies

This study included all participants who completed Wave 3 clinical assessment including individuals within all ranges of cognitive status in LCA. Future studies may use a similar approach but include data from a subsequent wave to examine incident dementia risk as a function of lifestyle latent class, with prevalent dementia cases excluded. Future studies may also examine factors that influence an individual choosing a pattern of lifestyle behaviors that also would affect dementia risk such as indicators of socioeconomic status, prior history of psychosocial stress, and depression. Smoking may be included in lifestyle behaviors as a risk factor in studies in other populations, but extremely low prevalence rates in this sample made inclusion of smoking history not useful. Identifying lifestyle patterns in other samples or more nationally representative samples to observe the nature of lifestyle behaviors in older adults and to examine their health outcomes might be in the interest of future studies. Additional studies could conduct multiple regression analyses in which lifestyle behavior measurement is on the original scale, thus eliminating loss of precision due to dichotomization as in the present study. Finally, studies examining co-trajectories of lifestyle behaviors, with health and functional status, and cognitive status over time could help understand how changes in lifestyle behaviors are associated with changes in the other domains.

Conclusions

The findings of the present study suggest that there are underlying patterns in lifestyle behaviors, and that engaging in healthy lifestyle behaviors may predict better cognitive function and lower rates of dementia in older adults. These relationships suggest that cognitive function might be an important indicator of dementia. The findings were consistent with the perspective of CR that individuals who engage in healthy lifestyle behaviors accumulate more CR than their counterparts and by increasing their ability to use the brain network efficiently, they can maintain higher cognitive function and reduce the risk of, or perhaps delay the onset of dementia.

The importance of this study is that it confirmed the possible effects of an engaged lifestyle in later life on preventing or delaying the onset of dementia. Because all of the behaviors examined in the present study are modifiable, this study further supports the argument that public health officials and healthcare providers should continue to promote these behaviors in older adults. Results from the present study, along with longitudinal studies consistently finding that the benefits of a healthy, engaged lifestyle extend not only to greater longevity (e.g., van Dam, Li, Spiegelman, & Hu, 2008) and lower depression (e.g., van Gool et al., 2003) and cardiovascular disease rates (e.g., Kurth et al., 2006), but also to lower risk for AD and other dementias. Such research may increase interest in the general population to engage in these protective behaviors, particularly if there is a family history of AD or other dementia.

The present study is the first to include the six lifestyle domains (i.e., cognitive activities, social activities, physical activities, religious involvement, diet, and alcohol consumption) and to demonstrate that it is possible to identify distinct patterns of these modifiable lifestyle behaviors in older adults. In the present sample, participants' behavioral patterns tended to align with one of the three patterns that were identified in this study. With the association between distinct lifestyle patterns and the risk of dementia, the present study helps to identify distinct patterns that define subpopulations who are most vulnerable to developing dementia or cognitive impairment and who can thus be more targeted for behavioral interventions to reduce dementia risk.

In summary, the findings of this study can be applied at the individual level, or at a policymaking level, through development of educational programs for older adults that encourage engagement in healthy lifestyles. Indeed, future studies that examine these same health-related lifestyle behaviors decades before the dementia risk period and prospectively follow participants to old age may extend the present findings to better understand whether such lifestyle behaviors need to begin earlier in life to have sustained effects with better cognitive health to lower dementia risk through the final decades of life.

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APPENDICES

Appendix A

Glossary of Terms

Glossary of Terms

Buccal scraping: A swap taken from the mouth epithelial cells for DNA analysis.

Comorbidity: The presence of one or more disease or disorders in addition to a primary disease or disorder.

Episodic memory: The memory of autobiographical events such as times, places, associated emotions, and other contextual knowledge that can be explicitly stated.

Executive function: A theorized cognitive system that controls and manages other cognitive processing.

Frontotemporal dementia (FTD): A clinical syndrome caused by degeneration of the frontal lobe of the brain and may extend back to the temporal lobe.

Information processing: The coding, retrieval, and combination of information in perceptual recognition, learning, remembering, thinking, problem solving, and performance of sensory-motor acts.

Lewy body dementia: Dementia in the presence of Lewy bodies clumps of alphasynuclein and ubiqutin protein in neurons, detectable in post-mortem brain biopsies.

Person year: A measure of the incidence rate of dementia in a population over an observed period of time that directly incorporates time into the denominator.

Appendix B

Sample Selection



Appendix C

Designated Subsample

Designated Subsample

Purpose

A panel of subjects was randomly selected to receive clinical evaluation regardless of their prior results on cognitive screening in the beginning of the CCSMHA. The purpose of this panel was: first, to establish sensitivity/specificity of dementia screening methods against the clinical assessment diagnosis; second, to increase the number and proportion of AD and other dementia cases identified from the population; third, to provide a control sample for case-control studies.

Selection protocol

(*Wave 1, 1995-1996*). Preliminary estimates of a sub-sample were designed to project the expected number of prevalent AD cases. The sub-sample was stratified by age group (65-69 years, 70-74 years, etc), gender, and number of APOE e4 alleles (36 strata). Sampling rates were calculated to yield a ratio of 2:1 sub-sample "controls" for each anticipated prevalent AD case within each of the 36 strata. The ratio of 4:1 was sought for the two youngest age strata with 0 or 1 e4 alleles. All AD cases were considered including subjects who were and were not part of the sub-sample.

The calculation of number of subjects to be selected included following steps: (1) Based on prior studies, approximately 80% of sub-sample members would be a non-case, or control. For that reason, if 160 controls were needed in one stratum, the corrected estimate was 160/.80 = 200 subjects. (2) Because of 85% clinical assessment (CA) participation rate in the sub-sample, the 200 subjects were adjusted to a total of 200/.85 = 235 subjects. The number of designated subsample for Wave 1 was 960 subjects among5,092 participants at Wave 1 screening.

Wave 2 (1998-1999). There had been some attrition of the sub-sample but no replacement was attempted. The number of designated subsample for wave 2 was 493 subjects among 3,411 participants at wave 2 screening.

Wave 3 (2002-2003). Additional subjects were randomly selected to replace subsample members who either were now deceased or who refused further participation in strata where remaining subjects would yield less than a 2:1 ratio. As the study's focus expanded from dementia to include prodromal AD, the definition of a "case" was extended to include dementia, mild/ambiguous, and MCI-Peterson diagnoses. This was conducted after approximately 700 subjects completed CA which was 60% of the eventual 1,216 subjects.

Stratum-specific incidence rates of "cases" were calculated and applied to the total number of subjects anticipated to complete Wave 3 screening visit, resulting in stratum-specific estimates for anticipated number of incident cases after all subjects completed CA. Stratum-specific sampling rates were calculated as the number of additional subjects needing to be selected, divided by the total number of study participants who completed Wave 3 screening within the stratum who had not yet been selected for the sub-sample. At the end of Wave 3, there were 422 "cases" including 222 incident dementia cases, 121 with mild/ambiguous, and 79 with MCI-Peterson diagnosis and a corresponding sub-sample participating in the CA of 664 subjects.

All participants aged 85 years and older were selected for CA in Wave 3, consequently, the replacement of designated subsample was conducted only for subjects whose age was younger than 85 years. This was because in effect, all persons aged 85 years and older were sampled as designated subsample at a rate of 100%, so no detailed sampling strategy was needed. The number of designated subsample for Wave 3 was 1,188 subjects (including n = 550 aged 85+ who might be considered as designated subsample because they were sampled without consideration of screening results but rather only age, gender, and/or genotype) among 2,350 participants at Wave 3 screening.
Appendix D

Generalizability of Designated Subsample

The subjects participating in Wave 3 CA were used to define the sample upon which to base hypothesis tests, with the clear advantage of a much more comprehensive set of variables available for analysis, spanning the six domains of interest (this is because the CA was the visit at which the lifestyle behavior domains, not collected at the screening visit, were collected). The potential disadvantage of this option was that the CA participants ("C3 completers") might be demographically different from the group completing the screening visit but not the CA ("C3 non-completers"). Although participants who were screen positive for possible dementia were examined at CA (n =552), there were participants who were randomly selected as designated subsample (n =664) in the CA subsample. The designated subsample that was stratified by age, gender, and APOE genotype were sampled to be more representative of the whole Wave 3 population than the C3 completers who had been selected for CA due to low cognitive screening score. In order to assess generalizability of the CA subsample, a series of comparisons between designated subsample and C3 non-completers were made, with both statistically and practically significant differences taken into consideration. Preliminary t tests for independent samples and chi-square tests were conducted to examine the differences between these two groups on demographic variables, depression, and APOE genotype and cognitive function, functional status, comorbidity (having at least one comorbid medical condition), and Body Mass Index (BMI, See Table D1 and Table D2).

The two groups were statistically significantly different on age, gender, education, cognitive status as measured by 3MS cognitive test, depressive symptoms and APOE genotype. Designated subsample was older, more males (47.9% versus 38.1%), more educated, lower on 3MS test score (cognitive function), less depressed and carried more APOE ɛ4 allele (46% versus 28.5%). Practical differences were significant in gender and APOE genotype, but minimal in age, education, 3MS test score, and depressive symptoms. For instance, age differed by only 2.32 years on average, 0.45 years in education, and 3MS test score differed by 1.68 points. The two groups did not differ in functional status, comorbidity, and BMI.

In conclusion, although designated subsample was different from the whole Wave 3 population, especially in APOE genotype, they were sufficiently representative of the entire surviving cohort and it was adequate to include the CA subsample in the present study. Most of all, good measures of cognitive activities, social interaction, and religious behaviors could be obtained by including the CA subsample (see Appendix D) which was very important lifestyle variables that contributed to the purpose of this thesis.

Table D1

Comparison For C3 Completer Designated Subsample and C3 Non-completers on

					t
	Designated	C3 non-	Mean		df
Variable	subsample	completers	difference	Overall mean	<i>p</i> -value
Age					
n	664	1108			<i>t</i> = 8.95
M	81.07	78.75	2.32	79.91	df = 1770
SD	5.26	5.28			<i>p</i> < .001
Education					
n	663	1108			<i>t</i> = 3.14
M	13.85	13.40	0.45	13.63	df = 1769
SD	3.02	2.75			p = .002
3MS					
n	652	1034			<i>t</i> = 3.73
M	90.28	91.96	1.68	91.12	df = 1684
SD	8.47	9.33			<i>p</i> < .001
IADL					
n	664	1108			<i>t</i> = 1.43
M	0.88	1.00	0.12	0.94	df = 1770
SD	1.73	1.98			p = .152
BMI					
n	652	1071			<i>t</i> = 1.88
М	26.03	26.45	0.42	26.24	df = 1721
SD	4.18	5.04			<i>p</i> = .061

Continuous	Measures
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Note. Designated subsample = participants who were randomly selected and who completed Wave 3 interview and clinical assessment (n = 664), C3 non-completers = participants who completed Wave 3 interview but did not complete clinical assessment (n = 1,108). 3MS = Modified Mini-Mental State Examination. IADL = Instrumental Activities of Daily Living. BMI = Body Mass Index.

Table D2

Comparison For C3 Completer Designated Subsample and C3 Non-completers on

ubsample (%)	completers n (%)	Difference (%)	Overall <i>n</i> (%)	$df \\ p-value \\ \varphi$
				2
18 (47.9)	422 (38.1)		740 (41.8)	$\chi^2 = 16.41$ df = 1 p < .001
46 (52.1)	686 (61.9)	9.8	1032 (58.2)	$\varphi = .096$
				2
41 (36.3)	400 (36.1)		641 (36.2)	$\chi^2 = 0.00$ df = 1 n = 959
23 (63.7)	708 (63.9)	0.2	1131 (63.8)	$\varphi = 0.00$
				2
88 (88.8)	931 (84.7)		1519 (86.3)	$\chi^2 = 5.88$ df = 1 p = .015
4 (11.2)	168 (15.3)	4.1	242 (13.7)	$\varphi = .058$
				2
58 (54.0)	787 (71.5)		1145 (64.9)	$\chi^2 = 55.96$ df = 1 p < .001
05 (46.0)	313 (28.5)	17.5	618 (35.1)	$\phi = .178$
	18 (47.9) 46 (52.1) 41 (36.3) 23 (63.7) 38 (88.8) 4 (11.2) 58 (54.0) 05 (46.0)	$(36, 3)$ $(23, 10)^{-1}$ $(36, 3)$ $(36, 1.9)$ $(48, (47.9)$ $422, (38.1)$ $(46, (52.1)$ $686, (61.9)$ $(41, (36.3)$ $400, (36.1)$ $(23, (63.7)$ $708, (63.9)$ (411.2) $168, (15.3)$ $(58, (54.0)$ $787, (71.5)$ $(55, (46.0)$ $313, (28.5)$	ExignatedC.5 holf completersDifference $(\%)$ Ibsamplecompleters $n (\%)$ Difference $(\%)$ I8 (47.9)422 (38.1)I8 (47.9)422 (38.1)I6 (52.1)686 (61.9)9.8I1 (36.3)400 (36.1)I23 (63.7)708 (63.9)0.2I8 (88.8)931 (84.7)I4 (11.2)168 (15.3)4.1I68 (54.0)787 (71.5)I65 (46.0)313 (28.5)17.5	ExignatedCS non- completersDifference (%)Overall n (%) $(\%)$ n (%) $(\%)$ n (%) 18 (47.9) 422 (38.1) 740 (41.8) 16 (52.1) 686 (61.9) 9.8 1032 (58.2) 141 (36.3) 400 (36.1) 641 (36.2) 23 (63.7) 708 (63.9) 0.2 1131 (63.8) 38 (88.8) 931 (84.7) 1519 (86.3) 4 (11.2) 168 (15.3) 4.1 242 (13.7) 58 (54.0) 787 (71.5) 1145 (64.9) 05 (46.0) 313 (28.5) 17.5 618 (35.1)

Categorical Measures

Note. Designated subsample = participants who were randomly selected and who completed Wave 3 interview and clinical assessment (n = 664), C3 non-completers = participants who completed Wave 3 interview but did not complete clinical assessment (n = 1,108). *APOE* = Apolipoprotein E; $\varepsilon 4$ carrier = persons with APOE allele combinations of $\varepsilon 2/\varepsilon 4$, $\varepsilon 3/\varepsilon 4$, and $\varepsilon 4/\varepsilon 4$; $\varepsilon 4$ noncarrier = persons with APOE allele combinations of $\varepsilon 2/\varepsilon 3$, $\varepsilon 3/\varepsilon 4$.

Appendix E

Instruments for Cognitive Activities, Social Interaction,

Religious Involvement, and Physical Activities

Instruments for Cognitive Activities, Social Interaction,

Religious Involvement, and Physical Activities

Cognitive activities

Please indicate how often in the past year you have spent time:

- 1. Reading the newspaper?
- 2. Talking about local or national problems or issues?
- 3. Playing cards or games with others?
- 4. Balancing a checkbook?
- 5. Drawing or painting?
- 6. Looking at paintings or other art?
- 7. Going to plays or concerts?
- 8. Doing crossword puzzles?
- 9. Taking courses or classes?
- 10. Reading books?
- 11. Writing in a journal?

Each question had six response options: Never or less than once a month/ once a month/

2-3 times a month/ once a week/ a few times a week/ every day. Total composite score

(11-50) was dichotomized into upper tertile (11-32) versus lower two tertiles (33-50).

Social interaction

Please indicate how often in the past year you have spent time:

- How often do you attend meetings of social clubs, groups, or organizations such as bridge clubs, book clubs, hospital volunteer, gardening clubs, Rotary club, Kiwanis, VFW, etc.
- 2. How often do you talk on the telephone with family, friends, or neighbors?
- 3. How often do you get together with family, friends, or neighbors? This includes meeting in your own home, meeting in other's home, or going out together.
- 4. Doing volunteer work?

Each question had six response options: Never or less than once a month/ once a month/ 2-3 times a month/ once a week/ a few times a week/ every day. Total composite score (4-23) was dichotomized into upper tertile (4-15) versus lower two tertiles (16-23).

Religious involvement

1. Please circle the number that most closely describes your religious belief on the following rating from 1 to 5.

Atheist		Unsure		Religious	
1	2	3	4	5	

How often do you participate in each activity?

- 2. Thinking about God
- 3. Praying
- 4. Meditating
- 5. Attending worship service
- 6. Reading scripture/holy writings

7. Having direct experiences of God

Each question had five response options: Never/ less than once a month/ once or twice a month/ once a week/ more than once a week. Total composite score (1-35) was dichotomized into upper two tertiles (1-28) versus lower tertile (29-35).

Physical activities

- In the past 12 months, have you walked for exercise? This includes either walking outside or walking on a treadmill. (Yes, No)
 - a. In the past 12 months, how many of those months did you walk for exercise? (__months)
 - b. During those months, how often did you walk for exercise?(number of times per day/ per week/ per month)
 - c. What was the average amount of time that you spent walking per session?
 (__hours __minutes)
 - d. When you walked for exercise, what was your usual pace? Would you say . . .
 - 1) Casual strolling; from 0 to 2 m.p.h.
 - 2) Average or normal; from 2 to 3 m.p.h.
 - 3) Fairly briskly; from 3 to 4 m.p.h.
 - 4) Briskly or striding more than 4 m.p.h.
- 2. In the past 12 months, have you done heavy house work including vacuuming, mopping or scrubbing floors or sidewalks, moving furniture or boxes?

- In the past 12 months, have you done garden or yard work including weeding, digging, cutting grass while walking, raking, or snow shoveling? DO NOT INCLUDE RIDING LAWN MOWER.
- 4. In the past 12 months, have you used an exercise machine including a treadmill for jogging or running but not walking, an exercise bicycle or some other machine? DO NOT INCLUDE TREADMILLL WALKING REPORTED IN THE FIRST QUESTION.
- 5. In the past 12 months, have you done calisthenics or lifted weights for exercise?
- 6. In the past 12 months, have you done other moderate or vigorous exercise such as swimming laps; aerobics; jogging running, or bicycling outside; dancing or tennis?

Question #2 to #6 had sub-questions a, b, and c that was identical to the sub-questions of Question #1. Total hours per week (0-95) were dichotomized into upper two tertiles (0-7) versus lower tertile (>7-95).

Appendix F

Proportion of Self-Report and Proxy Report For Lifestyle Behaviors

Table F1

Lifestyle behaviors	Self-report (%)	Proxy-report (%)	Total
Cognitive activities (CA)	540 (78.4)	149 (21.6)	689
Cognitive activities (Wave 3)	1,158 (95.3)	57 (4.7)	1,215
Social interaction	540 (78.5)	148 (21.5)	688
Physical activities	1,158 (95.3)	57 (4.7)	1,215
Religious involvement	530 (78.8)	143 (21.2)	673
Diet	1,156 (99.7)	3 (0.3)	1,159
Alcohol consumption	1,156 (99.7)	3 (0.3)	1,159

Proportion of Self-Report and Proxy Report For Lifestyle Behaviors

Appendix G

Descriptive Statistics

Table G1

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Variable		Ν	n (%)	Mean (min-max)	SD
Age		1,216		82.54 (73-101)	5.52
	Male		547 (45.0)		
Gender	Female	1,216	669 (55.0)		
Education (yrs	s)	1,215		13.64 (0-20)	2.94
	ε4 non-carrier	1 200	791 (65.4)		
apoe genotype	ε4 carrier	1,209	418 (34.6)		
IADL		1,216		1.11 (0-7)	1.92
Comorbidity	None 1 or more	1,216	436 (35.9) 780 (64.1)		
3MS		1,191		88.13 (26-100)	9.44
Cognitive acti	vities	835		28.5 (11-50)	6.4
Social interact	tion	919		13.5 (4-23)	3.4
Physical activities (hours/week)		1,197		7.4 (0-95)	10.2
Religious involvement		672		28.6 (7-35)	6.1
Diet		1,159		2.9 (1-5)	1.4
Alcohol const (moderate)	imption	1,159	64 (5.5)		

Descriptive Statistics for All Studied Variables

Notes. APOE = Apolipoprotein E; $1 = \epsilon 4$ noncarrier (persons with APOE allele combinations of $\epsilon 2/\epsilon 2$, $\epsilon 2/\epsilon 3$, and $\epsilon 3/\epsilon 3$), $2 = \epsilon 4$ carrier (persons with APOE allele combinations of $\epsilon 2/\epsilon 4$, $\epsilon 3/\epsilon 4$, and $\epsilon 4/\epsilon 4$; $\epsilon 4$). IADL (Instrumental Activities of Daily Living): 0 = all available without help, 7 = need at least some help for all. Comorbidity: 1 = no disease, 2 = at least 1 or more disease in hypertension, cholesterol, coronary bypass surgery, heart attack, coronary angioplasty, diabetes, Parkinson disease, stroke, severe head injury, and cancer. 3MS = Modified Mini-Mental State Examination. Means for cognitive activities, social interaction, and religious involvement are means of composite scores. Mean of diet is mean of DASH diet scores assigned in quintiles.

Appendix H

Pearson Correlation Matrix Among Lifestyle Behaviors and Covariates

Table H1

	Sex	Edu	APOE	IADL	Como	Cog	Soc	Phys	Relig	Diet	Alco
	(1216)	(1215)	(1209)	(1210)	(1216)	(835)	(919)	(1197)	(672)	(1159)	(1159)
Age	.144*	154**	127**	.377**	.010	123**	083*	133**	036	.031	039
Sex		258**	.000	.188**	007	.065	.069*	143**	.037	.156**	076**
Edu			.008	168**	.033	.204**	.109**	.015	029	.111**	.148**
APOE				038	070*	018	007	.047	.002	.005	025
IADL					.092**	392**	197**	234**	107**	033	076***
Como						046	085**	039	012	.049	.005
Cog							.382**	.108**	.215**	.175**	.024
Soc								.054	.337**	.100**	048
Phys									.044	.049	.002
Relig										.060	375**
Diet											.033

Pearson Correlation Matrix Among Lifestyle Behaviors and Covariates

Note. Sample sizes appear in parentheses.

*p < .05, **p < .01.

Appendix I

Attrition Analysis

Table I1

Variable	Respondent for religious involvement	Non-respondent for religious involvement	Mean difference	Overall mean	t df p-value
Age					
п	672	544			t = 6.14
M	81.68	83.60	1.92	82.64	df = 1214
SD	5.35	5.54			<i>p</i> < .001
Education					
n	672	543			t = 4.84
M	14.00	13.20	0.81	13.60	df = 1213
SD	2.98	2.82			p = < .001
3MS					
n	665	526			<i>t</i> = 5.59
М	89.48	86.44	3.04	87.96	df = 1189
SD	9.00	9.72			<i>p</i> < .001
IADL					
п	672	544			<i>t</i> = 3.38
M	0.94	1.32	0.38	1.13	df = 1214
SD	1.78	2.06			p = .001
BMI					
n	663	525			t = 0.48
M	26.03	25.91	0.12	25.97	df = 1721
SD	4.03	4.60			<i>p</i> = .634

Attrition Analysis of Selected Continuous Measures

Note. 3MS = Modified Mini-Mental State Examination. IADL = Instrumental Activities of Daily Living. BMI = Body Mass Index.

Table I2

Variable	Respondent for religious involvement n (%)	Non- respondent for religious involvement n (%)	Difference (%)	Overall n (%)	χ ² df p -value φ
Gender					2
Male	336 (50.0)	211(38.8)		547 (45.0)	$\chi^2 = 16.41$ df = 1 p < .001
Female	336 (50.0)	333 (61.2)	11.2	669 (55.0)	$\varphi = .096$
Comorbidity					v ² 1.42
None	231 (34.4)	205 (37.7)		436 (35.9)	$\chi = 1.43$ df = 1 n = 253
1 or more	441 (65.6)	339 (62.3)	3.3	780 (64.1)	$\varphi = .034$
Depressive symptom					2
No	586 (87.5)	476 (87.7)		1062 (87.6)	$\chi^2 = 0.01$ $df = 1$
Yes	84 (12.5)	67 (12.3)	0.2	151 (12.4)	p = .931 $\varphi = .003$
APOE genotype					$x^2 - 1.02$
ε4 non-carrier	446 (66.7)	345 (63.9)		791 (65.4)	df = 1 $n = 331$
ε4 carrier	223 (33.3)	195 (36.1)	2.8	418 (34.6)	$\varphi = .029$

Attrition Analysis of Selected Categorical Measures

Note. APOE = Apolipoprotein E; ϵ 4 carrier = persons with APOE allele combinations of ϵ 2/ ϵ 4, ϵ 3/ ϵ 4, and ϵ 4/ ϵ 4; ϵ 4 non-carrier = persons with APOE allele combinations of ϵ 2/ ϵ 2, ϵ 2/ ϵ 3, and ϵ 3/ ϵ 3.

Appendix J

Demographic Comparison of Three Latent Classes

Table J1

		Latent class		_		
		Moderately	Most engaged	_		
	Least engaged	engaged secular	religious			р-
Variable	<i>n</i> = 671	n = 59	<i>n</i> = 486	F	η^2	value
Age	82.94 _b	81.97 _{ab}	82.06 _a	3.96	.006	.02
	[82.49, 83.39]	[80.73, 83.21]	[81.62, 82.50]			
Education	13.20 _a	15.49 _c	14.03 _b	24.58	.039	<.001
	[12.98, 13.42]	[14.73, 16.25]	[13.77, 14.29]			
Functional	1.50 _a	0.25 _b	0.67 _b	34.69	.054	< .001
status	[1.34, 1.68]	[0.00, 0.50]	[0.54, 0.79]			

Analysis of Variance of Age, Education, and Functional Status for Latent Classes

Note. N = 1,216. Numbers in brackets are 95% confidence intervals of the means. Means with differing subscripts within rows are significantly different at p < .05 in the Tukey honestly significant difference comparisons.

Table J2

	Ge				
			_	Cramér's	
Latent class	Male	Female	χ^2	V	<i>p</i> -value
Least engaged	302	369	8.43	.083	<i>p</i> =.015
	(45.0)	(55.0)			
Moderately	37	22			
engaged	(62.7)	(37.3)			
secular					
Most engaged	208	278			
religious	(42.8)	(57.2)			
	APOE	genotype			
	ε4 non-carrier	e4 carrier	_		
Least engaged	414	251	6.63	.074	<i>p</i> = .036
	(62.3)	(37.7)			
Moderately	40	10			
engaged	40	(32.2)			
secular	(07.8)	(32.2)			
Most engaged	337	148			
religious	(69.5)	(30.5)			
	Com	- d- : d:4			
	Nona	At losst one	_		
	INOILE	At least one			
Least engaged	241	430	0.10	.009	p = .949
00	(35.9)	(64.1)			1
Moderately	20	39			
engaged	(33.9)	(66.1)			
secular					
Most engaged	175	311			
religious	(36.0)	(64.0)			

Crosstabulation of Gender, APOE Genotype, Comorbidity by Latent Class

Note. N = 1,216. Percentages appear in parentheses below group frequencies.