SOCIOCULTURAL DETERMINANTS OF SLEEP, COGNITIVE DECLINE, AND DEMENTIA AMONG AN INTERGENERATIONAL LATINO COHORT IN THE SACRAMENTO, CALIFORNIA REGION

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ABSTRACT

Erline E. Martinez-Miller: Sociocultural Determinants of Sleep, Cognitive Decline, and Dementia among an Intergenerational Latino Cohort in the Sacramento, California Region
(Under the direction of Allison E. Aiello)

Latinos in the US face higher proportions of dementia. Understanding how acculturation relates to cognition may provide insight to the mechanistic pathways driving this disparity. High US acculturation, when compared to an orientation towards another birth/ancestral country, has been linked to some poor health outcomes and may negatively shape cognition through these pathways. Poor sleep is an important risk factor that has been largely unexplored among Latinos, though evidence suggests a disproportionate burden. We addressed three gaps in our understanding of the Latino cognitive disparity within an intergenerational Sacramento, California cohort: (1) sociocultural mechanisms and sleep; (2) sociocultural mechanisms, cognitive decline, and dementia; and (3) sleep, cognitive decline, and dementia, with ApoE-ε4 genotype. Sacramento Area Latino Study on Aging comprised older age generation 1 (GEN1) and Niños Lifestyle & Diabetes Study comprised middle-age generation 2 (GEN2).

US acculturation may pattern sleep differentially by acculturative status of previous generations, socioeconomic context, and potentially age. High intergenerational US acculturation was associated with worse sleep among GEN2, but better sleep among GEN1. However, the beneficial association among GEN1 may be a function of lower SEP. Cognitive outcomes were explored among GEN1. High US acculturation was associated with better cognitive performance and reduced dementia/cognitive impairment, not dementia (CIND) risk. Fatigue was also associated with worse cognitive performance, but sleep, cognitive decline, or incident

dementia/CIND were not associated in this population. However, sleep-cognition associations need to be assessed bi-directionally and in larger populations to gain a full understanding.

High US acculturation may improve sleep and cognitive outcomes in low socioeconomic settings and acculturation across generations may differentially shape health, though a greater understanding of the underlying sociodemographic mechanisms is needed. If replicated, sociocultural pathways should be considered in sleep and cognitive research among Latinos. Pending further exploration of sleep and cognition, better sleep may link high US acculturation and improved cognitive outcomes. Future studies can build upon these findings as knowledge of broad sociocultural determinants can guide identification of modifiable intervention targets (e.g. sleep). Knowledge of a sociocultural framework can also guide the development of prevention and intervention efforts (e.g. community integration component).

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LIST OF ABBREVIATIONS

3MSE	Modified Mini-Mental State Examination
AIC	Akaike information criterion
AD	Alzheimer's disease
ApoE-ε4	Apolipoprotein-ε4
ARSMA	Acculturation Rating Scale for Mexican-Americans
AOS	Anglo orientation subscale
BIC	Bayesian information criterion
BMI	Body mass index
CI	Confidence interval
CIND	Cognitive impairment, not dementia
DAG	Directed acyclic graphs
df	Degrees of freedom
G^2	Likelihood ratio square statistics
GEE	General estimating equations
GED	General education diploma
GEN1	Generation 1
GEN2	Generation 2
HR	Hazard ratio
IQCODE	Informant Questionnaire on Cognitive Decline in the Elderly
IQR	Interquartile range
LCA	Latent class analysis
MOS	Mexican orientation subscale;
MCI	Mild cognitive impairment

NLDS	Niños Lifestyle and Diabetes Study
OR	Odds ratio
PR	Prevalence ratio
SALSA	Sacramento Area Latino Study on Aging
SE	Standard error
SENAS	Spanish and English Neuropsychological Assessment Scales
SEP	Socioeconomic positon
SEVLT	Spanish English Verbal Learning Test
US	United States

CHAPTER 1: SPECIFIC AIMS

1.1 Rationale

The overall goal of the proposed research is to disentangle a complex pathway leading to the disproportionate burden of cognitive impairment, cognitive decline, and dementia in US Latinos, with a focus on the contributing roles of sociocultural factors and sleep.

Cognitive impairment plagues more than 16 million people in the United States (US).[3] It is characterized by memory loss and other diminished cognitive abilities.[3] The progression to dementia among mild cognitive impairment (MCI) has been estimated as 12% annually among the general population.[4] Dementia is also marked by memory impairment, as well as difficulty with language, motor activity, object recognition, and disturbance of executive function.[5] Several studies have suggested that cognitive impairment and dementia are 1.5-2 times as common among Latinos as non-Hispanic Whites.[6-10] A wide range of socioeconomic and health risk factors of poor cognitive outcomes are more common among Latinos,[10-14] but the specific mechanisms of cognitive disparities have yet to be elucidated. As the population of elderly US Latinos rapidly expands,[15] the identification of modifiable risk factors of poor cognition and dementia is imperative to reduce the public health burden.

Sleep is crucial aspect of health that facilitates physiological and neurological functioning, resilience, and restoration,[16-20] and poor sleep has been linked to poor cognitive outcomes.[21-26] These associations are not well understood, but many behavioral and health risk factors (e.g. smoking and poor cardiovascular and mental health) are shared.[10-14,27-31] Gene-environment interactions also play a role in the sleep-cognition association as apolipoprotein E-

ε4 (ApoE-ε4) genotype and poor sleep measures have been shown to jointly increase the risk of poor cognitive performance and dementia.[32-36] These associations are also not well-studied among Latino populations, but limited sleep research among Latinos indicates they may also face higher rates of worse sleep than other race/ethnicities.[37-41] Given that the prevalence of ApoE-ε4 genotype has been found to be lower among Latino populations,[8,42] understanding the contribution of poor sleep to cognitive outcomes may provide insight into the disproportionate cognitive burden. Yet, given the complex web of shared risk factors, research is of limited value without an understanding of the broader framework of determinants for each disparity to interpret results, to guide identification of targetable underlying mechanistic behaviors, and to develop efficacious prevention and intervention tactics for poor sleep and cognitive outcomes among Latinos.

Health behaviors and conditions are shaped by upstream sociocultural factors that operate under an over-arching cultural orientation and structural socioeconomic determinants.[43,44] Latinos are comprised of many ancestral origins and can be characterized by cultural diversity that is often guided by the dynamic process of acculturation, or cultural change, that can become biologically embedded and reinforced across generations after exposure to culturally dissimilar people, groups, and social influences.[43-47] The concept of negative acculturation, whereby a strong cultural orientation to the US (vs. high orientation to another origin or ancestral country) is associated with worse health, is well-known,[43-46,48-51] but associations actually tend to vary in direction and magnitude depending upon the health outcome and socioeconomic context.[43-46,48-51] The health advantage among high socioeconomic populations is well-known.[52] Therefore, examining associations between acculturation and sleep and cognition provides an opportunity for greater understanding of the interplay between determinants and the complex pathways that

may lead to sleep and cognitive disparities among Latinos. Some studies have explored sleep[13,29,30,53-57] and cognitive associations[58-64] with unidimensional acculturative proxies, but these measures do not capture the multiple health pathways stemming from acculturation[45-47] and exploration of socioeconomic context has been limited.

We aimed to gain a greater understanding of the disproportionate burden of poor cognition and dementia among Latinos in the US via the broad sociocultural factors upstream from many of the known health determinants. We focused on the contribution of poor sleep as studies suggest Latinos may face higher rates of poor sleep and because if the known associations with poor cognitive outcomes, including with the ApoE-ε4 genotype, and overall health. We used a validated multidimensional measure of acculturation with intergenerational assessments, multiple self-reported sleep measures, repeated cognitive assessments, and multi-stage clinical dementia diagnoses to examine these associations within an intergenerational cohort of predominately Mexican-descent Latinos in the US: a first generation of older participants at study onset and a second generation of recruited offspring and other biological relatives of middle-age at study onset. Among our intergenerational Latino study population, we hypothesized that higher US cultural orientation was associated with poor sleep, accelerated cognitive decline, and increased dementia risk, and that poor sleep was also associated with accelerated cognitive decline and increased dementia risk.

1.2 Specific aims

1.2.1 Specific aim 1

Aim 1a. Examine the associations between high US acculturation, in single-generations and across generations, and poor sleep measures among adult Latinos in the US.

Hypothesis 1a. Single-generation and intergenerational high US acculturation will be associated with worse sleep outcomes than low US acculturation (i.e. a high acculturation towards another

origin or ancestral country). Across generations, parent-offspring pairs who both have high US acculturation (stable-high) will be associated with worse sleep outcomes than pairs with upwardly mobile high US acculturation (low parent-high offspring US acculturation) or low intergenerational US acculturation (low parent-low offspring or high parent-low offspring).

Aim 1b. Assess the socioeconomic context of these US acculturation-sleep associations within levels of educational attainment and major lifetime occupational category.

Hypothesis 1b. Among low socioeconomic indicators, high US acculturation will be associated with worse sleep when compared to low US acculturation, but among high socioeconomic indicators, high US acculturation will be associated with better sleep or not associate with sleep when compared to low US acculturation.

1.2.2 Specific aim 2

Aim 2a. Examine the associations between high US acculturation and rate of cognitive decline and incident dementia/cognitive impairment, not dementia (CIND) over a 10-year period among adult Latinos of older age in the US.

Hypothesis 2a. High US acculturation will be associated with an accelerated cognitive decline and an increased risk of dementia/CIND.

Aim 2b. Assess whether educational attainment modifies the US acculturation-cognition and dementia association.

Hypothesis 2b. Among low educational attainment, high US acculturation will be associated with an accelerated cognitive decline and an increased risk of dementia/CIND when compared to low US acculturation. Among high educational attainment, high US acculturation will be associated with a slower rate of cognitive decline and a reduced risk of dementia/CIND or not associate with either outcome when compared to low US acculturation.

1.2.3 Specific aim 3

Aim 3a. Examine the associations between poor sleep and rate of cognitive decline and incident dementia/cognitive impairment, not dementia (CIND) over a 10-year period among adult Latinos of older age in the US.

Hypothesis 3a. Poor sleep will be associated with an accelerated cognitive decline and an increased risk of dementia/CIND.

Aim 3b. Assess whether ApoE-ε4 modifies the sleep-cognition and dementia association.

Hypothesis 3b. Among non-ApoE-ε4 carriers, high US acculturation will be associated with an accelerated cognitive decline and an increased risk of dementia/CIND when compared to low US acculturation. Among ApoE-ε4 carriers, we will observe the same associations as among non-ApoE-ε4 carriers, though with a higher rate of cognitive decline and an increased risk of dementia/CIND.

1.3 Public health implications

Latinos in the US have been identified as disproportionately burdened by poor cognitive outcomes and there is also evidence of higher proportions of poor sleep. Cultural orientation and socioeconomic factors impact many health behaviors and outcomes. Understanding how US acculturation associates with sleep, cognitive performance, and dementia (1) provide a "big picture" understanding of how culture shapes health risk factors, including sleep, and ultimately cognitive outcomes; (2) offer future research potential modifiable underlying mechanistic pathways to explore, with the ultimate goal of identifying intervention targets for both sleep and cognition; (3) inform the development of prevention and intervention efforts with a cultural framework to reduce sleep and cognitive disparities. Additionally, we may set the framework for

future exploration of sleep as a key determinant of Latino cognitive disparities, potentially mediating the association between high US acculturation and cognitive outcomes, which would help gain a better understanding of the ways in which US acculturation can impact health

1.4 Conceptual framework

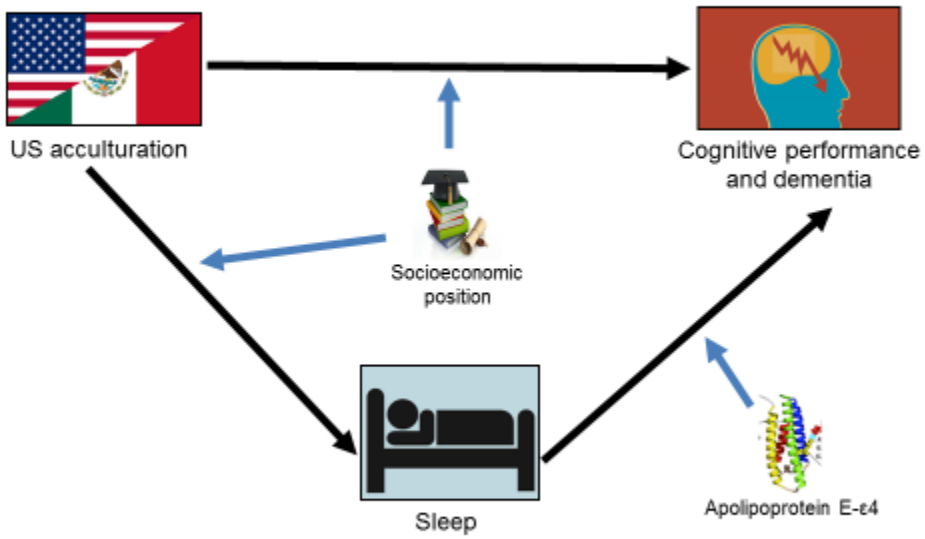

Figure 1. Conceptual framework of the hypothesized association of US acculturation and cognitive performance and dementia (Aim 2) via the mechanism of US acculturation-sleep (Aim 1) and sleep-cognitive performance and dementia (Aim 3), with potential effect modification by socioeconomic factors and ApoE-ε4 genotype.

CHAPTER 2: BACKGROUND AND SIGNIFICANCE

2.1 Background

2.1.1 Cognitive impairment, decline, and dementia

Cognitive impairment is twice as common among some Latino groups when compared to non-Hispanic Whites.[6,9] Cognitive function refers to processes crucial for daily living, including memory, concentration, coordination, and decision-making.[3,6,12] Cognitive impairment is a complex, multifaceted, poorly understood condition that plagues more than 16 million people in the US.[3] Common among the elderly,[3,6,65] it is characterized by memory loss and other diminished cognitive abilities[3] that exceeds what would be expected for the individual's age and level of education.[66] Cognitive impairment is also often related to health declines,[67,68] shortened lifespans, and a loss of independence.[3,32,69]

Cognitive impairment ranges from mild to severe,[3] and those with MCI often function independently in their daily lives in a manner that is indistinguishable from the past.[70,71] MCI is thought to reflect a transitional stage between normal cognitive aging and early dementia,[72] and 14% of individuals over age 70 have sufficient cognitive impairment that would qualify as dementia.[73] Women diagnosed with MCI have been shown to decline cognitively at faster rates than men.[74] Dementia is the loss of cognitive function, specifically of thought, recall, and reason, coupled with the loss of behavioral abilities, and interferes with an individual's daily living.

Multiple brain disorders lead to dementia (see *Supplemental Table 1.* Key brain disorders that cause dementia),[75] and Alzheimer's disease (AD) is the most common cause of dementia among elderly people, accounting for an estimated 60-80% of dementia cases.[32] AD is the 6th

leading cause of death for those aged 65 years and older and an estimated 5.2 million people in the US suffer from AD.[76] In the trajectory of problematic cognitive function, between 10–30% of adults aged 65 and older suffer from MCI, and 10–15% of those diagnosed with MCI progress to AD each year (see **Figure 2** for trajectories of cognition throughout the lifecourse).[77] Early symptoms of AD include difficulty remembering names and recent events, apathy, and depression, and as AD progresses, symptoms include impaired judgement, confusion, behavior changes, and loss of physical control and function, including speech.[6] The prevalence of AD is higher in women, but the incidence for AD is comparable for both sexes, which may be attributed to the longer lifespan of women.[78] When compared to non-Hispanic Whites, Hispanics are 1.5 times as likely to have AD and there is evidence that missed diagnoses are more common in this population.[76]

Previous research has found that MCI and AD share many of the same key modifiable risk factors[77] –which Latinos are more susceptible to,[6,24,65,79-82] including vascular disease,[83,84] low educational level,[6,85] and measures of poor sleep.[40,86] In addition to the heavier burden of modifiable risk factors, there is evidence that Mexican-Americans, the largest subpopulation of Latinos (65%),[87] are diagnosed at more advanced stages,[76] at younger ages,[42] and are less likely to carry the ApoE-ε4 allele[8] when compared to non-Hispanic Whites. One study found that among traditional risk factors for MCI, only age, sex, education, and the ApoE-ε4 gene were linked to an MCI diagnosis.[77] Importantly, Latinos comprise 17.4% of the total US population,[88] and are projected to increase to 29% of the population.[89] The elderly Latino population is expected to triple (19.8%) by the year 2050.[15] This demographic shift towards a larger elderly Latino population coupled with the disproportionate burden of cognitive impairment in this population will present critical health challenges in the US. Mexican-Americans comprise the

majority of Latinos, and there is a critical need to identify risk factors and pathways of MCI and dementia unique to this population. The identification of modifiable mechanisms of poor cognitive outcomes in US Latino groups will guide prevention and intervention efforts aimed at slowing progression, reducing risk, and diminishing disparities, and as well as to improving disease prediction tools in this population.[77]

2.1.2 Sleep

A modifiable risk factor of cognitive impairment that is also linked to the ApoE-ε4 genotype[90,91] is poor sleep.[24,65,92,93] Sleep is a crucial neurophysiologic state that is essential for overall health physiological and neurological functioning, resilience, and restoration.[16-20] Sleep has distinct stages that are characterized by brain patterns, and it can be measured subjectively or objectively across multiple dimensions: presence of disorders, quantity/duration, and quality.[94,95] Definitions of what constitutes adequate sleep health and sleep disorders also changes across the lifecourse.[17] Poor sleep health is a major public health problem that is difficult to define[96] and an estimated 50-70 million Americans suffer from some chronic sleep disorder.[97] Sleep apnea and insomnia are the most common sleep disorders and each are estimated to affect 15% of the population.[98] Sleep can be directly and indirectly influenced by many health factors: obesity, depression, anxiety, certain medical conditions and medications, and substances such as alcohol and nicotine are known predictors of poor sleep.[13] Not only do these factors influence sleep, but research suggests a bi-directional relationship between sleep and general health (see **Figure 3**) as poor sleep is also known to influence mental health, cardiovascular disease, diabetes, obesity, cancer, cognitive decline, and mortality.[13,20,21,24,93,97,99,100]

Importantly, most sleep research has been conducted in non-Hispanic populations, and research findings are therefore not generalizable to other racial/ethnic groups.[13] Thus, the

characterization of sleep in Latinos remains unclear as limited research has produced inconsistent results.[13,41,101] Still, when compared to non-Hispanic Whites, some Latino groups have shown widening gaps in sleep duration over time[40] and been found more likely to report insufficient sleep durations.[41] Additionally, some US Latino groups have been posited as disproportionately burdened by poor sleep because of elevated risks of 1) health conditions associated with impaired sleep,[29,102] and 2) adoption of negative predictive behaviors and poor habits of sleep.[29,103] Poor sleep has been hypothesized as a substantial contributor to racial/ethnic and socioeconomic inequalities in a wide range of health outcomes, yet it is understudied.[17,38,54,104] Recent reviews of sleep have called for more research on protective and adverse behaviors and outcomes that may link sleep to acculturation (cultural attitudes, beliefs, norms, practices), sociodemographic factors, and familial influence, with a focus on the role of a "Westernized" (or US) lifestyle, on sleep health in minority populations.[17,104]

2.1.2.a Sleep, cognition, and dementia

Poor sleep has been linked to differential risk of cognitive impairment, independently of the ApoE-ε4 genotype, via its impact on cellular ultrastructure, gene expression, metabolic and hormone regulation, mood, and vigilance, though these pathways are not completely understood.[24,92,105-108] While two recent meta-analyses concluded there was no association between the ApoE-ε4 allele and sleep apnea in the overall population,[109] Xu H et al. noted that there were associations between the two when considering risk of cognitive disorders.[110] The sleep-cognition link may be mediated by cardiovascular disease risk factors, and other health behaviors influenced by sleep.[111] As stated, the ApoE-ε4 allele and poor sleep jointly impact cognitive function, leading to elevated risks of cognitive impairment, while improved sleep seems to reduce the incidence of dementia and cognitive decline those with ApoE-ε4

allele.[34,36,111-114] It has been hypothesized that chronic systemic inflammation characterizes all these conditions and links poor sleep, ApoE-ε4, and AD, a pro-inflammatory condition itself.[115] While this three-way link provides critical guidance for intervening upon poor cognitive outcomes via modifiable sleep, this association has yet to be explored in the Latino population.

2.1.3 Apolipoprotein E-ε4

ApoE-ε4 is an established genetic risk factor for cognitive impairment and AD.[116-120] At least 60% of those diagnosed with AD have at least one allele,[78] and the ε4 allele accounts for at least 50% of the genetic attributable risk.[121,122] ApoE is a pleiotropic gene and lipid binding protein that transports triglycerides and cholesterol in multiple tissues, and its role is critical to the central nervous system and brain. The ApoE-ε4 allele specifically participates in metabolic interactions, especially when ε4 is delipidated, and is structurally different, which leads to different binding profiles and lipoprotein preferences, when compared to the other ApoE alleles. In turn, the ε4 allele leads to elevated pro-atherogenic lipoproteins, an accelerated trajectory towards atherogenesis, a higher likelihood of hyperlipidemia and cardiovascular disease, and thus, an increased risk of AD.[78]

A recent review found that ApoE-ε4 has a differential effect by age and sex: previous studies have found a reduction in risk after the age of 85 in both sexes, a risk curve five years earlier among women, and with the presence of two alleles, an increased and earlier risk curve by ten years for both sexes.[78] Additionally, differences in the acceleration of cognitive decline between men and women are greatest among women carrying the ε4 allele.[74] (For further information, please see *Supplemental Table 2*: ApoE genotype and AD by sex.) The underlying interactive mechanisms for increased risks among carriers remains unclear, and not all ApoE-ε4 carriers develop cognitive impairments.[123] Previous research has found a lower prevalence of the

ApoE-ε4 genotype in Latino groups when compared to non-Hispanic Whites,[8,42] which further suggests that unexplored and complex mechanisms may lead to Latinos' disproportionate burden, in both ε4 carriers and non-carriers. Gene-environment interactions, specifically those involving ApoE-ε4, may be key determinants of the development and progression of cognitive decline.[123,124] Disparities research should focus on the joint impacts of ApoE-ε4 and modifiable risk factors and the differential risk among carriers and non-carriers in Latino groups to provide insight into factors driving the disproportionate burden.

2.1.4 US acculturation

Culture is comprised of beliefs, traditions, language, and social interactions that shape health. Knowledge of one's broad cultural orientation provides insight about these compositional cultural factors and how they influence downstream health behaviors and conditions.[125] The Latino population has diverse ancestral origins (e.g. Mexico, Puerto Rico, etc.) and a large foreign-born population, leading to rich cultural variation that is often guided by the dynamic process of acculturation.[44]Acculturation defines the dynamic process by which individuals adapt to a new living environment and adopt the norms, values, and practices of that environment.[45] While the direction and magnitude of acculturation-health associations can vary by health factor, the concept of negative acculturation whereby a high cultural orientation to the US (vs. birth or ancestral country) is associated with worse health (i.e. many harmful health behaviors and poor health conditions) has been well-described [43-46,48-51]

In alignment with this concept, many risk factors of dementia such as alcohol use, smoking, poor sleep, diabetes, and other cardiovascular outcomes have been linked to high US acculturation.[8,10-14,43-46,48-51,92,108,126-132] Further, a growing body of literature has found that proxies of US acculturation are associated with worse sleep (e.g. too short or long sleep

durations, sleep complaints) among Latinos.[13,29,30,53-57] However, not all risk factors of sleep dementia are consistent with the negative acculturation hypothesis. For example, smoking, poor diet, high body mass index (BMI), and cardiovascular disease, have been linked to increased US Latino acculturation.[13,29,48,50,126-128,133-139] Conversely, healthy behaviors positively associated with sleep, like physical activity, are linked to US nativity (vs. foreign-born).[140] and for many chronic diseases and mental health disorders, the direction of influence of acculturation is unclear. Additionally, those who are more acculturated have been found to have improved access to care and use of preventative services, especially for women.[50] These behaviors and conditions have been found to be predictive of sleep health and cognitive function across the lifecourse.[12,65,131,141,142] Studies are often limited by the use of acculturative proxies that do not capture the complexities of acculturative change that measure adherence to American values and guide pathways between acculturation and health.[45-47] For example, increased US cultural orientation (i.e. higher US acculturation) in Latinos may be defined as being US-born, dominantly speaking the English language, number of years residing in the US, or as some combination of these factors.[13,29]

The acculturative experiences of preceding generations may impact sleep and health through separate mechanisms that a single-generation snapshot cannot capture.[44,46,143] For example, a US-born Latino may have one, both or no parents born outside the US resulting in varying degrees of acculturation and cultural transmission. First, acculturation can become biologically embedded and transmit to offspring via fetal programming (e.g. acculturative stress leads to elevated cortisol levels during pregnancy that impact offspring outcomes[144,145]) to impact subsequent generation health regardless of present life conditions.[143] Second, post-natally, parental acculturative behaviors and practices, including healthcare utilization, can be learned,

reinforced, and shape development to impact offspring health and sleep (e.g. parental sleep behaviors, diet, breastfeeding practices).[44,143] Therefore, single-generation cultural measures do not stand alone and intergenerational acculturation assessments provide context into how the culture and health of previous generations can become biologically embedded and shape the lifecourse culture and health of subsequent generations

The cultural exchange entailed in acculturation is facilitated and reinforced by structural socioeconomic determinants that are fundamental to the adaptation process.[45,49] Understanding how US acculturation operates across multiple spheres of influence (**Figure 4)** and along with socioeconomic factors, patterns cognitive functioning and sleep among Latinos may identify an over-arching cultural framework with specific underlying mechanistic pathways to explore in future research, the results of which would provide targetable points of intervention and inform the development of efficacious prevention and intervention efforts. Accounting for these complexities in Latino research enables us to effectively disentangle the influential role of acculturation on sleep, cognition, and dementia risk.

2.1.5 Socioeconomic position (SEP)

Socioeconomic position (SEP) is comprised of educational attainment, income, wealth, poverty, and other resource- and prestige-based characteristics.[146,147] The link between SEP and health is well-documented whereby SEP determines living and working conditions, social and psychological interactions in private and public settings, and health knowledge and access. Low SEP often leads to poor living and working conditions that harm health and reduce longevity.[147] These associations are not attributable to a single SEP component; rather, SEP components determine health through interconnected pathways that are dynamic across the lifecourse, and each component can shape health through different, though interrelated, pathways.[147] However,

single SEP components are often treated as proxies of SEP in research because SEP is challenging to quantify, though these proxies do not capture the complexities of SEP.[146]

2.1.5.a Educational attainment

Educational attainment is an important SEP component that influences other components- for example, educational attainment often sets an occupational and income trajectory, which can also be linked to working conditions.[146] More education is associated with better SEP and improved health outcomes, including cognitive performance and dementia risk.[148,149] More education has been hypothesized to improve cognitive outcomes via SEP pathways and enhanced cognitive reserve,[148-152] as an enhanced reserve may reduce the clinical expression of the physical brain degeneration that is characteristic of dementia.[151]

Education may modify the relationship between acculturation, health, and dementia as increased educational attainment is linked to measures of high US acculturation[47,51,153] and to reduced dementia risk.[148-150] Haan et al. (2011) found that more advantaged lifetime SEP trajectories, that included education, had better cognition, and that these advantages were greater in participants of fewer immigrant generations (i.e. less acculturated), indicating that a higher SEP confers a greater cognitive benefit in those with less US acculturation.[153] Similarly, Zeki al Hazzouri et al. (2015) found that low education across generations differentially increased poor metabolic outcomes, risk factors for poor sleep and cognitive outcomes, among US-born and foreign-born Latinos, whereby low educational trajectories were more harmful for foreign-born participants.[154] SEP has also been shown to modify the harmful association between cardiovascular risk factors and dementia/CIND; a protective benefit of high education can still be observed but to varying degrees dependent upon the exposure.[155,156]

2.1.5.b Occupational category

Occupation is another important indicator of SEP. There are clear gradients of health by occupation and the associations are complex and likely bi-directional. Occupations may enhance health through higher SEP trajectories (e.g. non-manual occupation), but individuals with higher education and improved health may also select into better working conditions. Broadly, more strenuous working conditions are associated with higher mortality and worse health outcomes (e.g. manual vs. non-manual). Manual and non-manual occupational categories are commonly used to group different types of working conditions whereby manual labor tends to require less education, more strenuous activity, and generally poorer working conditions.[157]

Occupation and working conditions can directly pattern sleep through shift work, job strain, and financial stress.[158] The prevalence of short sleep duration has been shown to vary by broad occupational category. Shift work has been linked to shorter sleep durations[159] and non-manual work has been linked to more sleep disturbances.[160] Associations between occupation and sleep duration among Latinos have been shown to vary by nativity and sex. A study by Jackson et al. (2014) found that among Latinos, the prevalence of short sleep duration increased with more professional/managerial roles, except for non-US-born women.[158] Conversely, short sleep duration tended to decrease with increasing professional/management roles among Whites. For women, the prevalence of short sleep was higher among US-born Latinos than non-US-born Latinos within all occupational categories, except laborers; there was not much variation observed by immigration status for men.[158]

2.2 Existing studies

2.2.1 US acculturation and sleep

Acculturation-sleep research in Latinos is limited, the existing studies have shown that being US-born (vs. both foreign born and non-Hispanic Whites),[29,30,53,54] living in the US for

longer durations,[29] and increased English language competence[55] were associated with increased sleep complaints and shorter duration of sleep. Research further hypothesized that these association were attributable to increased stress, increased prevalence of negative health behaviors such as smoking, differing attitudes towards sleep,[30] or a higher tendency to report sleep complaints among those categorized as highly acculturated towards the US.[29,30,54,55]

2.2.2 US acculturation, cognitive decline, and dementia

The relationship between US acculturation and cognition in Latinos is unknown, but associations between cognitive outcomes and known proxies have been examined.[58-64] For example, bilingualism has been explored as advantageous for cognition as some have hypothesized it may improve executive function and expand cognitive reserve, but findings have been inconsistent.[58-62,64] Others have focused on migration as a determinant for cognitive outcomes via different pathways, including more access to health and social services and improved socioeconomic status after migration, as well as detrimental factors like loss of social support, and increased stress and tobacco use. Xu et al. (2017) conducted a systematic review exploring migration-cognition research, and also found inconsistent results across the literature.[63] Again, while these proxies are closely linked to acculturation, they are single proxies that do not include assessments of beliefs, behaviors, and interactions that are essential for mapping the underlying behavioral and health mechanisms between culture, cognition, and dementia.[45,63]

A large body of literature has explored health behaviors and conditions that are shaped by acculturation as predictors of cognitive outcomes. For example, alcohol use, smoking, poor sleep, diabetes, and other cardiovascular outcomes linked to high US acculturation[13,45,48,50,126-129] are associated with worse cognition and dementia[8,10-12,14,92,108,130-132] Conversely, factors like social support and high education/SEP that are beneficial for cognition[10-12,148-150,161-163] have been

linked to high US acculturation or its proxies.[44,51,153] Moreover, risk factors for poor cognition and dementia like poor mental health and stress[11,12,164-169] have been linked to low host country acculturation.[170,171] Thus, pathways between high US cultural orientation and cognitive outcomes can characterize both harmful and advantageous associations.

2.3 Significance

The Latino population is disproportionately burdened by cognitive impairment in the US when compared to other racial/ethnic populations.[6,9,76] Research has found that some groups of Latinos suffer a greater incidence of AD then Whites in the US,[76,172] and this has been found across different adult age groups.[6] They are also more susceptible to delayed or missed medical diagnoses, which likely exacerbates the perceived greater burden.[76] As a whole, the Latino population is growing in the US, and as the elderly population increases in the US, the elderly Latino population is projected to increase dramatically.[15,89] The demographic shift to more elderly Latinos presents a critical need for cognitive research in this high-need minority population.[77] Not only is cognitive research in US Latinos limited, but there is evidence that Latinos have different risk profiles than other racial/ethnic populations.[8,42,76,77] For example, ApoE-ε4 is an established genetic risk factor for cognitive impairment and dementia, yet its prevalence appears to be slightly lower in Latino populations, raising questions as to what may be driving the disproportionate burden.[8,42] A lack of knowledge on the risk factors for cognitive impairment in the Latino population severely hinders prevention and intervention efforts and some of those identified in other populations may or may not be effective among Latinos.

The proposed research addresses sleep as a risk factor among Latino populations and acculturation, or cultural orientation, to the US as an over-arching concept to help understand what health factors are driving the disproportionate cognitive burden. Comprehensive sleep health research is lacking in the US Latino population[13] and sleep has been hypothesized to

contribute to substantially contribute to health disparities.[17,38,54,104] While current cognitive research often explores health behaviors and outcomes as risk factors, our proposed research seeks to explore modifiable upstream sociocultural exposures to disentangle the downstream risk behaviors and outcomes to guide future research seeking modifiable targets.[111]

The significance of the proposed research is also highlighted by our examination of cultural, socioeconomic, and familial influences, with consideration for gene-environment interactions, along this poorly understood pathway. The Latino population differs from other populations, and contains great diversity within itself, in terms of language use, resources, socialization, attitudes, and beliefs. When considering acculturation and health, we must account for the multiple spheres of influence and the structural socioeconomic determinants that facilitate health resources, behaviors, and outcomes.[45,49] The culturally-integrative approach of this research strengthened the ability to effectively target modifiable socioeconomic and behavioral risk factors of cognitive impairment and dementia in our primarily Mexican-origin US population.[44,173-176]

Thus, the proposed research:

(1) Examined over-arching individual and intergenerational sociocultural determinants of poor sleep, cognitive performance, dementia to disentangle the many health pathways that comprise the complex etiologies of both, and

(2) Explored sleep and cognitive associations, with consideration for contribution of ApoE-ε4 genotype, an association well-studied in another racial/ethnic population that lack the same sociocultural and health risk profiles of Latinos, and

Given reproducibility, these findings guide the exploration of modifiable targets in future research to ultimately inform poor sleep and dementia prevention and intervention efforts, and help shape these efforts with a cultural framework.

2.4 Supporting tables and figures

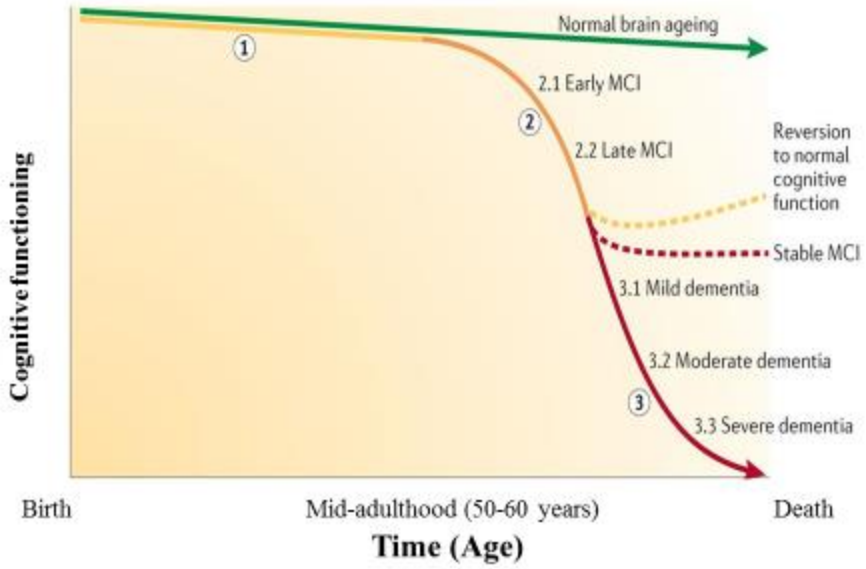

Figure 2. Cognitive functioning across the lifecourse.
Modified from: Hampel H, Lista S. Dementia: the rising global tide of cognitive impairment. Reviews Neurology. 2016; 12:131–132.[1] with Alzheimer's Disease: Unraveling the Mystery. National Institute on Aging. National Institutes of Health. US Department of Health and Human Services. [2]

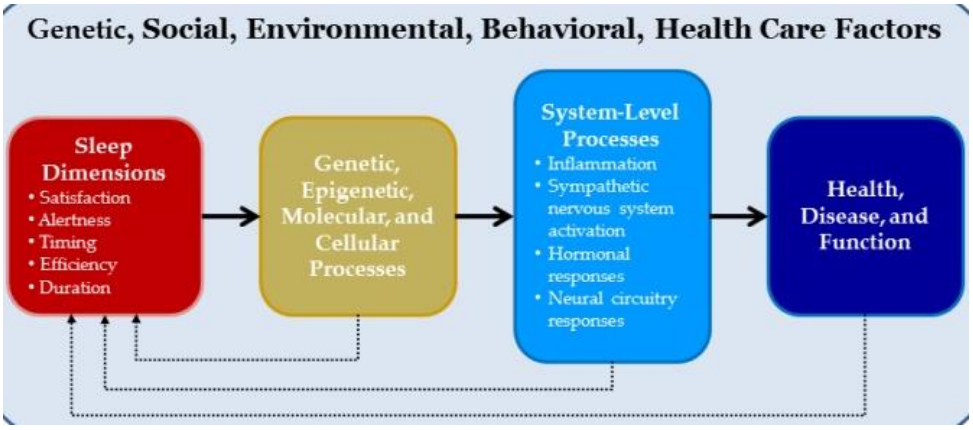

Figure 3. Simple conceptual model of the relationship between sleep dimensions and health.[94]

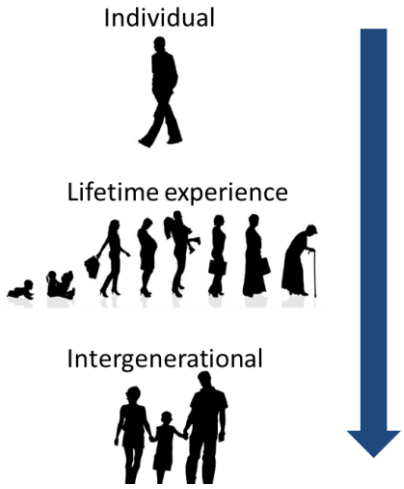

Figure 4. Levels of interpersonal influence across the lifecourse.

2.5 Supplemental tables

Supplemental Table 1. Key brain disorders that cause dementia.[75]

Brain disorders	Characteristics
Alzheimer's disease (AD)	Associated with the death of nerve cells (neurons) in important parts of the brain Brains develop deposits (known as plaques) of a protein called beta amyloid Develop disorganized masses of protein fibers within the brain cells known as neurofibrillary tangles. Unknown why and how AD develops
Vascular dementia	Lost or damaged areas of brain due to reduced blood flow → blood vessels in the brain get clogged with blood clots or fatty deposits More common among people who have had strokes or are at risk for strokes, especially those with longstanding high blood pressure and diabetes Can co-occur with AD
Dementia with Lewy bodies	Caused by abnormal protein structures (Lewy bodies) forming within brain cells Co-occurs with symptoms of Parkinson's disease, such as trembling, stiffness, and slowness Often causes vivid and long-lasting hallucinations. Can cause people to act out their dreams
Parkinson's disease (PD) dementia	Occurs later in the course of Parkinson's disease Similar symptoms to dementia with Lewy bodies
Frontotemporal dementia (FD)	Causes nerve cell loss in the brain- targeted in the frontal and temporal lobes Usually arises at an earlier age than AD *Three manifested forms are most common:* 1) Personality changes and abnormal social behavior 2) Impaired speech that leads to loss of speaking abilities 3) Difficulty understanding language
Mixed dementia	Common among more advanced older age (≥85 years) Often a combination of both AD and vascular damage
Other causes of dementia	Cumulative damage to the brain - can occur in people with chronic alcoholism or repeated head injuries (common among former professional boxers or football players)

Supplemental Table 2. Protective and risk factors of Alzheimer's disease associated with APOE genotype by sex**.***

Genotype	Sex	Findings
ε2/ε2	Males	More severe lipidemia and atherosclerosis due to high plasma ApoE.
	Females	Reduced AD risk in women <85, increased after age 85.
	General	Increased prevalence of hyperlipidemia and cardiovascular disease. ApoE concentrations are generally the highest in this group, protecting from AD.
ε2/ε3	Males	Increased AD risk due to higher incidence of insulin resistance.
	Females	Estrogen and estrogen replacement therapy improve insulin sensitivity, compensating for the increased risk in males. Reduced cardiovascular risk and AD risk in women <85, increased after age 85.
	General	Associated with increased longevity and protection from AD.
ε3/ε3	Males	Potentially protective against AD, although at higher risk than genotype-matched females.
	Females	MCI patients show lowest levels of phosphorylated tau, associated with delayed disease progression. More favorable cerebrospinal fluid amyloid profiles than ε3/ε3 men. Lowest AD risk compared to males and all other ApoE genotypes in females Increases in ApoE concentration with age provide protection from AD risk. Associated with increased longevity and protection from AD.
	General	Protective against AD.
ε2/ε4	Males	Increased risk of cardiovascular disease compared to ε3/ε3 individuals.
	Females	Protection from cardiovascular risk and AD.
	General	Greater AD risk in individuals of European descent. Evidence of brain amyloid accumulation occurs 10–15 years later than in ε4/ε4 carriers.
ε3/ε4	Males	Increased risk for MCI and AD, although slower decline.
	Females	Significant effects on risk for decline in episodic memory. Higher MCI and AD risk than non-ε4 carriers and male ε3/ε4, comparable to ε4/ε4 men. Increased likelihood of pathological levels of cerebrospinal fluid tau and tau/amyloid beta ratio Compared to ε3/ε4 men, faster age-related cognitive decline and longer survival rates.
	General	In 70+ normal ε4 carriers have greater amyloid positron emission tomography than other genotypes. Greater AD risk in individuals of European descent. Evidence of brain amyloid accumulation occurs 10–15 years later than for ε4/ε4 carriers.
ε4/ε4	Males	Higher risk of MCI and AD than ε3/ε4 or ε2/ε4 males or ε3/ε4 and ε4/ε4 females.
	Females	Comparable AD risk to ε3/ε4 females; longer survival rates following AD diagnosis.

Genotype	Sex	Findings
	General	Over 30% develop AD by age 75, with greater risk in individuals of European descent. ApoE concentrations are generally the lowest in this group, a predictor of AD risk. Highest risk for brain amyloid beta accumulation.
General ε4 findings	Males	Years of life lost in men ε4 carriers are greater than in genotype-matched women.
	Females	Greater prevalence of AD in female ε4 carriers than males. Greater alterations in precuneus and anterior cingulate cortex connectivity. Associations between ApoE and cognitive decline evident later in females. More prominent phenotypic features in female MCI ε4 carriers − reduced hippocampal volume and worse cognitive scores. Cerebrospinal fluid tau, phosphorylated tau, and tau/amyloid beta-42 levels highest in MCI ε4 carriers compared to non-carriers with MCI, particularly for females. Women ε4 with mild-AD are more likely to have both neurofibrillary tangles and amyloid than ε4 men, indicating greater pathology. Postmenopausal ε4 women on estrogen replacement therapy exhibit signs of neuroprotection and preservation of telomere length compared to ε4 women not receiving treatment.
	General	ApoE-ε4 show greater neural efficiency on episodic memory tasks and better performance in speed of processing, attention, and verbal fluency until mid-50′s when declines are evident. Reduced myelin integrity in AD-relevant regions evident in infancy. Increased dementia risk (AD, Parkinson's disease dementia, vascular dementia, and dementia with Lewy bodies) and cardiovascular risk. Carrying one ε4 allele shifts the AD risk curve 5 years earlier (OR=3.5–4). Two alleles shifts the AD risk curve by 10 years (OR=12-15). ApoE-ε4 exerts its maximal effects on AD risk by the early 70′s. Up to 65% of individuals with AD harbor at least one ε4 allele. Cerebrospinal fluid amyloid β less predictive of conversion from normal to MCI than for other genotypes. By age 40, 15% cognitively normal ApoE-ε4 carriers are amyloid positive.

*Adapted from Riedel BC, Thompson PM, Brinton RD. Age, ApoE and sex: Triad of risk of Alzheimer's disease. J Steroid Biochem Mol Biol. 2016;160:134-47.[78]
Abbreviations: AD: Alzheimer's disease; MCI: Mild cognitive impairment; OR: Odds ratio.

CHAPTER 3: METHODS

3.1 Overview

We aimed to disentangle the complex sociocultural and health pathways contributing to the disproportionate burden of poor cognition and dementia among US Latinos (see **Table 1** for overview of aims).

Specifically, we aimed to:

1) Investigate the associations between a validated measure of US acculturation in individuals and across generations and measures of sleep, including the modifying role of educational attainment and major lifetime occupational category;
2) Determine the influence of US acculturation at study onset with cognitive performance and incident dementia/CIND over a 10-year period, including the modifying role of educational attainment;
3) Analyze the influence of sleep measures at baseline with cognitive performance and incident dementia/CIND over a 10-year period, including the modifying role of the ApoE-ε4 genotype.

We utilized data from an intergenerational cohort comprised of two separate study populations of primarily Mexican-descent community-dwelling Latinos in California's Sacramento Valley: first generation older Latinos from the Sacramento Area Latino Study on Aging (SALSA) collected over 10 years and second generation (GEN2) middle-age Latinos from the Niños Lifestyle and Diabetes Study (NLDS), comprised of offspring and other biological relatives of the GEN1 SALSA participants. Results from this study provide an understanding of

how an over-arching cultural orientation, and its mechanistic socioeconomic and health pathways, associate with poor sleep, cognitive impairment and decline, and dementia in the understudied and disproportionately burdened US Latino population. It also provides future research with guidance for modifiable health pathways to explore as mediating mechanisms and to ultimately inform prevention and intervention tactics and reduce sleep and cognitive disparities. Poor sleep, cognitive impairment, and dementia are poorly understood disorders that negatively impact multiple health behaviors and outcomes.

3.2 Data source and study population

3.2.1 Description of the GEN1 SALSA and GEN2 NLDS cohorts

Sacramento Area Latino Study on Aging (SALSA), the first generation or GEN1 of the intergenerational cohort, is a longitudinal cohort study of 1,789 community-dwelling Mexican Americans residing in Sacramento, California region aged 60–101 years at baseline (1998–1999). The majority of the participants were born in Mexico (51%) or the United States (49%), less than half were male (41.7%), and participants were aged on average 70.65±7.13 years at baseline. Participants were followed every 12–15 months via home visits for a total of 7 follow-up visits, ending in 2008.[8] Participants reported health conditions, lifestyle and sociodemographic risk factors, medications, and provided clinical and cognitive assessments in interviews. Fasting blood samples were drawn for glucose, insulin, and lipids. Buccal cells were obtained for genetic analysis of ApoE.[8] Annual attrition from baseline through 2008 averaged 5%, including mortality and loss to follow up.[8,177]

Niños Lifesyle and Diabetes Study (NLDS), the second generation or GEN2 of the intergenerational cohort, were recruit offspring and other biological relatives of SALSA participants. Any living English- or Spanish-speaking biological relatives of the 1,789 SALSA parents aged 18+ years were eligible to participate in NLDS. The majority of participants were

born in the US (75%) or Mexico (23%), female (64%), and on average aged 53.45±11.83 years at baseline. Trained interviewers collected data at baseline (March–November 2013) and follow-up 12–18 months later (May–November 2014). New participants were also interviewed during Wave 2. Wave 1 baseline data was collected in 2013 (N=563) from offspring participants, and wave 2 follow-up data was collected in 2014 (N=495). Each wave of data collection included a 30-minute telephone interview, and a 2-hour home visit that included an interview, anthropometric measurements, blood draw, and medication inventory. The study collected data about health conditions, lifestyle and sociodemographic data, and clinical and cognitive assessments in these interviews.

3.2.1.a Preliminary findings

GEN1. Much research has been conducted on cognitive function and dementia in SALSA participants. GEN1 had a dementia prevalence of 4.8% for those aged 60 years and older, with an annual incidence of 0.8%.[8,178] The prevalence increased to 31% for those aged 85 years and older.[8] Among the 85% (N=1,614) of parents genotyped for ApoE-ε4, the prevalence of ApoE-ε4 has been reported as 4%, which is slightly lower than some studies examining ApoE-ε4 in other Mexican-descent populations.[8] However, this population is older than populations from other studies and research shows the frequency of ApoE-ε4 tends to decline with age, potentially as a function of differential population selection, which may explain the lower ε4 frequency. Additionally, participants homozygotic for ApoE-ε4 appear to have higher dementia risk and lower cognitive scores.[8]

When exploring risk factors of accelerated cognitive decline, research has shown links with type 2 diabetes;[179,180] obesity, modified by leptin;[181] lifecourse educational attainment;[153,182] lifecourse SEP;[183] depression and spousal depression, modified by sex;[184] and ApoE-ε4, often

modifying effects of other risk factors.[124] Previous SALSA studies examining baseline cognitive impairment have shown its associations with cardiovascular risk scores;[155] reduced heart rate variability;[185] stroke;[8] abdominal fat in late life;[186] homocysteine level,[187] modified by B-vitamin status;[178] red blood cell folate level;[188] white matter hyperintensities;[189] type 2 diabetes;[180,190] depression and spousal depression, modified by sex;[184] educational attainment, modified by migration status;[191] lifecourse SEP;[183] and neighborhood SEP.[182] When evaluating risk factors of dementia, findings have shown that stroke;[8] cardiovascular risk scores;[155] abdominal fat in late life;[186] homocysteine level, modified by B-vitamin status;[178] folate levels;[188,192] type 2 diabetes;[8,190,193] and lifecourse SEP[183] elevate the risk.

Previous SALSA studies exploring health outcomes associated with acculturation found that high US acculturation was associated with lower systolic blood pressure, better lipid profiles, a lower prevalence of cardiovascular disease[194] and a lower prevalence of depression[195] when compared to participants with low US acculturation, indicating a protective effect of high US acculturation. However, increased assimilation to the US, as measured by immigrant generation, was found to be associated with an increased diabetes risk in parents.[196]

3.2.2 Inclusion criteria

For Aim 1 analyses we included participants with acculturation data at baseline and any sleep measure at baseline. For Aim 2 analyses we included participants with acculturation data at baseline and cognitive assessments from at least on one occasion; for incident dementia/CIND analyses, we included participants with information on whether or not dementia/CIND was diagnosed. For Aim 3 analysis we included those with self-reported sleep data at baseline and cognitive assessments from at least on one occasion; for incident dementia/CIND analyses, we included participants with information on whether or not dementia/CIND was diagnosed.

3.2.3 Exclusion criteria

We excluded participants who lacked the data needed for inclusion as noted in **Section 3.2.2. Inclusion criteria.** To evaluate the association between US acculturation and incident dementia/CIND, we excluded participants with dementia/CIND at study onset.

3.3 Measures

3.3.1 Exposure definition and assessment

3.3.1.a US acculturation

GEN1 and GEN2. Acculturation was measured using the Acculturation Rating Scale for Mexican-Americans – Version II (ARSMA-II)[197] at baseline in parents and at both waves of data collection in offspring. ARSMA-II measures acculturation among three main factors: language, ethnicity identity, and ethnic interaction.[198] The primary ARSMA-II scale consists of 30 items within two subscales that quantify orientation towards the Anglo (herein referred to as US) culture (AOS) and the Mexican culture (MOS) within four factors: 1) language use and preference, 2) ethnic identity and classification, 3) cultural heritage and ethnic behaviors, and 4) ethnic interaction.[198] Each item is scored on a Likert scale from 1 (not at all) to 5 (extremely often or almost always); the AOS contains 13 items (Cronbach's alpha for internal consistency=0.83) and the MOS contains 17 items (Cronbach's alpha=.88).[197,198] Each participant received a mean MOS score and a mean AOS score. The MOS mean was subtracted from the AOS mean to obtain a score along a Mexican to Anglo/US cultural orientation continuum. A lower score indicates a higher Mexican cultural orientation and a higher score indicates a higher US cultural orientation.[198] We defined a "high" US cultural orientation score as greater than or equal to 0. Scores below 0 were defined as "low" US cultural orientation.

3.3.1.b Intergenerational US acculturation

GEN1. We used immigrant generation as an intergenerational acculturation proxy among SALSA participants. Participants reported their nativity and the nativity of their parents. We used this information to create a three-level immigrant generation variable[196] as a proxy of intergenerational US acculturation. A foreign-born participant was categorized as a first generation immigrant; a US-born respondent with at least one foreign-born parent was categorized as second immigrant generation; and US-born participant with two US-born parents was categorized as third generation.

GEN2. Measures of intergenerational acculturation were classified into three parent/offspring acculturation categories: low US acculturation, stable-low (low /low) and downwardly mobile (high/low); upwardly mobile (low/high); and stable-high (high/high). We grouped stable-low and downwardly mobile acculturation into one low US acculturation category due to the low prevalence of downwardly mobile pairs.

3.3.2 Outcome definition and assessment

3.3.2.a Cognitive performance

GEN1. Cognitive impairment was assessed using two tests: Modified Mini-Mental State Examination (3MSE) and Spanish English Verbal Learning Test (SEVLT). Diagnosis of cognitive impairment or significant cognitive decline from either test determined a positive diagnosis. The 3MSE is a 0-100 point cognitive exam composed of several cognitive domains that provides an assessment of global cognitive function. It offers a brief assessment of attention span, concentration, orientation to time and place, long- and short-term memory, language capabilities, abstract thinking, and list-generating fluency.[199] The 3MSE has been validated and field tested in both English and Spanish and been found to have strong test-retest properties[199,200]

and high inter reliability with a standardized alpha of 0.90.[201] Higher scores indicate higher cognitive function. A score below 78 was considered cognitively impaired (treated as dichotomous).[202] The SEVLT was administered to assess verbal memory recall with four 15-word memory trials, an interference list, and a fifth trial which was usually used as the test score.[203,204] SEVLT was developed for use in the SALSA study,[204] validated in both English and Spanish, and has been used in other studies.[185] Higher scores indicate better cognitive performance.[185,203] For the SEVLT, a score of ≤ 5 indicated cognitive impairment and a significant decrease from baseline was treated as ≥ 3 points. The 3MSE and SEVLT were administered at baseline, the first annual visit, and at five follow-up visits for a total of seven times. We log-transformed scores for decline and examined the errors (log[(high score+1)–score]); an increase in log(errors) over time indicates decline.[179,205]

3.3.2.b Dementia/CIND

GEN1. Dementia was determined at all home visits by a multistage assessment protocol with 3MSE and SEVLT.[203] At baseline, a participant was referred for further evaluation if his or her score on either test fell below the 20th percentile. At follow-up, a participant was referred for a neuropsychological test battery and a standard neuropsychological examination if the score declined from baseline by more than eight 3MSE points or more than three SEVLT points, or if it was below the 20th percentile. A team of neurologists and a neuropsychologist reviewed all potential cases and gave a diagnosis based on standard diagnostic criteria for dementia (Diagnostic and Statistical Manual of Mental Disorders-IV),[206] AD,[207] and vascular dementia.[208] For participants who died during the study period without a previous diagnosis of any type of dementia, dementia diagnoses were ascertained from death certificates based on the following causes of death listed anywhere on the death certificate: dementia in AD, vascular dementia,

other dementia, or unspecified dementia. We treated the presence of an incident dementia diagnosis (vs. no diagnosis) as dichotomous.

3.3.2.c Poor sleep and disorders.

Sleep measures differed between GEN1 and GEN2. GEN1 had more and different measures than GEN2, though an identical measure of restless sleep was available for both.

GEN1. We used five dichotomous (yes/no) measures: restless sleep; overall fatigue (a wake-time measure linked to sleep quality)[209]; waking up far too early; trouble falling asleep; and waking up several times a night. We examined restless sleep and overall fatigue as individual outcomes due to the literature base and interpretable connection to daily functioning and health[94,210] and all measures were used in a latent class analysis.

GEN2. We used five dichotomous (yes/no) measures: restlessness; three duration variables; and a self-reported sleep apnea medical diagnosis. Participants answered how long they sleep on weekdays and weekends and we created a weighted average of sleep per night throughout a week. We created three separate duration variables with the average dichotomized at informative cut points (averages of <5, <6, and <7 hours of sleep/night) based on sleep recommendations and sleep duration-health literature.[97,211-214] In GEN2, restless sleep data was collected via phone survey for all NLDS participants; sleep duration and sleep apnea data were collected at home visits for a sub-sample of NLDS participants consenting to a home visit (N=483). NLDS participants who agreed to a home visit were similar in sociodemographic and cultural factors to the total NLDS population.

3.3.3 Covariate definitions and assessments

3.3.3.a Educational attainment, potential effect measure modifier.

GEN1 AND GEN2. Participants were asked to provide the highest completed degree of education. We dichotomized educational attainment as "low" for less than 12 years (no high school degree/general education diploma [GED]) and "high" as more than or equal to 12 years for parents. This cut point has also been used previously in other SALSA (GEN1) studies and in studies with similar populations.[154,215] For GEN2, we dichotomized education as low (<13 years) or high (≥13 years). This cut point is higher for offspring than for parents because there are age- and location-related differences in education levels between the two generations/cohorts,[216] and offspring have a higher median educational attainment.

3.3.3.b Major lifetime occupational category, potential effect measure modifier.

GEN1. Participants were asked "what job did you do most of your life?" and responses were categorized with census codes: manual, non-manual, and other (which included housewives and unemployed).[182,217]

3.3.3.c ApoE-ε4, potential effect measure modifier.

GEN1. Participants provided serum samples or buccal cell swabs for ApoE-ε4) genotyping at baseline. DNA was extracted using the PureGene DNA Extraction Kit (Gentra Systems). Genotype and allele frequencies (ε2, ε3, or ε4) were determined by polymerase chain reaction amplification followed by restriction enzyme digestion.[218] The ApoE genotype was in Hardy-Weinberg equilibrium. We dichotomized the presence of any ApoE-ε4 allele (ε2/4, ε3/4, and ε4/4) as 1, and 0 (ε2/3 and ε3/3) if absent.

3.3.3.d Other covariates.

GEN1 and GEN2. We considered sociodemographic variables, lifestyles factors, general health, and anthropometric measures. Sociodemographic variables included nativity, age, sex, education, income, employment status, major lifetime occupation, and marital status. We considered acculturative factors like language use, duration in the US, age of arrival in the US, and immigrant generation. We also considered self-reported health, mental health disorders (depression, anxiety), chronic health, body mass index (BMI), medication use, insurance status, and lifestyle factors such as diet, physical activity, smoking status, and alcohol use. These factors were self-reported in home visit and phone surveys or measured and recorded by trained data collectors. Depression was measured by the Center for Epidemiologic Studies Depression scale.[216,219] Diagnosis of chronic diseases, including diabetes and cardiovascular health as measured by occurrence of myocardial infarction, angina, catheterization or coronary artery bypass grafting, stroke, heart failure, or atrial fibrillation.[220] BMI was calculated using the formula weight in kilograms divided by the square of height in meters with data measured and recorded by trained data collectors.[196]

3.3.4 Sensitivity measures

We conducted sensitivity assessments to explore whether language acculturation drove acculturation and cognitive outcome associations. Language is an important driver of the acculturative process that also shapes cognitive development and performance through multiple mechanisms [47,58-62,64]. We parsed apart the ARSMA-II acculturative scale into two groups of questions: 1) *language* (media and communication language preferences) and 2) *practice and identity* (i.e. non-language measures of social interactions, ethnic identity, and traditions), and calculated acculturation scores for each group to produce a language US acculturation score and

a practice and identity US acculturation score. We dichotomized each score for high/low categories and treated each as a sensitivity exposure to compare results between language acculturative factors and practice and identity acculturative factors.

3.4 Statistical approach

The overall goal of dissertation was to address three gaps in our understanding of Latino cognitive disparities: the associations between (1) sociocultural mechanisms and sleep, (2) sociocultural mechanisms, cognitive decline, and dementia, and (3) sleep, cognitive decline, and dementia, with exploration of ApoE-ε4 genotype. Briefly, the proposed analytical approach consists of cross-sectional and longitudinal analyses that account for family clustering within intergenerational analyses, latent class methods for a multidimensional sleep measure, and competing risk regression models to account for the competing risk of death in dementia/CIND analyses. We also assessed effect measure modification by socioeconomic factors and ApoE-ε4 genotype throughout our research aims. Statistical analyses were performed with SAS 9.4 (SAS Institute, Inc., Cary, North Carolina).

3.4.1 Variable selection

For all research aims and models, we first assessed selected covariates in directed acyclic graphs (DAGs) based on our theoretical knowledge of the literature to determine an adjustment set.[221] We then considered the adjustment set in the context of the literature to determine if there was a need to consider multiple adjusted sets. When considering whether covariates that were informative to our research question as explanatory variables, we considered a change-in-estimate approach of 10% or more as an important explanatory variable.[222]

3.4.2 Specific aim 1 (GEN1 and GEN2)

Aim 1a. Examine the associations between high US acculturation, in single generations and across generations, and poor sleep measures among adult Latinos in the US.

Hypothesis 1a. Single-generation and intergenerational high US acculturation will be associated with worse sleep outcomes than low US acculturation (i.e. a high acculturation towards another origin or ancestral country). Across generations, parent-offspring pairs who both have high US acculturation (stable-high) will be associated with worse sleep outcomes than pairs with upwardly mobile high US acculturation (low parent-high offspring US acculturation) or low intergenerational US acculturation (low parent-low offspring or high parent-low offspring).

Aim 1b. Assess the socioeconomic context of these US acculturation-sleep associations within levels of educational attainment and major lifetime occupational category.

Hypothesis 1b. Among low socioeconomic indicators, high US acculturation will be associated with worse sleep when compared to low US acculturation, but among high socioeconomic indicators, high US acculturation will be associated with better sleep or not associate with sleep when compared to low US acculturation.

3.4.2.a Approach

We used log-binomial models (**Equation 1**) to produce prevalence ratios (PRs) and 95% confidence intervals (CIs) to examine cross-sectional associations between a dichotomous measure of acculturation and dichotomous sleep measures. For intergenerational education, we compared each level of intergenerational acculturative mobility to low offspring US acculturation (combined stable-low and downwardly mobile categories).

Equation 1. Log-binomial equation:

$$ln(E[Y]) = \beta_0 + \beta_1 X_1 + \ldots . \beta_k X_k$$

Where Y = outcome ~ binomial; β_0 = log of the risk of Y among the unexposed; β_1 = difference in log risk of Y between the exposed and unexposed; X_1 = exposure; $\beta_k = X_k$ regression coefficient; X_k = covariate k.

We used generalized estimating equations (GEEs) to account for within-family clustering[223] for intergenerational analyses (GEN1 parent-GEN2 offspring linked pairs). GEEs enable estimation of parameters even when there is correlation between observations and produces parameter estimates that quantify population-average effects, by estimating and modeling the **covariance structure of the correlated responses (Equation 2).**[223-225] GEEs are robust to misspecification of the correlation structure, unlike the alternative mixed model regression.[223,226] We used GEEs to account for correlation between offspring from the same family and clustered by GEN1 identification number. The Huber-White sandwich estimator was used for robust standard errors.[227,228]

Equation 2. Model for generalized estimating equation J x J covariance matrix for outcome Y:

$V_i = \phi A_i^{1/2} R(\alpha) A_i^{1/2}$

Where $j = j$th outcome (for j=1,.,J); $i = i$th participant (for i=1,.,N); ϕ = GLM dispersion parameter; A = diagonal matrix of variance functions; $R(\alpha)$ = the working correlation matrix of outcome Y.

We used latent class analyses (LCA)[229] in GEN1 with five sleep measures (**Table 1**) to create latent classes of sleep. LCA provides an opportunity to capture the complex, interrelated, and perhaps unobservable, components of sleep that are difficult to measure.[94] We fit baseline models for multiple numbers of latent sleep classes (2-5 classes) and assessed the best statistical fit (likelihood ratio square statistics [G^2] relative to degrees of freedom [df]; Akaike information criterion [AIC]; Bayesian information criterion [BIC]). We used multinomial logistic regression and reported odds ratios (ORs) and 95% CIs for the odds of latent sleep class membership given US acculturation status in demographic- and sociodemographic-adjusted models.[230]

In all models, we used DAGs and substantive knowledge to identify confounders (**3.5.1 Variable Selection**).

In GEN1, we assessed effect measure modification by educational attainment and major lifetime occupational category by completing analyses within strata and comparing estimates.

3.4.2.b Statistical power

Aim 1a: With two-sided tests, alpha=0.05, and 80% power we are able to detect a minimum expected mean difference of 1.02 in sleep health between participants with high US acculturation (40-50%) and low US acculturation (N=1638). For offspring (N=390), we are able to detect a minimum expected difference of 1.04 in sleep health between the US acculturated and non-US acculturated participants.

Aim 1b: To examine the impact of intergenerational acculturation on offspring sleep health (N=390) with two-sided tests, alpha=0.05, and 80% power, we were able to detect a minimum expected difference of 1.05 in sleep health between offspring participants who have high US acculturation and those who have low US acculturation.

3.4.3 Specific aim 2 (GEN1)

Aim 2a. Examine the associations between high US acculturation and rate of cognitive decline and incident dementia/cognitive impairment, not dementia (CIND) over a 10-year period among adult Latinos of older age in the US.

Hypothesis 2a. High US acculturation will be associated with an accelerated cognitive decline and an increased risk of dementia/CIND.

Aim 2b. Assess whether educational attainment modifies the US acculturation-cognition and dementia association.

Hypothesis 2b. Among low educational attainment, high US acculturation will be associated with an accelerated cognitive decline and an increased risk of dementia/CIND when compared to low US acculturation. Among high educational attainment, high US acculturation will be associated with a slower rate of cognitive decline and a reduced risk of dementia/CIND or not associate with either outcome when compared to low US acculturation.

3.4.3.a Approach

Cognitive performance. We examined the association between dichotomized US cultural orientation (low/high) and log-transformed errors of cognitive performance and cognitive decline over 10 years with hierarchical linear mixed models[231] and repeated measures to model changes over time (**Equation 3**).[232,233] The data structure for this analysis included two levels: baseline and six follow-up time points (level 1) nested within participants (level 2). At level 1, we modeled the cognitive scores (logarithms of 3MSE errors) as a function of time. Time was operationalized as grand mean-centered age of cognitive measurement instead of calendar time, primarily cognition function changes as a function of age.[234] Baseline cognitive function (intercept) and linear rate of cognitive change (slope) were treated as random effects. 3MSE errors were log transformed (natural logarithm) to closely correspond to normal distributions as required by assumptions of the linear mixed model.[179,181]

Equation 3. Hierarchal linear mixed models:

Level-1 model (repeated measures):

$Y_{ti} = \beta_{0i} + \beta_{1i}(time_{ti}) + \varepsilon_{ti}$

Where β_{0i} = outcome for *i*th individual at initial time point when $time_{ti} = 0$; β_{1i} = average unit change in outcome for *i*th individual over time; ε_{ti} = within-individual random error with variance equal σ^2, capturing within-individual variation (i.e. $e_{ti} \sim N[0, \sigma^2]$).

Level-2 model (individual)

$\beta_{0i} = \gamma_{00} + U_{0i}$

$\beta_{1i} = \gamma_{10} + U_{1i}$

Where γ_{00} = average outcome at the initial time point (i.e. $time_{ti}$= 0); γ_{10} = average unit change in the outcome over all participants; U_{0i} and U_{1i} = between-individual random effects, assumed to be normally distributed.

Variance-covariance matrix: $\begin{pmatrix} U_{0i} \\ U_{1i} \end{pmatrix} \sim N\left[\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \tau_{00}\tau_{01} \\ \tau_{10}\tau_{11} \end{pmatrix}\right]$

Where U_{0i} = difference between the intercept (β_{0i}) of *i*th participant from the average intercept γ_{00}; U_{1i} = difference between the estimated unit change in outcome (β_{1i}) of *i*th participant from the average unit change in outcome across all participants; variances of U_{0i} and U_{1i} are τ_{01} and τ_{11}, capturing between-individual variation.

Incident dementia/CIND. We used competing risk regression models with the method proposed by Fine and Gray (**Equation 4**)[235] to assess the association between US acculturation (high/low) and incident dementia/CIND with cumulative incidence functions and hazard ratios (HRs) in participants free of dementia/CIND at study onset. Participants were observed from study entry until the date of dementia (the event of interest), death (the competing event), or censoring (last date of contact). Because of the strong association between dementia and age for all models, we used age at diagnosis, death, or censoring as the timescale and adjusted for baseline age.[234] Our method accounted for the fact that individuals who die prior to developing dementia will never develop dementia, and the association between acculturation and dementia depends on the association between acculturation and death.[236,237]

Equation 5. Fine and Gray's extension of Cox regression that models the hazards of the cumulative incidence function:

Sub-distribution hazard:

$\tilde{h}_k(t,x) = -\frac{d}{dt} log(1-F_k(t,x))$

Where $\tilde{h}_k(t,x)$ = hazard of the cumulative incidence function, "~" denotes sub-hazard for sub-cause *k*; *d* = outcome events of interest; *t* = time; $F_k(t,x)$ = cumulative incidence function for events of type *k* given a vector of covariates *x*;

Proportional hazards assumption on the sub-distribution hazards:

$\tilde{h}_k(t,x) = \tilde{h}_{k,0} exp(\beta'_k x)$

The estimation of regression coefficients is based on modified risk sets, where participants that experience a competing event are retained after the event. The weight of participants artificially retained in the risk sets is gradually reduced according to the conditional probability of being under follow-up had the competing event not occurred.

In all models, we used DAGs and substantive knowledge to identify confounders (**3.4.1 Variable Selection**).

We assessed effect measure modification by educational attainment by completing analyses within strata and comparing estimates.

3.4.3.b Statistical power

Aim 2: For a hierarchical linear mixed model including a random intercept with an average of N=1070 participants, seven cognitive observations per participant, and an assumed sample with 50% high US acculturation, we had 80% power to detect cognitive outcomes over time of 0.010, 0.014, and 0.018 for each unit change in time when between variance explains 67%, 50%, and 40% of the total variance, respectively.

3.4.4 Specific aim 3 (GEN1)

Aim 3a. Examine the associations between poor sleep and rate of cognitive decline and incident dementia/cognitive impairment, not dementia (CIND) over a 10-year period among adult Latinos of older age in the US.

Hypothesis 3a. Poor sleep will be associated with an accelerated cognitive decline and an increased risk of dementia/CIND.

Aim 3b. Assess whether ApoE-ε4 modifies the sleep-cognition and dementia association.

Hypothesis 3b. Among non-ApoE-ε4 carriers, high US acculturation will be associated with an accelerated cognitive decline and an increased risk of dementia/CIND when compared to low US acculturation. Among ApoE-ε4 carriers, we will observe the same associations as among non-ApoE-ε4 carriers, though with a higher rate of cognitive decline and an increased risk of dementia/CIND.

3.4.4.a Approach

Cognitive performance. We used hierarchical linear models with repeated cognitive assessments to examine the association between baseline measures of poor sleep (restless sleep and overall fatigue) and cognitive performance at baseline and decline over a 10-year period. (**Equation 3**).[231]

Incident dementia/CIND. We used Fine and Gray's competing risk regression models to assess whether baseline measures of poor sleep were associated with risk of dementia/CIND over a 10-year period in participants free of dementia/CIND at study onset (see **Equation 4**).[235]

In all models, we used DAGs and substantive knowledge to identify confounders (**3.4.1 Variable Selection**).

We assessed effect measure modification by ApoE-ε4 by completing analyses within strata and comparing estimates.

3.4.4.b Statistical power

Aim 3: We used a SAS simulation to fit a log-binomial model for cognitive impairment and dementia under assumptions that 50% of participants had poor sleep health and 50% had any ApoE-ε4 allele. Participants with better than poor sleep health and no allele had a 0.10 probability of cognitive impairment diagnosis. For a sample size of N=1548 and significance level of 0.05, we had 80% power to detect a PR of 1.25 for those with poor sleep and any allele vs. those with better than poor sleep and no allele. For measures over time, we fit a linear mixed model with a random intercept for a sample size N=1070, and seven cognitive observations per participants. Under assumptions that 50% of participants had poor sleep health and 50% had any ApoE-ε4 allele, we had 80% power to detect a mean log change for participants with both sleep poor health and any ApoE-ε4 allele of 0.027, 0.036, and 0.042 for each unit change in time when between variance explains 67%, 50%, and 40% of the total variance, respectively).

3.5 Supporting tables

Table 1. Summary of variable roles by research aims along the proposed pathway to poor cognitive outcomes.

Aim	Exposure	Outcome	Effect measure modifier
1	Single-generation and intergenerational US acculturation	Poor sleep measures	1. Level of educational attainment 2. Major lifetime occupational category
2	Single-generation US acculturation	Cognitive decline and incident dementia/CIND	Level of educational attainment
3	Poor sleep measures	Cognitive decline and incident dementia/CIND	ApoE-ε4 genotype status

Abbreviations: CIND, cognitive impairment, not dementia; ApoE-ε4, apolipoprotein E-ε4.

CHAPTER 4: US ACCULTURATION AND POOR SLEEP AMONG ADULT LATINOS IN THE SACRAMENTO, CALIFORNIA REGION

4.1 Overview

Acculturation may shape the disproportionate burden of poor sleep among Latinos in the US. Existing studies are limited by unidimensional acculturation proxies that fail to capture the dynamic complexities of cultural change across generations. Understanding how acculturation relates to sleep may lead to identification of modifiable intervention targets. We used multivariable regression and latent class methods to examine cross-sectional associations between high US acculturation, compared to high acculturation towards another origin/ancestral country, and multiple self-reported poor sleep measures. We used a multidimensional US acculturation scale for assessments in both generations. We analyzed an intergenerational cohort: first generation (GEN1) older Latinos (Sacramento Area Latino Study on Aging; N=1716; median age: 69.5) and second generation (GEN2) middle-age offspring and relatives of GEN1 (Niños Lifestyle and Diabetes Study; N=670; median age: 54.0) in Sacramento, California. Among older Latinos, high US acculturation was associated with less restless sleep (PR[95%CI]: 0.67[0.54, 0.84]) and a higher likelihood of best sleep class membership than worst (OR[95% CI]: 1.62[1.09, 2.40]); among non-manual occupations, more immigrant generations was associated with more fatigue (PR[95%CI: 1.86[1.11, 3.10]). Among middle-age Latinos, intergenerational high US acculturation was associated with shorter sleep durations (PR[95% CI]: 2.86[1.02, 7.99]). US acculturation shaped sleep differentially by generational cohort and socioeconomic context. High US acculturation was associated with better sleep among older lower socioeconomic Latinos, and worse sleep outcomes among middle-age higher

socioeconomic Latinos. Future studies should incorporate prospective and intergenerational designs to elucidate the sociobehavioral pathways by which acculturation may influence sleep, which, if replicated, may inform intervention efforts.

4.2 Background

Sleep is a multidimensional vital neurophysiologic state that changes across the lifecourse and facilitates biological functions for health maintenance, longevity, and restoration.[16-20] Poor sleep has been linked to harmful health behaviors and conditions, including mortality.[17,26,214,238,239] In the US, poor sleep is a public health crisis[94,95] where 50-70 million suffer from a chronic sleep disorder[97] and one-third of adults report sleeping less than the recommended amount.[20] Some Latino populations may be disproportionately burdened by poor sleep when compared to other race/ethnicities,[37-41] which is not surprising since they face higher proportions of risk factors like obesity and depression.[13,27-31] Yet the underlying mechanisms driving poor sleep in Latinos remain poorly understood as these associations are complex, interdependent, and rooted in cultural and sociodemographic context.[13,29,30]

Culture is comprised of beliefs, traditions, language, and social interactions that shape health. Knowledge of one's broad cultural orientation provides insight about these compositional cultural factors and how they influence downstream health behaviors and conditions.[125] The Latino population has diverse ancestral origins (e.g. Mexico, Puerto Rico, etc.) and a large foreign-born population, leading to rich cultural variation that is often guided by the dynamic process of acculturation.[44] Acculturation, or cultural change, takes place over time and across generations after exposure to culturally dissimilar people, groups, and social influences.[43-47] US acculturation may play a role in patterning sleep among Latinos as a cultural orientation towards the US (vs. orientation towards another birth or ancestral country) has been linked to many harmful health behaviors and conditions that predict poor sleep.[13,29,30] This concept is known as

negative acculturation,[43-46,48-51] but socioeconomic factors like education and occupation can modify how new cultures are internalized and influence health via mechanisms of differential knowledge, values, and opportunities established by each.[43-47] Understanding how US acculturation, along with socioeconomic factors, patterns sleep among Latinos may identify an over-arching cultural framework with specific underlying mechanistic pathways to explore in future research, the results of which would provide targetable points of intervention and inform the development of efficacious prevention and intervention efforts.

A growing body of literature has found that proxies of US acculturation are associated with worse sleep (e.g. too short or long sleep durations, sleep complaints) among Latinos.[13,29,30,53-57] However, unidimensional acculturative measures like immigration status, language use and competency, and length of residence are of limited utility as they do not capture the complexities of acculturative change that measure adherence to American values and guide pathways between acculturation and health.[45-47] Varying measures of sleep and limited exploration of sociodemographic context (e.g. education, adult age) also make it challenging to draw clear conclusions of how US acculturation influences sleep.

While a genetic contribution to sleep is known,[240] the acculturative experiences of preceding generations may impact sleep and health through separate mechanisms that a single-generation snapshot cannot capture.[44,46,143] For example, a US-born Latino may have one, both, or no parents born outside the US, resulting in varying degrees of acculturation and cultural transmission. First, acculturation can become biologically embedded and be transmitted to offspring via fetal programming (e.g. acculturative stress leads to elevated cortisol levels during pregnancy that impact offspring outcomes[144,145]) to shape subsequent generation health regardless of present life conditions.[143] Second, post-natally, parental acculturative behaviors and

practices, including healthcare utilization, can be learned, reinforced, and shape offspring development to ultimately influence offspring health and sleep (e.g. parental sleep behaviors, diet, breastfeeding practices).[44,143] Therefore, single-generation cultural measures do not stand alone and intergenerational acculturation assessments provide context into how the culture and health of previous generations can become biologically embedded and shape the culture and health of subsequent generations.

In this study of predominately Mexican-descent US Latinos, we sought to estimate the association between US acculturation and poor sleep in two generations: parents of older age at study onset and their offspring and other biological relatives of middle-age at study onset. We used a validated multidimensional acculturation measure,[197] acculturative proxies,[45-47] and several subjective sleep measures for an in-depth exploration of US acculturation and sleep. We hypothesized that high US acculturation, in single generations and across two generations, would be associated with measures of worse sleep quality and sleep apnea among US Latinos.

4.3 Methods

4.3.1 Study population

We utilized baseline data from an intergenerational cohort spanning two studies of community-dwelling predominately Mexican-American adults in the Sacramento Valley region of California.[8] The first generation (GEN1) was drawn from the Sacramento Area Latino Study on Aging (SALSA), a 10-year longitudinal cohort study of N=1,789 Latinos aged 60–101 years at baseline (1998–1999). The second generation (GEN2) was drawn from the Niños Lifestyle and Diabetes Study (NLDS), which consists of N=728 biological relatives (N=534 offspring; 73.4%) of SALSA/GEN1 participants aged 48-60 years at baseline (2013). Participants reported health conditions, lifestyle, and sociodemographic factors via interviewer-administered surveys in self-selected Spanish or English language; clinical and cognitive assessments were collected at

home visits. Analyses were conducted in sub-samples with acculturation and sleep data: N=1716 older SALSA GEN1 participants and N=670 midle-age NLDS GEN2 participants for single-generation analyses to explore differences between acculturation and sleep,[241,242] and N=534 GEN2 offspring linked to GEN1 parents to explore the intergenerational influence of acculturation on sleep.[143] The sub-sample of parent-linked offspring pairs were similar in sociodemographic and cultural factors to the full SALSA and NLDS samples (**Table 3**).

4.3.2 Measures

Acculturation measures. Acculturation was measured using the Acculturation Rating Scale for Mexican-Americans–Version II (ARSMA-II), an established measure of language use and ethnic identity and interaction. The scale consists of two subscales totaling 30 items to measure Anglo orientation (AOS) and Mexican orientation (MOS). The subscales are then averaged and subtracted (AOS-MOS) for an overall mean score. AOS and MOS have strong internal reliability (Cronbach's alpha=0.83 and 0.88, respectively), test-retest reliability at 1-week intervals (correlation coefficient=0.94 and 0.96, respectively), and concurrent validity (correlation coefficient with original ARSMA=0.89). We modified Cuellar et al. (1995)'s suggested cut points for a dichotomous US acculturation measure where ≥0 indicates "high" US cultural orientation and <0 indicates "low" (or "high" Mexican orientation). We had a small sample size of bicultural (score=0) participants (<1%) and combined them with participants scoring ≥0 for a high US acculturation score because the study is US-based.[197,198,216]

Intergenerational acculturation. We linked GEN2 offspring to GEN1 parents and created a three-level intergenerational parent/offspring US acculturation measure: stable-high intergenerational US acculturation (high parent US acculturation/high offspring US acculturation); upwardly mobile (low parent/high offspring); and low, which was a combination

of stable-low (low parent/low offspring) and downwardly mobile (high parent/low offspring) as downwardly mobile pairs constituted <2% of the parent-linked offspring sample.

Immigrant generation. In GEN1, participants reported their nativity and the nativity of their parents. We used this information to create a three-level immigrant generation variable[196] as a proxy of intergenerational US acculturation. A foreign-born participant was categorized as a first generation immigrant; a US-born respondent with at least one foreign-born parent was categorized as second immigrant generation; and US-born participant with two US-born parents was categorized as third generation.

Sleep. Briefly, availability of sleep measures differed between GEN1 and GEN2. GEN1 had more measures and different measures than GEN2, though an identical measure of restless sleep was available for both (see **Table 2** for a summary comparison of GEN1 and GEN2 sleep measures). In GEN1, we used five dichotomous (yes/no) measures of poor sleep: restless sleep; overall fatigue (a wake-time measure linked to sleep quality)[209]; waking up far too early; trouble falling asleep; and waking up several times a night. We examined restless sleep and overall fatigue as individual outcomes due to the literature base and interpretable connection to daily functioning and health[94,210] and all measures were used in a latent class analysis. In NLDS, we used five dichotomous (yes/no) measures of poor sleep: restless sleep; three duration variables; and a self-reported sleep apnea medical diagnosis. Participants answered how long they sleep on weekdays and weekends and we created a weighted average of sleep per night throughout a week. We created three separate duration variables with the average dichotomized at informative cut points (averages of <5,<6, and <7 hours of sleep/night) based on sleep recommendations and sleep duration-health literature.[97,211-214] In GEN2, restless sleep data was collected via phone survey for all participants; sleep duration and sleep apnea data were collected at home visits by a

sub-sample of NLDS participants consenting to a home visit (N=483). NLDS participants who agreed to a home visit were similar in sociodemographic and cultural factors to the total NLDS population (*Supplemental Table 3*).

Covariates. We considered the following factors in directed acyclic graphs (DAGs)[221] of the association between US acculturation and poor sleep: sociodemographic variables (nativity, age, sex, income, education, employment, major lifetime occupation, language use, duration in the US, immigrant generation), lifestyle factors (diet, physical activity, smoking status, alcohol), other health indicators (self-reported health, mental health disorders [e.g. depression, anxiety], body mass index [BMI], medication use, and insurance status). Education. We used different cut points for "high" and "low" education in GEN1 and GEN2 to account for cohort and location differences that relate to educational attainment.[216] In GEN1, we dichotomized education as "low" for <12 years and "high" as ≥12 years, a recurring cut point in GEN1 research and studies with similar populations.[154,215] In GEN2, "low" education was categorized as <13 years and "high" as ≥13 years. Major lifetime occupation. Participants were asked "what job did you do most of your life?" and responses were categorized with census codes: manual, non-manual, and other (which included housewives and unemployed).[182,217]

Effect measure modifiers. Acculturation, sleep, and related health factors are embedded in socioeconomic context.[43] We examined educational attainment and major lifetime occupation as effect measure modifiers in the larger GEN1 population to determine whether cross-sectional acculturation-sleep associations varied in direction and magnitude. While education and occupation are interrelated, each provides insight into different individual and societal dynamics. Education can indicate skillset and predict socioeconomic trajectory, while occupation can indicate factors like workplace responsibility and daily activity.[243,244]

4.3.3 Statistical analysis

All analyses were conducted in SAS 9.4 (SAS Institute, Inc., Cary, North Carolina). We explored descriptive characteristics of GEN1, GEN2, and the sub-sample of parent-offspring linked pairs. We then explored the interdependence of restless sleep across generations, the only sleep measure available in both cohorts, with a chi-square test of independence in parent-offspring linked pairs to inform our interpretation of the intergenerational results.

Cross-sectional multivariable regression analysis. First, we used log-binomial regression to assess associations between single-generation US acculturation and poor sleep measures (GEN1 and GEN2 cohorts examined separately) and then intergenerational US acculturation and poor sleep measures (GEN1 parent-linked GEN2 offspring). General estimating equations were used to account for within family clustering in intergenerational analyses.[224,245] Results were exponentiated to report prevalence ratios (PRs) and 95% confidence intervals (CIs). If models did not converge, we used a modified log-Poisson approach to approximate PRs.[246] We ran a model adjusted for demographics (Model 1: age, sex) and a sociodemographic-adjusted model (Model 2: age, sex, education) where we added education as the direction of influence between acculturation and education is debatable and likely bi-directional.[43,44]

Second, in parent-offspring linked pairs, we conducted an *intergenerational sleep sensitivity assessment* to explore whether parental sleep accounted for any association between intergenerational US acculturation and offspring sleep. Parental sleep can directly influence offspring sleep as a learned and reinforced behavior and we sought to determine if any acculturation-sleep association was driven by parental sleep rather than other acculturative or mediating health factors. We additionally adjusted for parental restless sleep (GEN1), the only sleep measure in both cohorts for comparability, in an intergenerational US acculturation-NLDS

offspring restless sleep analysis to isolate a measure of parental sleep measure from the same measure in offspring (i.e. restless sleep) and observe any changes in association.

Latent class analysis (LCA). Second, in GEN1 we conducted a LCA[229] with five sleep measures (**Table 1**) to create latent sleep classes. LCA provides an opportunity to capture the complex, interrelated, and perhaps unobservable, components of sleep that are difficult to measure.[94] We fit baseline models for a range of two to five latent sleep classes and chose the final number of classes based on the best statistical fit (G^2 relative to *df*; AIC; BIC). We used multinomial logistic regression and reported odds ratios (ORs) and 95% CIs for the odds of latent sleep class membership given US acculturation status in demographic- and sociodemographic-adjusted models.[230]

Effect measure modification. Fourth, in GEN1 we explored the modifying roles of education and major lifetime occupation as both socioeconomic factors confer different levels of values, knowledge, opportunities, and experience that may modify the direction and magnitude of US acculturation-poor sleep associations.

4.4 Results

4.4.1 Descriptive characteristics

Table 3 displays participant descriptive characteristics. In GEN1, the median age was 69.5 years and 58.3% were female. Education was low (<12 years) for 70.3% and 59.8% worked in manual occupations. Less than half were highly acculturated to the US (35.1%), and 54.4% were first generation immigrants. Restless sleep and overall fatigue were reported by 23.5% and 28.9%, respectively. In GEN2, the median age was 54.0 years (IQR: 48.0, 60.0) and 62.4% were female. Education was low (<13 years) for 36.8% of participants and 67.8% had high US acculturation. Restless sleep, average sleep duration of less than 6 hours/night, and sleep apnea were reported by 39.9%, 16.9%, and 12.0%, respectively. In parent-offspring linked pairs,

intergenerational US acculturation was low for 32.8%, upwardly mobile for 34.1%, and stable-high for 33.2%. As shown in **Table 3**, parent-offspring linked pairs were similar in culture and sociodemographic factors and sleep to the overall populations. We examined how sleep relates across generations with a chi-square test for independence between parental restless sleep (SALSA/GEN1) and offspring restless sleep (NLDS/GEN2). We rejected the null hypothesis of independence (p=0.03) and concluded parental and offspring restless sleep were statistically associated.

4.4.2 Cross-sectional multivariable analyses

In GEN1 (**Table 4**), single-generation high US acculturation (vs. low US/more oriented towards Mexico or other origin/ancestral country) was associated with less restless sleep (PR[95%CI]: 0.67[0.54, 0.84]), even when adjusting for age, sex, and education. Participants of third and greater immigrant generation reported less restless sleep than first generation immigrants (PR[95%CI]: 0.60[0.39, 0.91]); we observed no association for second immigrant generation participants (vs. first generation immigrants). We did not find an association between overall fatigue and US acculturation or immigrant generation. For example, high US acculturation-overall fatigue Model 2 estimates were null (PR[95%CI]: 1.03[0.87, 1.23]).

In NLDS (**Table 5**), single-generation US acculturation and sleep outcomes were not associated. For example, high US acculturation-restless sleep Model 2 estimates were null (PR[95%CI]: 1.06[0.86, 1.31]). *Parent-linked offspring*. Participants with stable-high intergenerational US acculturation had a higher prevalence of <5 hours of sleep/night than participants with low intergenerational US acculturation (PR[95%CI]: 2.86[1.02, 7.99]), but this estimate was imprecise. Upwardly mobile intergenerational US acculturation (vs. low intergenerational US acculturation/more culturally oriented towards Mexico or other

origin/ancestral country across generations) was not associated with sleep durations.

Intergenerational sleep sensitivity assessment. We explored the role of parental sleep in intergenerational US acculturation-offspring sleep associations with restless sleep. Though associations between intergenerational US acculturation and offspring restless sleep were null (**Table 5**), we explored how additional adjustment for parental restless sleep influenced results (*Supplemental Table 4*). The estimate changed by <10% and we concluded that parental restless sleep was not an important explanatory variable for the observed intergenerational US acculturation-offspring restless sleep results.

4.4.3 Latent class analysis (LCA)

Baseline latent classes. In GEN1, three latent classes of sleep were the best statistical fit for the data (*Supplemental Table 5*) and each class had clear interpretability: best sleep, 36.9% (standard error[SE]: 0.05) of the study population; average sleep, 40.7% (SE: 0.11); and worst sleep, 22.4% (SE: 0.10). **Figure 5** presents conditional probabilities of a "yes" response for each of the five measures of poor sleep given latent class membership (*Supplemental Table 6*). Participants in the worst sleep class had the highest probability of a "yes" response to all poor sleep measures, and those in the best sleep class had the lowest, except for responses to waking up several times a night. The probability of "yes" response to waking up several times a night was higher for participants in the best sleep class (probability[SE]: 0.063[0.016]) than the average sleep class (probability[SE]: 0.027[0.127]), but this did not substantially detract from the meaningfulness of the latent class labels.

LCA classes and covariates. We examined whether US acculturation level or immigrant generation predicted latent sleep class membership when adjusting for age, sex, and education (**Table 6**). Acculturative level was a significant predictor of latent class membership (p=0.00),

while immigrant generation was not (p=0.11). When compared to low US acculturation participants, high US acculturation participants had a higher odds of membership in the best sleep class than the worst sleep class (OR[95%CI]: 1.62[1.09, 2.40]) and a higher odds of membership in the average sleep class than the best sleep class (OR[95%CI]: 1.86[1.00, 3.48]).

4.4.4 Effect measure modification by educational attainment level

In GEN1 (**Table 7**), there was some evidence that education modifies the relationship between immigrant generation and restless sleep. Though CIs overlapped slightly, low education-third and greater immigrant generation participants reported a lower prevalence of restless sleep than low education-first generation immigrants (PR[95%CI]: 0.35[0.17, 0.72]), and the association was null for high education participants (PR[95%CI]: 1.31[0.67, 2.58]). We did not observe significant effect modification for restless sleep among second immigrant generation participants compared to first generation immigrants. For fatigue, the education stratified estimates were not statistically significant and CIs overlapped. However, the direction of the point estimates suggested high education-third and greater immigrant generation individuals reported more fatigue than high education-first generation immigrants (PR[95%CI]: 1.30[0.82, 2.04]), while low education-third and greater immigrant generation participants reported less fatigue than low education-first generation immigrants (PR[95%CI]: 0.67[0.42, 1.09]).

4.4.5 Effect measure modification by major lifetime occupational category

In GEN1 (**Table 8**), we did not observe modification between acculturative measures and restless sleep. Conversely, we did observe modification of immigrant generation-fatigue associations by occupational category. When adjusting for age, sex, and education, non-manual labor-third and greater immigrant generation participants reported more fatigue than non-manual labor-first generation immigrants (PR[95%CI]: 1.86[1.11, 3.10]); the same associations for

manual laborers and other laborers were null (PR[95%CI]: 0.74[0.46, 1.20] and 0.61[0.28, 1.32], respectively). We did not observe modification by occupational category for reported fatigue among second immigrant generation participants when compared to first generation immigrants.

4.5 Discussion

This is the first study, to our knowledge, to examine the association between a validated acculturation scale and multiple measures of sleep among two generations of Latinos. Overall, associations between US acculturation and poor sleep varied by generational cohort, acculturation status of previous generations (i.e. intergenerational acculturation), and socioeconomic context. Specifically, among GEN1, those with high US acculturation had better sleep outcomes than those with low US acculturation overall, but we then found associations were modified by educational and occupational status. Conversely, among GEN2, high intergenerational US acculturation was associated with shorter sleep durations (i.e. worse sleep) than low intergenerational US acculturation. Results for GEN2 supported a negative acculturation hypothesis for sleep, while associations among GEN1 refuted a negative influence. The differential results by generational cohort may be attributable to differing sociocultural profiles and trajectories, differing age groups, or both.

More specifically, GEN1 participants with single and intergenerational (i.e. number of immigrant generations) measures of high US acculturation reported better sleep (i.e. less restless and more likely to be in the best sleep class than the worst) than participants with low US acculturation measures. We used immigrant generations as a proxy of intergenerational US acculturation whereby more familial US generations indicated higher intergenerational US acculturation. When compared to first generation immigrants, the lowest measure of intergenerational US acculturation, an acculturative advantage for sleep was observed among third and greater immigrant generations, but not among second immigrant generation

participants. This highlights the importance of intergenerational measures to fully capture the range of acculturative influence on health and sleep. It also suggests that an acculturative advantage for sleep may not extend to more bicultural orientations like that of second immigrant generation Latinos (i.e. US-born participants with at least one foreign-born parent).

Multiple factors may explain these findings. First, poor sleep is associated with psychosocial stress[247,248] and poor mental health,[31,249] and these factors may be more prevalent among individuals residing in the US with low US acculturation due to more daily acculturative stressors (e.g. low community integration and social support, language barriers).[170,171,250-252] Perceived discrimination is an acculturative stressor that may mediate this association as it is linked to low acculturation towards a country where one resides, poor mental health,[171,250] and worse sleep.[248,253,254] In the context of high US acculturation, the same opposing factors (i.e. strong social support and community integration)[44] may improve sleep by the reverse mechanisms (i.e. enhanced mental health, and less stress and loneliness).[31,255]

Second, these results may be a function of age as some studies exploring US acculturation and health among the older GEN1 have found no associations or improved outcomes.[194,256,257] For example, in our study population, Lopez et al. identified better cardiovascular outcomes among the highly acculturated,[194] and an extensive body of literature has linked poor cardiovascular health to poor sleep.[258] Those highly acculturated are also likely to have a higher SEP and more healthcare access to better manage the chronic illnesses and disabilities that are characteristic of older age.[31,256] Third, findings may also be attributable to sociocultural characteristics specific to GEN1 as the cohort can be characterized by generally low SEP (e.g. **Table 3**: 70.3% had <12 years of educational attainment), and some research has shown high US acculturation may associate with better health in low SEP settings.[194,259-263] Thus,

we may not expect to see these same associations in GEN2 at older age due to differences in sociocultural profiles and trajectories. For example, at middle-age, GEN2 already had a higher SEP and acculturative level than the older GEN1 cohort (**Table 3**), indicating that at middle-age GEN1 and GEN2 were not socioculturally similar. Each cohort has a unique sociocultural trajectory that is likely to differentially influence lifecourse health.

Results for GEN2 were in line with the negative acculturation hypothesis and previous literature.[13,29,30,53-57] High intergenerational US acculturation participants reported shorter sleep durations than low intergenerational US acculturation participants. There are multiple underlying health behaviors (e.g. poor diet, more alcohol use and smoking) and outcomes (e.g. obesity, diabetes, cardiovascular disease) associated with both high US acculturation and poor sleep that may explain our findings.[13,29,48,50] We found that restless sleep among parents was statistically associated with restless sleep among offspring, but our sensitivity assessment provided little evidence that parental sleep was an important explanatory variable between intergenerational US acculturation and offspring sleep in our study population. Future studies should first seek to replicate these results and to understand the mechanisms underlying the intergenerational contributions, and then explore mediating health factors and the sociocultural mechanisms that facilitate these pathways. For example, if we found that poor diet and obesity mediated these findings and that familial and social networks facilitated diet, poor sleep prevention and intervention efforts could target these factors.

Among GEN2, we found associations between intergenerational acculturation and sleep duration, but we did not find single-generation acculturation associations, again highlighting the importance of intergenerational assessments. As with intergenerational measures among GEN1, though in the opposite direction, we did not observe clear differences in sleep between upwardly

mobile (i.e. the intermediate level) and low intergenerational acculturation participants. When cultural orientations are more bicultural in nature (i.e. influenced by the country where they reside and the origin or ancestral country), the positive and negative influences of acculturation on sleep may counteract.

We then explored the socioeconomic context of acculturation and sleep among the larger GEN1 population with measures of educational attainment and major lifetime occupational category. There was evidence that both education and occupation modified associations between immigrant generations, our proxy for intergenerational acculturation, and poor sleep measures, but we did not observe modification for single-generation acculturation. Among lower education participants, high intergenerational US acculturation (i.e. three or more immigrant generations in the US) was associated with better sleep (i.e. less restless), but among higher education participants, the association was null among higher education participants, providing further support for a beneficial association between high US acculturation and sleep in a low SEP setting.[194,259-263]

Among participants with non-manual lifetime occupations, high intergenerational US acculturation participants (i.e. three or more immigrant generations in the US) reported more fatigue, an indicator of worse sleep quality, than low intergenerational US acculturation participants (i.e. first generation immigrants); the same association was null for other occupational categories. Among GEN1, this is the only finding that aligns with the negative acculturation hypothesis.[43-46,48-51] Non-manual labor may capture a higher SEP in our population that we were unable to capture with education given the low educational attainment overall of GEN1, providing support for the negative acculturation hypothesis with sleep outcomes in a higher SEP setting.[194,259-263] Non-manual laborers often have more workplace responsibilities and

resulting work-related psychosocial stress than manual laborers,[264,265] which when combined with poor health behaviors associated with high US acculturation (e.g. alcohol use, smoking)[43-46,48-51] may jointly impact sleep negatively.[13,29,30,247] The sedentary nature of non-manual labor may also partially bias our findings as fatigue can be prolonged, more noticeable, and thus more reportable in sedentary settings.

This study had several limitations. First, we used cross-sectional data and were therefore unable to determine temporality or discount reverse causality, as sleep can also influence the adoption of cultural behaviors and trends. However, the intergenerational findings provide some confidence that we are measuring temporal changes with parent to offspring acculturation. Second, the scope of our multidimensional acculturation measure was limited as we were unable to assess biculturalism and downwardly mobile intergenerational acculturation due to limited sample sizes in both categories. Third, subjective unidimensional measures are not the gold standard for sleep,[94] but we used latent class methods to create a multidimensional measure that also captured underlying and unobservable sleep characteristics.[230] Fourth, comparability between our two cohorts is limited as each cohort can be characterized by unique sociocultural characteristics that have accumulated over time to differentially shape health. Differing results between the two cohorts may be partially attributable to differing sociocultural cohort profiles rather than age-related differences, or both factors. However, our exploration of socioeconomic context in GEN1 provided some insight into how acculturation and sleep may associate among older Latinos in a high SEP setting (i.e. non-manual labor) that was more comparable to the socioeconomic make-up of the GEN2 cohort.

Our study had several strengths. First, we used a well-validated multidimensional measure of acculturation to account for the intricacies of culture across multiple domains of

identity, behaviors, and interpersonal relationships.[197] Second, we examined acculturation and sleep within a rich intergenerational cohort to account for acculturative shifts across generations and to explore how parental sleep may contribute to this association. We were then also able to examine cohort and age-related differences between acculturation-sleep associations. Third, we used sseveral unidimensional measures and created a multidimensional latent class measure for an in-depth exploration of the different dimensions and complexities of sleep.[94,230] Fourth, our use of PRs provided conservative and consistent estimates for intepretation.[266]

4.6 Conclusions

Overall, our results suggest that US acculturation may pattern sleep differentially by socioeconomic context and by age cohort, and that the acculturative status of previous generations (i.e. intergenerational acculturation) is a contributing factor. Among GEN2, high intergenerational US acculturation was associated with shorter sleep durations (i.e. worse sleep) than low intergenerational US acculturation. Conversely, among GEN1, single and intergenerational measures of high US acculturation were associated with better sleep (i.e. less restless and more likely to be in the best sleep class the worst) than low acculturation measures. However, among higher SEP GEN1 participants, we found some evidence of a negative acculturation association with sleep (i.e. more reported fatigue among non-manual laborers), which was also consistent with findings for GEN2.

In conclusion, our findings add to our understanding of the ways in which cultural orientation shapes Latino sleep across generations. Associations varied by generational cohort, the acculturation status of previous generations, and socioeconomic context. Future research should utilize prospective and intergenerational designs to parse out the temporal relations between acculturation, SEP, and sleep over time and to elucidate the specific mechanisms underlying these associations to guide prevention and intervention efforts.

4.7 Main tables and figures

Table 2. Summary of sleep measures and treatments in Generation 1 (GEN1), Sacramento Area Latino Study on Aging (SALSA) and Generation 2 (GEN2), Niños Lifestyle and Diabetes Study (NLDS).

Survey question	Responses	Study treatment	Use in analysis
	GEN1		
In the past week, was your sleep restless?	Never; little of the time; some of the time; most of the time	Yes=some of the time or most of the time; No=never or little of the time	Outcome and latent variable
In the past month, have you ever had an overall sense of fatigue?	Yes; No	Yes; No	Outcome and latent variable
Do you usually wake up far too early?	Yes; No	Yes; No	Latent variable
Do you usually have trouble falling asleep?	Yes; No	Yes; No	Latent variable
Do you usually wake up several times a night?	Yes; No	Yes; No	Latent variable
	GEN2		
During the past week, on how many days was your sleep restless?	Never; little of the time; some of the time; most of the time	Yes=some of the time or most of the time; No=never or little of the time	Outcome variable
About how many hours of sleep do you usually get at/per night on weekdays? About how many hours of sleep do you usually get at night on weekends?	Fill in the blank hours	Hours summed and averaged for a single hours/day/week measure. If weekday or weekend was missing, the available duration was used. Dichotomized at three clinically significant cut points: less than 5, less than 6, and less than 7 hours/day/week.	Three separate outcome variables (<5 hours sleep/night; <6 hours sleep/night; <7 hours sleep/night)
Has a doctor (ever) told you that you have sleep apnea?	Yes; No	Yes; No	Outcome variable

Abbreviations: GEN1, generation 1; SALSA, Sacramento Area Latino Study on Aging; GEN2, generation 2; NLDS, Niños Lifestyle and Diabetes Study.

Table 3. Sociodemographic, health, acculturative, and sleep characteristics for an intergenerational cohort of adult Latinos in the Sacramento, California region: Generation 1 (GEN1), Sacramento Area Latino Study on Aging (SALSA) and Generation 2 (GEN2), Niños Lifestyle and Diabetes Study (NLDS).

	Overall		**Parent-offspring linked pairs**	
	GEN1	GEN2	GEN1 parents	GEN2 offspring
	N=1716	N=670	N=543	
	Median (IQR) or N (%)			
Sociodemographic and health measures				
Age at baseline	69.5 (65.0, 74.7)	54.0 (48.0, 60.0)	69.9 (64.6, 75.1)	54.0 (49.0, 60.0)
Sex				
Male	715 (41.7)	252 (37.6)	172 (32.2)	201 (37.6)
Female	1001 (58.3)	418 (62.4)	362 (67.8)	333 (62.4)
Nativity				
Non-US (Mexico or other)[a]	869 (50.1)	165 (24.6)	263 (49.3)	136 (25.5)
US	847 (49.4)	505 (75.4)	271 (50.8)	398 (74.5)
Educational attainment (years)				
High: GEN1 ≥12; GEN2 ≥13	510 (29.7)	411 (63.2)	176 (33.0)	333 (63.9)
Low: GEN1 <12; GEN2 <13)	1206 (70.3)	239 (36.8)	358 (67.0)	188 (36.1)
Missing	0	20	0	13
Current working status				
Employed	292 (18.4)	348 (53.1)	81 (16.9)	283 (53.3)
Looking for work/unemployed/unretired[b]	26 (1.6)	58 (8.9)	3 (0.6)	46 (8.7)
At home full time to take care of family		44 (6.7)		37 (7.0)
Retired, sick leave, or disability[c]	1269 (80.0)	207 (31.5)	395 (82.5)	165 (31.1)
Missing	129	13	55	3
Major lifetime occupational category				
Non-manual	367 (21.6)		106 (20.0)	
Manual	1016 (59.8)		287 (54.2)	
Other[d]	315 (18.6)		137 (25.9)	
Missing	18		4	
Self-rated health				
Good and better than good	873 (50.1)	531 (79.3)	260 (50.0)	431 (80.7)
Worse than good	840 (49.0)	139 (20.8)	260 (50.0)	103 (19.3)
Missing	3	0	14	0
Depressive symptoms[e]				
Low	1006 (79.9)	505 (83.9)	346 (78.5)	416 (88.3)
High	253 (20.1)	98 (16.3)	95 (21.5)	55 (11.7)
Missing	457	67	93	63
Acculturative measures				
US acculturation				
Low	1113 (64.9)	216 (32.2)	348 (65.2)	175 (32.8)
High	603 (35.1)	454 (67.8)	186 (34.8)	359 (67.2)
Intergenerational US acculturative mobility[f]				
Low				175 (32.8)
Upwardly mobile				182 (34.1)

	Overall		Parent-offspring linked pairs	
	GEN1	GEN2	GEN1 parents	GEN2 offspring
	N=1716	N=670	N=543	
	Median (IQR) or N (%)			
Stable-high				177 (33.2)
Primary language				
Spanish	977 (56.9)	65 (9.7)	294 (55.1)	52 (9.7)
English	739 (43.1)	605 (90.3)	240 (44.9)	482 (90.3)
Immigrant generation				
First	869 (54.4)		263 (54.0)	
Second	579 (36.2)		159 (32.6)	
Third and greater	150 (9.4)		65 (13.4)	
Missing	118		47	
Poor sleep measures				
Restless sleep in past week: yes (vs. no)	404 (23.5)	267 (39.9)	100 (19.2)	215 (40.3)
Missing	0	0	13	0
Overall sense of fatigue: yes (vs. no)	496 (28.9)		180 (34.6)	
Missing	0		13	
Wake up far too early: yes (vs. no)	756 (44.1)		246 (47.2)	
Missing	1		13	
Trouble falling asleep: yes (vs. no)	681 (39.7)		217 (41.7)	
Missing	1		13	
Wake up several times a night: yes (vs. no)	1100 (64.1)		311 (59.7)	
Missing	0		13	
Duration (hours)		7.0 (6.0, 8.0)		7.0 (6.0, 8.0)
Less than 5 hours		25 (5.9)		21 (6.0)
Less than 6 hours		72 (16.9)		63 (18.0)
Less than 7 hours		182 (42.8)		152 (43.4)
Missing		245		184
Sleep apnea diagnosis: yes (vs. no)		51 (12.0)		42 (12.0)
Missing		245		185

Abbreviations: GEN1, generation 1; SALSA, Sacramento Area Latino Study on Aging; GEN2, generation 2; NLDS, Niños Lifestyle and Diabetes Study; IQR, interquartile range; US, United States.

[a]Percentage of non-US study population from Mexico (vs. other): total population, GEN1= 89.0, GEN2= 88.5; linked population, GEN1= 92.4, GEN= 89.0.

[b]GEN1: Unemployed and unretired; GEN2: Looking for work or unemployed.

[c]GEN1: Retired only.

[d]Other major lifetime occupational category includes housewives and unemployed participants.

[e] Center for the Epidemiological Studies of Depression Scale; GEN1: 20-item, score ≥16 = high depressive symptoms; GEN2: 10-item, score ≥10 = high depressive symptoms.

[f]Breakdown of GEN2 low intergenerational US acculturation (%): stable-low, 94.9; downwardly mobile, 5.1.

Table 4. Adjusted[a,b] prevalence ratios of poor sleep measures and US acculturation measures for first generation older Latino adults in the Sacramento, California region: Sacramento Area Latino Study on Aging (SALSA; N=1716), 1998-1999.

	Restless sleep				**Overall fatigue**			
	PR 95% CI							
	Model 1[a]		*Model 2*[b]		*Model 1*[a]		*Model 2*[b]	
US acculturation: high (vs. low)	0.60	0.49, 0.74	0.67	0.54, 0.84	0.98	0.84, 1.15	1.03	0.87, 1.23
Immigrant generation								
First	1	Referent	1	Referent	1	Referent	1	Referent
Second	0.87	0.72, 1.05	0.97	0.80, 1.18	0.95	0.80, 1.12	0.97	0.82, 1.16
Third and greater	0.52	0.34, 0.80	0.60	0.39, 0.91	0.90	0.67, 1.20	0.93	0.69, 1.25

Abbreviations: US, United States; SALSA, Sacramento Area Latino Study on Aging; PR, prevalence ratio; CI, confidence interval.

[a]Model 1. Adjusted for age and sex,

[b]Model 2. Adjusted for age, sex, and education.

Table 5. Adjusted[a,b] prevalence ratios of poor sleep measures and US acculturation level for second generation middle-age Latino adults (N=665) and parent-linked offspring for intergenerational assessments (N=530) in the Sacramento, California Region: Niños Lifestyle and Diabetes Study (NLDS), 2013.

	Restless sleep		**Sleep duration: less than 5 hours/night**		**Sleep duration: less than 6 hours/night**		**Sleep duration: less than 7 hours/night**		**Sleep apnea diagnosis**	
					PR 95% CI					
					Model 1[a]					
US acculturation: high (vs. low)	1.08	0.88, 1.33	1.28	0.54, 3.01	0.97	0.62, 1.51	1.03	0.81, 1.30	1.11	0.65, 1.92
Intergenerational US acculturation										
Low[c]	1	Referent	1	Referent	1	Referent	1	Referent	1	Referent
Upwardly mobile	0.97	0.76, 1.24	1.20	0.37, 3.82	0.94	0.53, 1.68	0.88	0.64, 1.20	1.12	0.57, 2.21
Stable-high	1.10	0.86, 1.39	1.90	0.68, 5.36	1.02	0.60, 1.74	1.11	0.85, 1.46	1.09	0.53, 2.24
					Model 2[b]					
US acculturation: high (vs. low)	1.06	0.86, 1.31	1.42	0.58, 3.47	0.93	0.59, 1.48	0.99	0.78, 1.27	0.89	0.52, 1.55
Intergenerational US acculturation										
Low[e]	1	Referent	1	Referent	1	Referent	1	Referent	1	Referent
Upwardly mobile	0.98	0.76, 1.26	1.34	0.41, 4.37	0.90	0.50, 1.63	0.85	0.61, 1.17	0.89	0.45, 1.74
Stable-high	1.14	0.89, 1.46	2.86	1.02, 7.99	1.06	0.60, 1.88	1.09	0.81, 1.48	0.87	0.41, 1.87

Abbreviations: US, United States; NLDS, Niños Lifestyle and Diabetes Study; PR, prevalence ratio; CI, confidence interval.

[a]Model 1. Adjusted for age, sex, and in intergenerational models, clustering at family level.

[b]Model 2. Adjusted for age, sex, education, and in intergenerational models, clustering at family level.

[c]Low intergenerational US acculturation: stable-low (low parent/low offspring) and downwardly mobile (high parent/low offspring).

Table 6. Adjusted[a] odds ratios of poor sleep latent class and US acculturation measures for first generation older Latino adults in the Sacramento, California region: Sacramento Area Latino Study on Aging (SALSA; N=1716), 1998-1999.

	US acculturation: high (vs. low)		Immigrant generation (vs. first)			
			Second		Third and greater	
Sleep class	**OR**	**95% CI**				
Average versus best	1.86	1.00, 3.48	1.3	0.85, 1.99	1.14	0.59, 2.20
Worst versus best	0.62	0.42, 0.92	0.95	0.68, 1.33	0.56	0.32, 0.99
Best versus average	0.54	0.29, 1.00	0.77	0.50, 1.18	0.88	0.45, 1.70
Worst versus average	0.33	0.16, 0.68	0.73	0.46, 1.16	0.49	0.23, 1.06
Best versus worst	1.62	1.09, 2.40	1.05	0.75, 1.47	1.78	1.01, 3.12
Average versus worst	3.02	1.48, 6.18	1.36	0.86, 2.15	2.02	0.94, 4.34
p-value	0.001		0.109			

Abbreviations: US, United States; SALSA, Sacramento Area Latino Study on Aging; OR, odds ratio; CI, confidence interval.

[a]Model adjusted for age, sex, and education.

Table 7. Adjusted[a] prevalence ratios of poor sleep measures and US acculturation measures by strata of educational attainment[b] for first generation older Latino adults in the Sacramento, California region: Sacramento Area Latino Study on Aging (SALSA; N=1716), 1998-1999.

	Educational attainment							
	Low education		High education		Low education		High education	
	PR 95% CI							
	Restless sleep				*Overall fatigue*			
US acculturation: high (vs. low)	0.66	0.50, 0.87	0.70	0.47, 1.03	1.03	0.84, 1.27	1.03	0.75, 1.41
Immigrant generation								
First	1	Referent	1	Referent	1	Referent	1	Referent
Second	0.94	0.76, 1.16	1.38	0.81, 2.34	0.99	0.81, 1.20	1.02	0.70, 1.48
Third and greater	0.35	0.17, 0.72	1.31	0.67, 2.58	0.67	0.42, 1.09	1.30	0.82, 2.04

Abbreviations: US, United States; SALSA, Sacramento Area Latino Study on Aging; PR, prevalence ratio; CI, confidence interval.

[a]Models adjusted for age and sex.

[b]Educational attainment level: low, <12 years; high, ≥12 years.

Table 8. Adjusted[a,b] prevalence ratios of poor sleep measures and US acculturation measures by strata of occupational category for first generation older Latino adults in the Sacramento, California region: Sacramento Area Latino Study on Aging (SALSA; N=1716), 1998-1999.

	Major lifetime occupational category											
	Manual		**Non-manual**		**Other**		**Manual**		**Non-manual**		**Other**	
	PR 95% CI											
	Restless sleep						*Overall fatigue*					
	Model 1[a]											
US acculturation: high (vs. low)	0.66	0.50, 0.89	0.59	0.38, 0.92	0.65	0.42, 1.00	0.99	0.79, 1.25	1.16	0.81, 1.67	0.90	0.66, 1.22
Immigrant generation												
First	1	Referent	1	Referent	1	Referent	1	Referent	1	Referent	1	Referent
Second	0.92	0.72, 1.18	1.11	0.66, 1.86	0.84	0.57, 1.24	1.01	0.80, 1.27	1.07	0.69, 1.65	0.92	0.68, 1.26
Third and greater	0.54	0.30, 0.94	0.71	0.28, 1.78	0.59	0.24, 1.45	0.72	0.45, 1.15	1.84	1.11, 3.06	0.59	0.27, 1.28
	Model 2[b]											
US acculturation: high (vs. low)	0.72	0.54, 0.96	0.62	0.40, 0.98	0.70	0.45, 1.08	1.04	0.82, 1.32	1.19	0.82, 1.71	0.92	0.68, 1.26
Immigrant generation												
First	1	Referent	1	Referent	1	Referent	1	Referent	1	Referent	1	Referent
Second	0.98	0.76, 1.25	1.24	0.73, 2.10	0.88	0.60, 1.30	1.03	0.82, 1.31	1.08	0.69, 1.68	0.93	0.68, 1.27
Third and greater	0.58	0.33, 1.02	0.77	0.30, 1.94	0.68	0.28, 1.66	0.74	0.46, 1.20	1.86	1.11, 3.10	0.61	0.28, 1.32

Abbreviations: US, United States; SALSA, Sacramento Area Latino Study on Aging; PR, prevalence ratio; CI, confidence interval.

[a]Model 1. Adjusted for age and sex.

[b]Model 2. Adjusted for age, sex, and education.

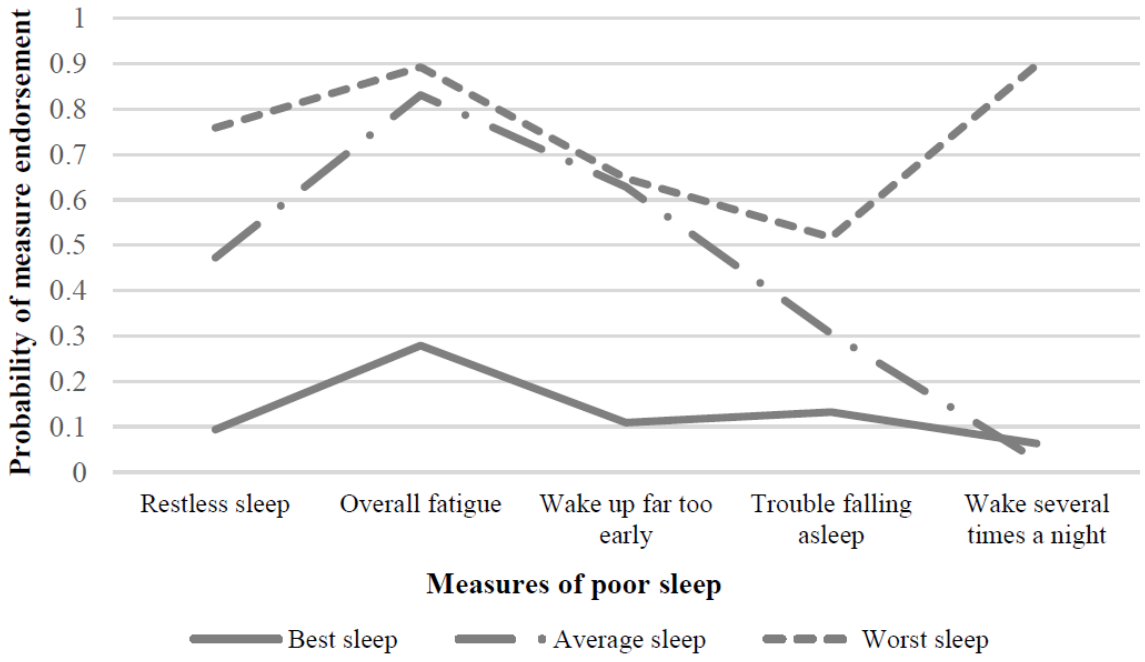

Figure 5. Conditional probability of endorsement in the baseline model for each sleep measure given membership in the latent sleep class: Sacramento Area Latino Study on Aging (SALSA; N=1716).

4.8 Supplemental tables

Supplemental Table 3. Comparison of sociodemographic and cultural characteristics for phone Survey and home visit participants: second generation (GEN2), Niños Lifestyle and Diabetes Study (NLDS), 2013.

	Phone survey N=670	**Home visit** N=425
Age at baseline	54.0 (48.0, 60.0)	54.0 (48.0, 60.0)
Sex		
Male	252 (37.6)	156 (36.7)
Female	418 (62.4)	269 (63.3)
Nativity		
Non-US (Mexico or other)	165 (24.6)	108 (25.4)
US	505 (75.4)	317 (74.6)
Educational attainment (years)		
High: ≥13	411 (63.2)	265 (64.8)
Low: <13	239 (36.8)	144 (35.2)
Missing	20	16
Current working status		
Employed	348 (53.1)	210 (50.4)
Looking for work/unemployed	58 (8.9)	38 (9.1)
At home full time to take care of family	44 (6.7)	29 (7.0)
Retired, sick leave, or disability	207 (31.5)	140 (33.6)
Missing	13	8
US acculturation		
Low	216 (32.2)	142 (33.4)
High	454 (67.8)	283 (66.6)
Primary language		
Spanish	65 (9.7)	51 (12.0)
English	605 (90.3)	374 (88.0)

Abbreviations: NLDS, Niños Lifestyle and Diabetes Study; IQR, interquartile range; US, United States.

Supplemental Table 4. Adjusted[a] prevalence ratio of offspring restless sleep and intergenerational US acculturation for parent-linked offspring of second generation middle-age Latino adults in the Sacramento, California region: Niños Lifestyle and Diabetes Study (NLDS; N=504), 2013.

	Restless sleep	
	PR 95% CI	
Intergenerational US acculturation		
Low[b]	1	Referent
Upwardly mobile	0.96	0.74, 1.25
Stable-high	1.16	0.90, 1.49

Abbreviations: US, United States; NLDS, Niños Lifestyle and Diabetes Study; PR, prevalence ratio; CI, confidence interval.

[a]Adjusted for age, sex, education, parental restless sleep, and clustering at the family level.

[b]Low intergenerational US acculturation: stable-low (low parent/low offspring) and downwardly mobile (high parent/low offspring).

Supplemental Table 5. Baseline model fit statistics for latent class models of poor sleep for first generation older Latino adults in the Sacramento, California region: Sacramento Area Latino Study on Aging (SALSA; N=1716), 1998-1999.

Number of classes	G^2	*df*	AIC	BIC	Adjusted BIC	Log-Likelihood	Entropy
2	84.73	20	106.73	166.66	131.71	-5090.05	0.57
3	23.03	14	57.03	149.64	95.64	-5059.2	0.61
4	11.98	8	57.98	183.28	110.21	-5053.67	0.59

Abbreviations: SALSA, Sacramento Area Latino Study on Aging; G^2=likelihood-ratio chi-square statistic; *df*, degrees of freedom; AIC, Akaike information criterion; BIC, Bayesian information criterion.

Supplemental Table 6. Frequency of poor sleep measures and latent class assignments with probabilities of endorsing item given class membership for first generation older Latino adults in the Sacramento, California region: Sacramento Area Latino Study on Aging (SALSA; N=1716), 1998-1999.

		Best sleep	**Average sleep**	**Worst sleep**
			Percentage (SE)	
		36.9 (0.05)	40.7 (0.11)	22.4 (0.10)
Poor sleep measure: yes (vs. no)	*N (%)*		*Probability (SE)*	
Restless sleep	404 (23.5)	0.0940 (0.0269)	0.4723 (0.0689)	0.7588 (0.0695)
Overall fatigue	496 (28.9)	0.2789 (0.0441)	0.8309 (0.0409)	0.8924 (0.0237)
Wake up far too early	756 (44.1)	0.1088 (0.0351)	0.6287 (0.0433)	0.6469 (0.0303)
Trouble falling asleep	681 (39.7)	0.1327 (0.0209)	0.3051 (0.0515)	0.5172 (0.0557)
Wake several times a night	1100 (64.1)	0.0632 (0.0155)	0.0272 (0.1274)	0.8971 (0.2913)

Abbreviations: SALSA, Sacramento Area Latino Study on Aging; SE, standard error.

Fit statistics: Likelihood-ratio chi-square statistic (G^2)=23.03 with 14 degrees of freedom; Akaike information criterion=57.03; Adjusted Bayesian information criterion=95.64 .

CHAPTER 5: CULTURAL ORIENTATION AND EDUCATION AS DETERMINANTS OF COGNITION AND DEMENTIA AMONG OLDER LATINOS IN THE SACRAMENTO, CALIFORNIA REGION

5.1 Overview

Latinos are disproportionately burdened by dementia. As the elderly Latino population grows, the identification of modifiable determinants for intervention targets is needed. The etiology of dementia is complex and acculturation provides an opportunity to disentangle the health pathways that can shape dementia under over-arching cultural orientations. We examined how high US acculturation, when compared to high acculturation towards another origin/ancestral country, associated with cognitive performance and incident dementia/CIND in an older Sacramento, California Latino cohort (Sacramento Area Latino Study on Aging; N=1778; median age: 69.8 years). We used hierarchical linear mixed models and Fine and Gray's competing risk regression models to assess associations between a multidimensional US acculturation measure, repeated cognitive assessments, and a multistage clinical dementia diagnosis, as well as the modifying role of education. Participants were followed up to 7 visits (1998-2008). In adjusted models, high US acculturation participants made 0.20 fewer log-transformed errors on the cognitive assessment at baseline (i.e. better cognitive performance) than low US acculturation participants (β[standard error]: -0.20[0.05]). High practice and identity US acculturation had a 44% lower risk of incident dementia/CIND than low practice and identity US acculturation (HR[95% confidence interval]: 0.56[0.32, 0.98]). Among older Latinos, measures of high US acculturation were associated with improved cognitive performance and reduced dementia/CIND risk. Acculturative components like social support and networks, rather

than language, may drive associations with dementia/CIND. If replicated, future studies should determine which modifiable mechanisms stemming from high US acculturation may explain these findings for intervention targets.

5.2 Introduction

Dementia is a major source of morbidity and mortality in the US and worldwide.[32,267] AD, which constitutes 60-80% of dementia cases, is the 5th leading cause of death for those aged 65 years and older. An estimated 5.2 million people in the US suffer from AD.[32,76,267] Elderly Latinos are a rapidly growing population and expected to constitute ~20% of the total elderly population in the US by 2020.[268] Latinos are also 1.5 times as likely to have AD as non-Hispanic Whites.[76,267] The underlying causes of this disparity are only partially understood as studies have shown that a wide range of risk factors for dementia are more prevalent among Latinos (e.g. diabetes and other poor vascular outcomes, smoking, poor sleep, low educational attainment).[10-14,102,155,193,269,270] However, Latino populations contain great diversity in culture and health outcomes as many are foreign-born, of recent immigrant generations, or different countries of ancestry and origin.[44] An exploration of the broader sociocultural determinants of dementia within Latinos may provide more insight into the causes of these risk differentials.

Acculturation, the dynamic process of change in cultural orientation after exposure to culturally dissimilar people, groups, and social influences, has been extensively linked to health outcomes among Latinos. Knowledge of cultural orientation provides insight to attitudes, beliefs, behaviors, and social interactions that shape health behaviors and conditions.[43-51] Language use has been recognized as a leading acculturative component that drives cultural change, facilitates all aspects of daily life, and measures functional community integration.[47] While the direction and magnitude of acculturation-health associations can vary by health factor, the concept of negative acculturation whereby a high cultural orientation to the US (vs. birth or ancestral

country) is associated with worse health (i.e. many harmful health behaviors and poor health conditions) has been well-described.[43-46,48-51] In alignment with this concept, many risk factors of dementia such as alcohol use, smoking, poor sleep, diabetes, and other cardiovascular outcomes have been linked to high US acculturation.[8,10-14,43-46,48-51,92,108,126-132] However, not all risk factors of dementia are consistent with the negative acculturation hypothesis. For example, poor mental health and stress have been linked to low resident country acculturation,[11,12,164-171] and factors associated with improved cognitive outcomes like social support and high socioeconomic status have been linked to high US acculturation.[10-12,44,51,148-150,153,161-163] An understanding of how an over-arching cultural orientation relates to cognitive performance over time and incident dementia may help disentangle the multiple health pathways leading to cognitive disparities among Latinos and shape prevention and intervention efforts.

To fully elucidate the associations between US acculturation and poor cognitive outcomes, validated and multidimensional measures are needed to capture the complexities of the acculturative process, as well consideration for socioeconomic context and the accumulation of these factors across the lifecourse, Some studies have explored how acculturative proxies like migration status and bilingualism (i.e. a measure of acculturative language use) associate with cognitive outcomes, but overall findings have been inconsistent.[58-64] These unidimensional proxies fail to capture the range of acculturative factors that comprise cultural orientation and as a result, the health pathways stemming from these factors.[45-47] Acculturation-health associations have also been shown to vary by socioeconomic context and the health advantage among high socioeconomic populations is well-known.[43,52] Educational attainment may play a key modifying role as more attainment has been linked to worse cognitive outcomes and the influence of acculturation may vary by education level.[43,148,149,151] Additionally, acculturation changes over

time and may also differentially influence health across the lifecourse. For example, an extensive body of literature has linked high US acculturation to poor cardiovascular health and related harmful behaviors, but when populations are restricted to older adults, associations have been found to be protective or null.[194,257] Further, the onset of age-related cognitive decline begins during the 20s or early 30s[271] and the importance of lifecourse and mid-life health in late-life cognitive outcomes has been recognized.[150,272-276] We must then consider the dynamic interplay of acculturation and accumulation of health across the lifecourse rather than at one life stage in isolation to understand how acculturation may shape cognitive performance over time and dementia risk.

We sought to examine the association between a validated multidimensional measure of US acculturation,[197] cognitive decline, and incident dementia, with exploration of the modifying role of education, in a cohort of older Latino adults in the Sacramento, California region over ten years. Given the disproportionate burden of dementia risk factors in US Latinos and their associations with high US acculturation, we hypothesized that high US acculturation was associated with more dementia and accelerated cognitive decline, and that high education would attenuate this association.

5.3 Methods

5.3.1 Study population

We utilized data from the Sacramento Area Latino Study on Aging (SALSA), a ten-year longitudinal cohort study of community-dwelling predominately Mexican-American adults representative of the Latino community living in the Sacramento Valley.[8] SALSA consists of N=1,789 Latinos aged 60–101 years at baseline (1998–1999). Participants were followed every 12–15 months via home visits for a total of 7 follow-up visits, ending in 2008. Average annual attrition was 5%, including mortality and loss to follow up.[8,177] Participants selected Spanish or

English language for all data collection and reported health conditions, lifestyle, and sociodemographic risk factors via interviewer-administered surveys; clinical and cognitive assessments were also collected at home visits.

5.3.2 Measures

Acculturation. Acculturation was measured at baseline using the Acculturation Rating Scale for Mexican-Americans–Version II (ARSMA-II), an established measure of language, ethnic identity, and ethnic interaction. There are scored two subscales that quantify Anglo orientation (herein referred to as US) (AOS) and Mexican orientation (MOS) for one final score. Both have strong internal reliability (Cronbach's alpha= 0.83 and 0.88, respectively), test-retest reliability at 1-week intervals (correlation coefficient= 0.94 and 0.96, respectively), and concurrent validity (correlation coefficient with original ARSMA = 0.89). We modified Cuellar et al. (1995)'s suggested cut points for a dichotomous US acculturation measure, where ≥0 indicates "high" US cultural orientation and <0 indicates "low" (or "high" Mexican orientation). We combined bicultural (score=0) participants with high US acculturation participants due to small sample size (<1%) and because our study population is US-based.[197,198,216]

We conducted sensitivity assessments to explore whether language acculturation drove acculturation and cognitive outcome associations. Language is an important driver of the acculturative process that also shapes cognitive development and performance through multiple mechanisms.[47,58-62,64] We parsed apart the ARSMA-II acculturative scale into two groups of questions: 1) *language* (media and communication language preferences) and 2) *practice and identity* (i.e. non-language measures of social interactions, ethnic identity, and traditions), and calculated acculturation scores for each group to produce a language US acculturation score and a practice and identity US acculturation score. We dichotomized each score for high/low

categories and treated each as a sensitivity exposure to compare results between language acculturative factors and practice and identity acculturative factors.

Cognitive function and dementia/CIND. Cognitive function was assessed with the 3MSE and SEVLT at all study visits. Higher scores on both tests indicate better cognitive function. The 3MSE is a 100-point global cognitive function test validated and field-tested in English and Spanish. The 3MSE shows better reliability, test–retest properties, sensitivity, and specificity than the Mini-Mental State Exam (MMSE), and has fewer ceiling effects.[199,200] The 3MSE was used to measure cognitive decline over the follow-up and was treated as the log-transformation of errors (log(101–3MSE score)) for a normal distribution. More errors indicate poorer cognitive function and an increase in log(3MSE errors) over time indicates decline. The SEVLT is a 15-point verbal memory recall test with four 15-word memory trials and a fifth trial that is usually used as the score. SEVLT was developed for SALSA, has been validated in English and Spanish, and used in other studies.[204,277]

A multistage screening process was used for incident dementia or CIND diagnosis over the 10-year follow-up period. First, 3MSE and SEVLT were administered. If participants scored below the 20th percentile on either test or if their scores declined by >8 or >3 points, respectively, from the previous examination, participants were referred for more neuropsychological testing. Second, the Spanish and English Neuropsychological Assessment Scales (SENAS)[278] and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)[279] were used to determine the need for further neurologic testing with the following scoring criteria: ≥3.40 on the IQCODE and below the 10th percentile on ≥1 of the SENAS tests; below the 10th percentile on ≥4 SENAS tests; or >4.0 on the IQCODE. Third, potential dementia cases were diagnosed by neurologists and neuropsychologists using the Diagnostic and

Statistical Manual of Mental Disorders–IV and National Institute of Neurologic and Communicative Disorders and Stroke-Alzheimer Disease and Related Disorders Association criteria. Participants were classified as normal, cognitively impaired, not dementia (CIND), or demented. Demented participants were subject to magnetic resonance imaging and laboratory tests. In this analysis, we combined dementia and CIND cases into a single outcome (dementia/CIND).

Covariates. We considered the following covariates based on previous literature and substantive knowledge in directed acyclic graphs (DAGs)[221]: sociodemographic (age, sex, nativity, chosen English/Spanish survey language, age of US arrival, duration in the US, marital status, education, major lifetime occupation, employment status), lifestyle (diet, physical activity, smoking status, alcohol, sleep), general health (self-reported health, depression, BMI, and insurance status.

We explored the role of educational attainment throughout the analyses as acculturation, cognition, and health are embedded in socioeconomic context and associations are complex and likely bi-directional. Differing levels of education can confer divergent experience, knowledge, values, opportunities, and lifestyles that modify how acculturation influences health and cognition.[43,44,148-150] More educational attainment has been linked to a reduced dementia risk via enhanced cognitive reserve and an elevated SEP.[148-151] Education level is also a source of bias in cognitive testing.[280] We dichotomized attainment and treated <12 years (no high school/GED) as "low" and ≥12 years as "high," a cut point chosen based on the data distribution that is recurring in SALSA research and similar populations.[154,215,216]

5.3.3 Statistical analysis

All analyses were conducted in SAS 9.4 (SAS Institute, Inc., Cary, NC). We assessed the association of acculturation with cognitive decline and dementia/CIND over a 10-year follow up period. We ran three adjusted models based on DAGs and substantive knowledge and included baseline age as recommended when using an age timescale[221,234]: demographic (Model 1: baseline age, sex, marital status); sociodemographic (Model 2: Model 1 + education); and sociodemographic with survey language (Model 3: Model 2 + survey language). Model 2 examined the confounding role of education due to complexities previously described.[43,44,148-150] Model 3 examined chosen survey language (English/Spanish) as a cofounder to account for known cultural biases in cognitive testing.[172,281] We also completed exploratory analyses to assess whether education level modified the direction and magnitude of acculturation-cognition/dementia associations in all analyses.[43,44,148-150]

First, we used *hierarchical linear mixed models for longitudinal associations* between high US acculturation and the rate of cognitive decline over ten years. We used a liberal unstructured correlation structure for within-subject associations, random intercept (baseline cognitive function) and slope (linear rate of cognitive change), and time was operationalized as grand mean centered age at visit. We included indicators for the first and second assessment to account for practice effects in cognitive testing. This method uses maximum likelihood estimation which requires that data be missing completely at random or at random for unbiased estimates.[282] Cognitive impairment and decline can be associated with attrition that is non-ignorable as those with high impairment and an accelerated decline may be unable to complete evaluations or drop-out for reasons related to poor cognition.[283] However, missing at random can be satisfied if patterns of missing data can be accounted for with observed model variables, and

repeated measures of cognition provide insight about decline, which minimizes bias of missing observations.[61]

Second, we evaluated the association between US acculturation and incident dementia/CIND in participants without dementia/CIND at study onset with *Fine and Gray's competing risk regression models.* We examined cumulative incidence functions and produced HRs and 95% CIs.[235] This approach accounts for death as a competing risk that prevents the development of dementia/CIND in participants and produces a more realistic estimation of the hazard. Participants were observed from study entry until date of dementia/CIND diagnosis (the event of interest), death (the competing event), or censoring (last date of contact). Time was operationalized as grand-mean centered age (70 years).

Third, we conducted a *sensitivity assessment* to determine whether cognitive associations varied between two groupings of the acculturative scale questions: language acculturation (i.e. high/low US acculturation score for ARSMA-II language questions) and practice and identity acculturation (i.e. high/low US acculturation score for ARSMA-II non-language measures of social interactions, ethnic identity, and traditions questions). In the first sensitivity assessment we treated high language US acculturation as the exposure (vs. low language US acculturation) and assessed associations with cognitive decline (hierarchical linear mixed model) and incident dementia/CIND (Fine and Gray's competing risk regression model). We did the same in a second assessment where we treated practice and identity acculturation (vs. low practice and identity US acculturation) as the exposure.

5.4 Results

5.4.1 Descriptive characteristics

Descriptive characteristics for SALSA participants with acculturative and cognitive data are displayed in **Table 9** overall and by US acculturation status. The median age was 69.8 years,

58.5% were female, and almost half were born in the US (48.9%). The median educational attainment overall was 6 years and 29.2% of the total population had a high education level (≥high school/GED education). Half of participants (51.0%) reported good or better health. English was the chosen survey language for 42.3% of participants and 34.5% had a high US acculturation level based on ARSMA-II scale score. Dementia/CIND was diagnosed in 6.5% of the total population and 88 was the median 3MSE score.

5.4.2 Hierarchical linear mixed models

Hierarchical linear mixed models assessed associations between baseline high US acculturation and cognitive performance over a ten-year period (**Table 10; Figure 6**). Overall. When adjusting for sociodemographic characteristics and survey language in the total study population (Model 3), high US acculturation participants made 0.20 fewer log-transformed errors on the 3MSE cognitive assessment at baseline (i.e. a better cognitive performance) than low US acculturation participants (high US acculturation β[SE]: -0.20[0.05]). Fewer errors indicates a higher score which indicates a better cognitive performance. However, as the population aged, the rate of cognitive decline did not differ between high US acculturation and low US acculturation participants. For example, when adjusting for sociodemographic characteristics and survey language (Model 3), low US acculturation participants had an average slope of 0.13 log-transformed 3MSE errors (more errors over time indicates decreasing score and cognitive performance; Age β[SE]: 0.13[0.01]) and high US acculturation participants also had an average slope of 0.13 log-transformed 3MSE errors ([Age β(SE): 0.13(0.01)] + [high US acculturation*age β(SE):-0.00(0.00)]). When comparing adjusted models, adjustment for education attenuated the association between high US acculturation and baseline cognitive score by >10% (Model 2 high US acculturation β compared to Model 1 high US acculturation β), as

did language adjustment (Model 3 high US acculturation β compared to Model 2 high US acculturation β). Educational strata. When comparing results between low education and high education strata, we did not observe modification by educational attainment for US acculturation-cognitive performance associations at baseline or over time.

5.4.3 Competing risk regression models

We assessed the association between high US acculturation and incident dementia/CIND using *competing risk models* (**Table 11; Figure 7**). Overall. When adjusting for sociodemographic characteristics and survey language, we did not find a statistically significant association between high US acculturation and dementia/CIND (Model 3 HR[95% CI]: 0.81[0.51, 1.30]). When comparing adjusted models, adjustment for education attenuated the association between high US acculturation and dementia/CIND by >10%, but when we additionally adjusted for language there was less change in estimate (10%). Educational strata. We did not observe modification of the high US acculturation-incident dementia/CIND association by educational attainment.

5.4.4 Sensitivity assessment

Longitudinal analyses (*Supplemental Table 7*). In contrast with the main analyses (**Table 10**) measures of US acculturation were not consistently associated with baseline cognitive score. Specifically, among high education participants, high language US acculturation was not associated with baseline cognitive score and among low education participants, high practice and identity US acculturation was not associated with baseline cognitive score (high US acculturation β[SE]: -0.11[0.12] and -0.00[0.09], respectively). Competing risk regression models (*Supplemental Table 8*). In main analyses (**Table 11**), we did not find an association between high US acculturation and incident dementia/CIND. We also did not observe an association

between high language US acculturation and incident dementia/CIND. Conversely, high practice and identity US acculturation was associated with a decreased risk of incident dementia/CIND in the overall study population and among high education participants (HR[95%CI]: 0.56[0.32, 0.98] and 0.35[0.14, 0.92], respectively).

5.5 Discussion

This is the first population-based study to examine the association between a validated multidimensional measure of US acculturation, cognitive performance, and dementia/CIND in older US Latinos. High US acculturation, when compared to a stronger orientation towards Mexico or other birth/ancestral country, was associated with fewer errors on the 3MSE cognitive assessment (i.e. better cognitive score) at study onset but was not associated with rate of cognitive decline. High practice and identity US acculturation (e.g. social interactions and self-identity) was protective against incident dementia/CIND in the total population and among more educated participants (e.g. social interactions and self-identity, while language acculturation was not association with incident dementia/CIND. These findings conflicted with our hypothesis that there would be a negative association between acculturation and health.[43-46,48-51] Specifically, we conjectured that high US acculturation would be associated with worse cognitive outcomes. Overall, our results suggested that high US acculturation among older Latinos was associated with improved cognitive performance regardless of education level and that social interaction and identity measures of acculturation (as opposed to language measures) were associated with reduced dementia/CIND risk overall and among the more educated. These findings indicate high US acculturation may be protective against poor cognitive outcomes among older Latinos.

Multiple pathways may help us understand why high US acculturation was associated with better cognitive outcomes among the older Latino population. In our study population of older Latinos, we found that high US acculturation was associated with improved levels of some

health outcomes linked to cognition. Cardiovascular risk factors and disease play key roles in the etiology of cognitive decline and dementia and their management may significantly reduce risk for poor cognitive outcomes.[11,155,284] Extensive research has linked high US acculturation to more cardiovascular risk factors and disease in Latino adults,[10-12,14] but more recent studies have found the association may differ for older Latinos.[194,285] Specifically, in our study population, Lopez et al. (2014) found that high US acculturation was associated with improved levels of some cardiovascular factors and behaviors (e.g. blood pressure, cholesterol, physical activity) and not associated with others (e.g. diabetes, obesity, smoking).[194] Previous research has found inconsistent results between physical activity and US acculturation[140,286,287] and that smoking tends to increase.[128] Further, we expected more alcohol consumption and worse sleep for high US acculturation participants based on the research.[13,129] We found this was only true for alcohol in our univariate analyses and that poor sleep was more evenly distributed across acculturative strata (**Table 9**). Consistent with prior findings,[47,50,51,153] we observed more insurance coverage and higher SEP among highly acculturated participants (**Table 9**).

In the context of low US acculturation, we expected some risk factors for poor cognition or dementia to be linked to low US or resident country acculturation, and we found evidence of this in our study population. Depression is a predictor of poor cognition and dementia[165,168] and studies have demonstrated that low resident country acculturation may be associated with worse mental health.[170,171] Accordingly, we observed more depressive symptoms among low US acculturation participants (**Table 9**). Also, elevated acculturative stress is common among those less culturally oriented to a resident country, and this may be attributed to a lack of community integration, perceived discrimination, or more socioeconomic challenges.[250-252,288,289] While we did not measure stress specifically, we observed a lower prevalence of English as chosen survey

language (i.e. an indicator of less community integration) and lower SEP (i.e. more socioeconomic disadvantage) among low US acculturation participants (**Table 9**), suggesting that those with lower US acculturation carried a higher burden of stress-related risk factors.

As noted, language use drives acculturation and can shape cognitive development.[47,58-62,64] Greater exposure to American culture and language is also a source of cultural bias in cognitive testing as it associated with better scores.[172,281] Our main findings were robust to language adjustment, providing confidence that neither cultural bias nor chosen language, an acculturation proxy, drive these associations. Additionally, the sensitivity assessment suggested language acculturation did not fully explain the observed associations between acculturation and cognitive performance or dementia/CIND. Rather, acculturation-dementia associations may be driven by practice and identity acculturative factors, like strong social support and networks. For cognitive performance, a larger indicator of the acculturative process, like community integration which can be a part of language and practice and identity acculturation, may drive associations.

Importantly, education provides socioeconomic context to our research and has been linked to measures of high US acculturation[47,50,51,153] and to reduced dementia risk via mechanisms of enhanced cognitive reserve and the socioeconomic advantages implicit in high education (e.g. more healthcare access).[148-151] Based on changes in estimates across adjusted models, education was an important explanatory variable between high US acculturation, cognitive performance, and dementia/CIND. Still, associations between high US acculturation and cognitive performance were robust to education adjustment, and estimates for cognitive performance did not vary by educational strata. However, education was low overall in our population and there may be residual confounding from our broad educational categories that did not explore variation in low education below attainment of a high school degree. Still, pending

further exploration, our results suggests cultural factors may predict cognitive level independently of education and its benefits (i.e. cognitive reserve and socioeconomic advantage).[148] For example, while some socioeconomic benefits of education are closely tied to high US acculturation,[47,50,51,153] cultural factors and pathways separate from education and SEP, such as social support, community integration, or cardiovascular health, should be explored to better understand acculturation-cognition associations.

Conversely, in sensitivity analyses, high education and high practice and identity US acculturation jointly reduced the dementia/CIND risk in our study population, while there was no association for low education participants. This aligns with the known protective effect of high education against poor cognitive outcomes.[148,149] The lack of educational modification observed for cognitive score may point to the importance of cognitive reserve in dementia/CIND. Large cognitive reserve and improved SEP are both beneficial for general cognition,[148-152] but cognitive reserve plays a more specific role in dementia as high reserve is posited to limit clinical expression by offsetting the physical brain degeneration characteristic of dementia.[151] Therefore, cognitive reserve may drive the modification observed for incident dementia/CIND via a clinical pathway of high education (i.e. more cognitive stimulation) and the enhanced propensity for future stimulation, more cognitive reserve, and then reduced clinical expression of dementia.[151]

While we explored the mechanistic health pathways by which a high US acculturation may associate with better cognition, the reason high US acculturation may have a beneficial association with health in older age has not been well-studied. However, previous work on life satisfaction and SEP may help us understand how high US acculturation may benefit health. Castro et al. (2010) examined assimilation across the lifecourse and found that a trajectory of upward US assimilation was associated with improved health in adulthood, including life

satisfaction.[290] They hypothesized that the development of human and social capital early in life may enhance late-life health, which may be mirrored in our population. The higher education observed and likely established before late-life (**Table 1**) and stronger social networks expected among high US acculturation participants[10-12,148-150,161-163] may have built more human and social capital[291,292] and then enhanced late-life health. This helps us understand the results of our sensitivity assessment whereby practice and identity acculturation may drive US acculturation-cognitive associations as social networks are a key measure of practice and identity acculturation.[47] Our findings may also be explained by associations between life satisfaction, mental health, and physical health as higher life satisfaction has been linked to better mental health[293] (i.e. lower levels of depressive symptoms among high US acculturation participants [**Table 9**]), and poor mental health has been linked to poor physical health.[294] Moreover, the increased healthcare access among those more acculturated likely improves general health and cognitive outcomes with the early detection of poor health conditions, including advanced cognitive decline; more access to medications, therapeutic treatments, and health management; and prevention and intervention of risk factors for poor cognitive outcomes.[10,43,295-297] Finally, in our study population, SEP is low as 44.8% of participants had an income of <$1000/month and the median educational attainment was 6 years (**Table 9**), and previous studies have shown that among low SEP populations, US acculturation may be protective against poor health outcomes.[194,259-263]

Studies beginning earlier in life may provide insight into how sociocultural and health trajectories across the lifecourse interplay to shape late-life cognition and dementia in Latinos. We assessed acculturation-health-cognitive associations in late-life, but acculturative differences in cognitive performance were clearly established before study onset (**Figure 6**). Acculturation

takes place over time and the etiology of dementia is comprised of many health and socioeconomic mechanisms that interact and intervene across the lifecourse.[44,276,298] Both mid- and late-life health influence late-life cognition and dementia status.[299] Mid-life is an important period for cognition as cognitive decline begins during the 20s and 30s[273,275,300] and has been found to accelerate approximately three years before dementia diagnosis, which usually occurs in late-life.[301] Study onset began at a median age of 69.8 years (**Table 9**) and though we lacked mid-life acculturation and health measures, SEP indicators like education and occupation are often already established by mid-life. We are then able to speculate that if these study participants had consistently high US acculturation, they may have exhibited an improved health trajectory across the lifecourse that has led to the observed better cognitive outcomes, via the aforementioned protective effect of US acculturation in low SEP settings.[194,259-263] Still, if mid-life health was worse among high US acculturation participants, improved late-life health combined with strong social support and better access to health services among those highly acculturated[44,47,50,51,153] may counteract any harmful influence high mid-life acculturation may have had on health and cognition. Further, while health among the highly acculturated may improve over time (e.g. cardiovascular health), health among those with low acculturation may remain poor into late-life (e.g. poor mental health, low social support and healthcare access), contributing to poorer cognitive performance observed among low US acculturation participants.

Our study had several limitations. The scope of our acculturation exposure was limited as we were unable to assess biculturalism due to limited sample size. Our study population is older and attrition and selection bias are concerns. For example, poor cognitive functioning is likely associated with increased morbidity or mortality, leading to higher loss to follow up among individuals with cognitive impairment. This attrition could lead to underestimate of the

associations observed in our study.[302] However the repeated cognitive assessments informed this missingness and minimized bias whereby if someone drops out due to reasons related to poor cognition the most recent cognitive performance is likely to be low and inform our analyses.[61] Second, our older population is susceptible to survivor bias whereby participants surviving to age of inclusion are likely healthier than individuals excluded from participation due to morbidity or mortality.[303] This can also lead to depletion of susceptibles whereby the exposure is linked to the morbidity and mortality preventing study enrollment and exposed participants susceptible to disease are depleted.[304] Studies have shown this can lead to a reversal of association.[302] Though our findings refuted our hypothesis, we do not believe depletion of susceptibles has resulted in a reversal of estimate as many plausible health pathways may explain the beneficial association of high US acculturation, and acculturation-health literature has shown that direction of association varies by health factor and socioeconomic context.[43-46,48-51]

Additionally, there may be residual confounding from our high/low treatment of education and variation of associations within the "low" (i.e. <12 years) category may provide further insight to the contributing role of education in this population. However our sample size was limited and this cut point aligned with previous research. Further, we had limited power in educational modification assessments due to smaller sample sizes within educational strata. Dementia/CIND analyses were also underpowered as few participants were diagnosed with dementia/CIND. Finally, the study population was of predominately Mexican ancestry and results may not be generalizable to Latinos overall or other sub-groups.

Our study also had several strengths. Earlier studies have predominantly utilized unidimensional measures of acculturation, such as language use and nativity. We employed a validated multidimensional measure of acculturation to better characterize the multifaceted

process of acculturation.[197] We then separated out language from practice and identity measures of acculturation to explore the role of language and other acculturative factors in cognitive outcomes.[47,58-62,64] We also accounted for bias in cognitive testing with survey language adjustment[172,280,281] and for the competing risk of death in dementia/CIND analyses.[235] Additionally, SALSA data was collected over 10 years with rich sociocultural and clinical health measures, including repeated measures of global cognitive function and a thorough multistage clinical dementia/CIND diagnosis.

5.6 Conclusion

In conclusion, our findings refuted our negative acculturation research hypothesis as we found that high US acculturation was associated with better cognitive outcomes overall, even after adjusting for education and survey language in our study population of older US Latinos. We also found that among those with more education, high practice and identity US acculturation significantly reduced the risk of dementia/CIND overall and in those with higher education, even when adjusting for survey language. Research on the public health implications of acculturation may help identify key components of cultural change that influence health and well-being.[45] For example, we used a multidimensional measure of acculturation and explored which cultural pathways, language acculturation (e.g. language preference with friends) or practice and identity acculturation (e.g. social interactions), may drive the association with cognitive performance and dementia/CIND.[197] If replicated, future studies should examine the underlying mechanistic pathways between culture and cognition highlighted in this research to identify novel points of intervention. For example, the process of acculturation may influence cognitive function through social support and community integration. In addition, cardiovascular risk factors may mediate the associations between acculturation and cognition. In conclusion, our results suggest that high US acculturation was associated with better cognitive performance and

reduced dementia/CIND risk. Future studies should build upon these findings by exploring the modifiable pathways that linking US acculturation, cognition, and dementia to reduce poor cognitive outcomes in Latinos.

5.7 Main tables and figures

Table 9. Baseline sociodemographic and health characteristics[a] of participants with acculturation and cognition data, overall and by US acculturation status: Sacramento Area Latino Study on Aging.

	Overall (N=1778)	US acculturation	
		Low (N=1164)	High (N=614)
	Median (interquartile range) or N (%)		
Sociodemographic factors			
Age	69.8 (65.1, 75.2)	70.1 (65.2, 75.5)	69.2 (64.9, 74.6)
Female sex (vs. male)	1040 (58.5)	705 (60.6)	335 (54.6)
US nativity (vs. non-US[b])	870 (48.9)	325 (27.9)	545 (88.8)
Migration age[c]	29.9 (20.0, 45.0)	32.0 (21.2, 48.0)	2.0 (1.0, 13.9)
Marriage/domestic partnership (vs. none)	1046 (58.9)	688 (59.2)	358 (58.3)
Missing	1	1	
High education (vs. low)[d]	519 (29.2)	167 (14.4)	352 (57.3)
Number of years	6.0 (3.0, 12.0)	4.0 (1.0, 8.0)	12.0 (8.0, 14.0)
Major lifetime occupation			
Non-manual	372 (21.2)	140 (12.2)	232 (38.2)
Manual	1056 (60.1)	769 (66.8)	287 (47.3)
Other[e]	330 (18.8)	242 (21.0)	88 (14.5)
Missing	20	13	7
Gross household income per month			
<$1000	784 (44.8)	651 (57.1)	133 (21.8)
$1000-$1999	557 (31.8)	339 (29.7)	218 (35.8)
≥$2000	409 (23.4)	151 (13.2)	258 (42.4)
Missing	28	23	5
English survey language (vs. Spanish)	752 (42.3)	192 (16.5)	560 (91.2)
Measures of health			
Insurance coverage (vs. none)	1610 (90.7)	1013 (87.2)	597 (97.4)
Missing	3	2	1
Good or better self-rated health (vs. worse than good)	873 (51.0)	478 (43.1)	395 (65.5)
Missing	65	54	11
Body mass index			
>25	310 (19.1)	191 (18.3)	119 (20.5)
25-29	629 (38.7)	417 (39.9)	212 (36.5)
≥30	688 (42.3)	438 (41.9)	250 (43.0)
Missing	151	118	33
Any alcohol consumption (vs. none)[f]	945 (53.2)	558 (48.0)	387 (63.0)
Missing	1	1	0

	Overall (N=1778)	US acculturation	
		Low (N=1164)	High (N=614)
	Median (interquartile range) or N (%)		
Smoking status			
Never	818 (46.1)	540 (46.5)	278 (45.3)
Former	754 (42.5)	486 (41.9)	268 (43.7)
Current	203 (11.4)	135 (11.6)	68 (11.1)
Missing	3	3	0
Overall fatigue in past month (vs. none)			
Baseline	496 (28.9)	327 (29.4)	169 (28.0)
Missing	62	51	11
Ever during study period	804 (46.5)	530 (47.0)	274 (45.4)
Missing	47	36	11
Restless sleep in past week (vs. none)			
Baseline	404 (23.5)	307 (27.6)	97 (16.1)
Missing	62	51	11
Ever during study period	857 (49.5)	611 (54.2)	246 (40.8)
Missing	48	37	11
High depressive symptoms (vs. low)[g]			
Baseline	439 (25.5)	342 (30.6)	97 (16.0)
Missing	54	46	8
Ever during study period	916 (52.8)	640 (56.6)	276 (45.5)
Missing	42	34	8
Diabetes diagnosis (vs. none)			
Baseline	586 (33.0)	380 (32.7)	206 (33.6)
Ever during study period	810 (45.6)	529 (45.5)	281 (45.8)
Mortality during study period (vs. living)	641 (36.1)	421 (36.2)	220 (35.8)
ARSMA-II acculturation scores			
High US acculturation (vs. low)	614 (34.5)	0 (0.0)	100 (100.0)
High language US acculturation (vs. low)	809 (45.5)	205 (17.6)	604 (98.4)
High practice and identity US acculturation (vs. low)	278 (15.6)	9 (0.8)	269 (43.8)
Cognitive outcomes			
3MSE (raw score)	88.0 (80.0, 93.0)	85.0 (76.0, 91.0)	92.0 (87.0, 97.0)
Dementia diagnosis (vs. none)			
Baseline	68 (3.8)	51 (4.4)	17 (2.8)
Ever	184 (10.4)	135 (11.6)	49 (8.0)
CIND diagnosis (vs. none)			
Baseline	47 (2.6)	34 (2.9)	13 (2.1)
Ever	115 (6.5)	79 (6.8)	36 (5.9)
Dementia/CIND diagnosis (vs. none)			

	Overall (N=1778)	US acculturation	
		Low (N=1164)	High (N=614)
	Median (interquartile range) or N (%)		
Baseline	115 (6.5)	85 (7.3)	30 (4.9)
Ever	274 (15.4)	197 (16.9)	77 (12.5)

Abbreviations: US, United States; 3MSE, Modified Mini-Mental State Exam; CIND, cognitive impairment, no dementia.

[a]Characteristics collected at baseline unless otherwise stated.

[b]Non-US birth country: Mexico, 88.8%; other, 11.2.

[c]Migration age restricted to non-US born participants.

[d]Educational attainment: high ≥12 years/high school/GED education; low <12 years/high school/GED education.

[e]Includes participants categorized as unemployed or housewives.

[f]Beer, wine, or liquor.

[g]20-item Center for the Epidemiological Studies of Depression Scale score ≥16 = high.

Table 10. Change in errors on the Modified Mini-Mental State Exam from linear mixed models by US acculturation status overall and by educational attainment strata[a]: Sacramento Area Latino Study on Aging (N=1778).

	High US acculturation (vs. low)			
	Crude	Model 1[b]	Model 2[c]	Model 3[d]
	β (standard error) of log-transformed 3MSE errors			
	Overall			
High US acculturation	-0.60 (0.04)	-0.57 (0.04)	-0.31 (0.04)	-0.20 (0.05)
Age	0.04 (0.00)	0.13 (0.01)	0.13 (0.01)	0.13 (0.01)
High US acculturation*Age	0.00 (0.00)	0.00 (0.00)	-0.00 (0.00)	-0.00 (0.00)
	Low education			
High US acculturation	-0.41 (0.06)	-0.39 (0.06)		-0.18 (0.07)
Age	0.04 (0.00)	0.12 (0.01)		0.12 (0.01)
High US acculturation*Age	-0.00 (0.01)	-0.00 (0.01)		-0.00 (0.01)
	High education			
High US acculturation	-0.21 (0.06)	-0.17 (0.06)		-0.20 (0.08)
Age	0.05 (0.01)	0.17 (0.01)		0.17 (0.01)
High US acculturation*Age	-0.01 (0.01)	-0.00 (0.01)		-0.01 (0.01)

Abbreviations: CIND, cognitive impairment, not dementia; US, United States.

[a]Educational attainment: high ≥12 years, low <12 years.

[b]Adjusted for age, sex, marital status.

[c]Adjusted for age, sex, marital status, and educational attainment.

[d]Adjusted for age, sex, marital status, survey language, and in overall models, educational attainment.

Table 11. Hazard ratios from Fine and Gray's competing risk regression models for incident dementia/CIND and US acculturation status, overall and by educational attainment strata[a]: Sacramento Area Latino Study on Aging (N=1663).

	High US acculturation (vs. low)		
	Overall	Low education	High education
	Hazard ratio (95% confidence interval)		
Crude	0.78 (0.56, 1.09)	0.74 (0.34, 1.63)	0.95 (0.64, 1.40)
Model 1[b]	0.79 (0.56, 1.10)	0.95 (0.63, 1.41)	0.72 (0.32, 1.60)
Model 2[c]	0.90 (0.63, 1.31)		
Model 3[d]	0.81 (0.51, 1.30)	0.90 (0.52, 1.55)	0.53 (0.22, 1.27)

Abbreviations: CIND, cognitive impairment, no dementia; US, United States.

[a]Educational attainment: high ≥12 years, low <12 years.

[b]Adjusted for age, sex, marital status.

[c]Adjusted for age, sex, marital status, and educational attainment.

[d]Adjusted for age, sex, marital status, survey language, and in overall models, educational attainment.

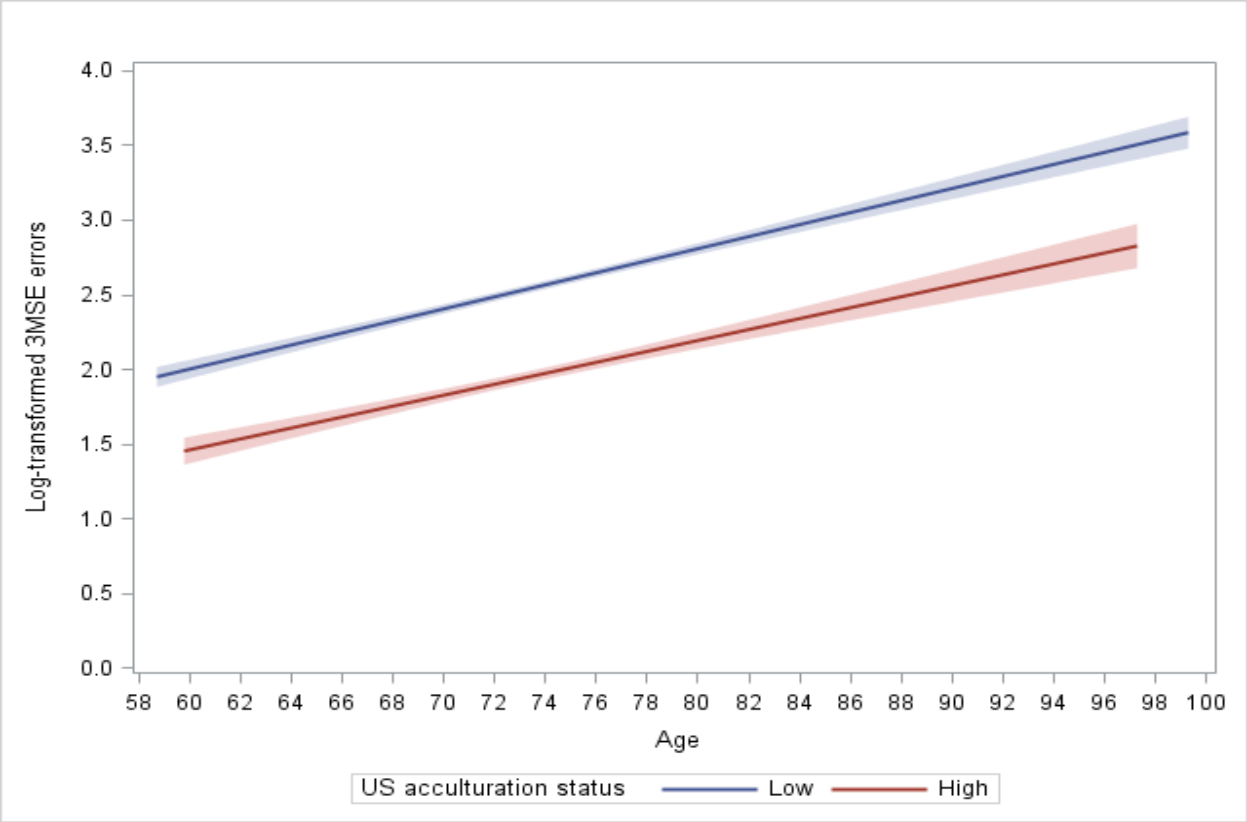

Figure 6. Predicted mean log-transformed 3MSE errors over time (age)[a] by US acculturation status: Sacramento Area Latino Study on Aging.

[a]Adjusted for age, sex, and educational attainment.

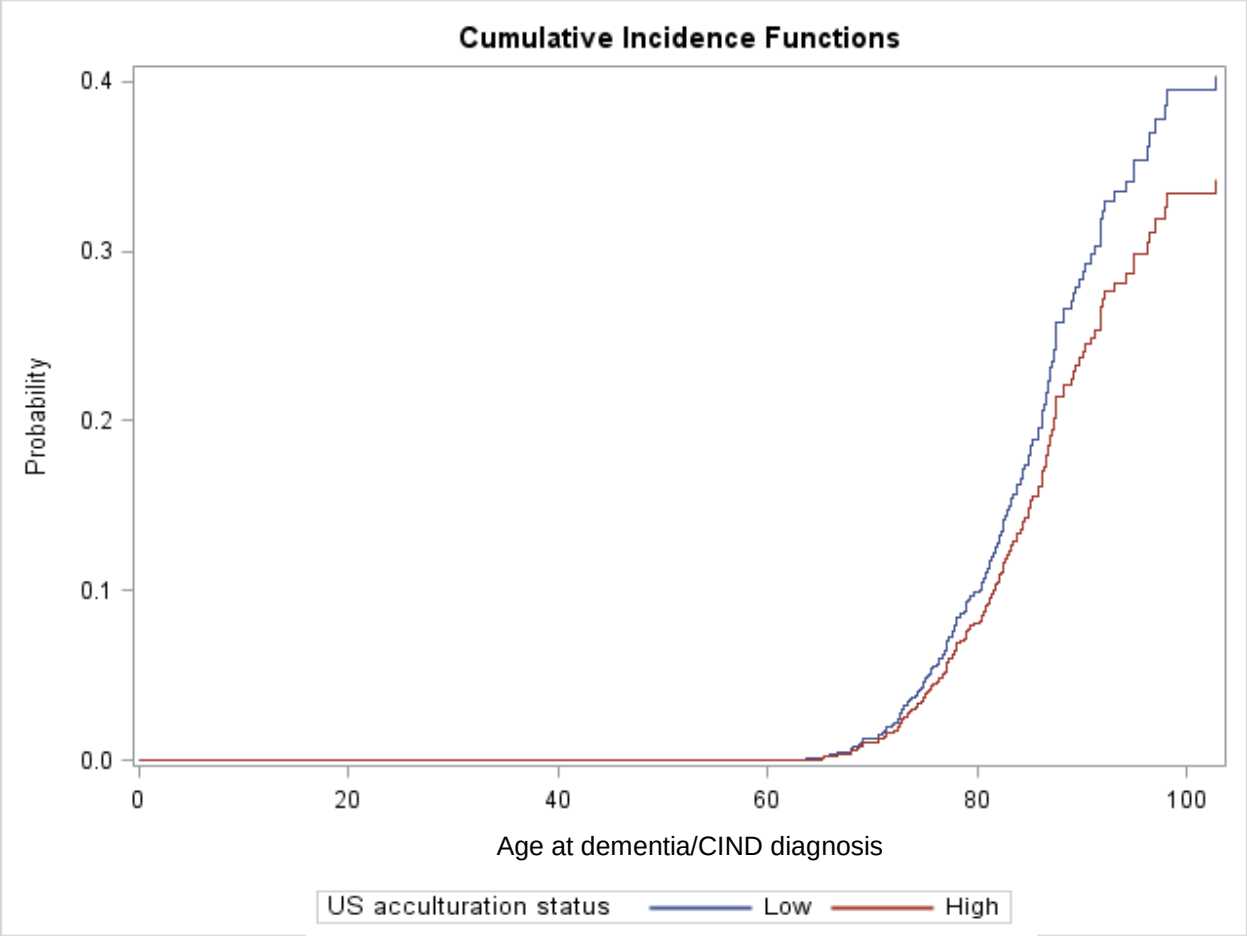

Figure 7. Cumulative incidence functions[a] for dementia/CIND by acculturation status, accounting for the competing risk of death: Sacramento Area Latino Study on Aging.
Abbreviations: CIND, cognitive impairment, not dementia; US, United States.
[a]Adjusted for baseline age, sex, marital status, educational attainment, and survey language.

5.8 Supplemental tables

Supplemental Table 7. Change in errors on the Modified Mini-Mental State Exam from adjusted linear mixed models for language US acculturation and for practice and identity US acculturation, overall and by educational attainment strata[b]: Sacramento Area Latino Study on Aging (N=1778).

	Overall	Low education	High education
	β (standard error) of log-transformed 3MSE errors		
	High language US acculturation (vs. low)		
High US acculturation	-0.19 (0.06)	-0.19 (0.07)	-0.11 (0.12)
Age	0.13 (0.01)	0.12 (0.01)	0.17 (0.01)
High US acculturation*Age	-0.00 (0.00)	-0.00 (0.01)	-0.00 (0.01)
	High practice and identity US acculturation (vs. low)		
High US acculturation	-0.12 (0.05)	-0.00 (0.09)	-0.19 (0.07)
Age	0.13 (0.01)	0.12 (0.01)	0.16 (0.01)
High US acculturation*Age	0.00 (0.01)	0.00 (0.01)	0.00 (0.01)

Abbreviations: CIND, cognitive impairment, not dementia; US, United States.

[a]Adjusted for age, sex, marital status, survey language, and in overall models, educational attainment.

[b]Educational attainment: high ≥12 years, low <12 years.

Supplemental Table 8. Hazard ratios from adjusted[a] Fine and Gray's competing risk regression models for incident dementia/CIND, language US acculturation, and practice and identity US acculturation, overall and by educational attainment strata[b]: Sacramento Area Latino Study on Aging (N=1663).

	Overall	Low education	High education
	Hazard ratio (95% confidence interval)		
High language US acculturation (vs. low)	0.88 (0.57, 1.36)	0.93 (0.58, 1.48)	0.58 (0.17, 2.01)
High practice and identity US acculturation (vs. low)	0.56 (0.32, 0.98)	0.72 (0.37, 1.40)	0.35 (0.14, 0.92)

Abbreviations: CIND, cognitive impairment, no dementia; US, United States.

[a]Adjusted for age, sex, marital status, survey language, and in overall models, educational attainment.

[b]Educational attainment: high ≥12 years, low <12 years.

CHAPTER 6: SLEEP, COGNITIVE DECLINE, AND DEMENTIA AMONG OLDER LATINOS IN THE SACRAMENTO, CALIFORNIA REGION

6.1 Results

In adjusted models, participants with overall fatigue at baseline made 0.09 more log-transformed errors on the 3MSE cognitive assessment at baseline (i.e. worse cognitive performance) than participants without overall fatigue (overall fatigue adjusted model, sleep measure β[SE]: 0.09[0.04]). More errors indicates a lower score which indicates worse cognitive performance. As the population aged, the rate of cognitive decline did not differ between participants who did and did not report overall fatigue at baseline. Restless sleep at baseline was not associated with cognitive performance at baseline or cognitive decline over the ten-year period. In exploratory analyses, we did not observe clear modification of sleep-cognitive performance associations by ApoE-ε4 genotype status at baseline or over time, but we were underpowered.

In adjusted models, neither restless sleep not overall fatigue were associated with incident dementia/CIND. In exploratory analyses, we did not observe clear modification of sleep-incident dementia/CIND associations by ApoE-ε4 genotype status at baseline or over time, but we were underpowered.

6.2 Discussion

We found that participants with overall fatigue had worse cognitive performance at baseline than those without overall fatigue in this study population of older Latinos. We did not observe associations between sleep measures, cognitive decline, and dementia. However, these

associations should be explored in larger US Latino populations and with methods that account for changes in sleep over time.

We had several limitations for this aim. We used subjective unidimensional measures which are not the gold standard for sleep measurement,[94] but we used two different measures to capture more than one dimension. Further, sleep changes over time and can worsen with age, and cognitive outcomes are a result of an accumulation of many health factors over time.[241,242,276,305,306] This approach only used baseline measures of sleep and therefore did not capture the full scope of interplay between sleep, cognitive decline, and dementia/CIND. Given our repeated assessments and older population, attrition and selection bias are also concerns as out cognitive outcomes are likely linked to these factors. The repeated cognitive assessments inform missingness and minimize bias.[61,302] We are also susceptible to survivor bias whereby participants surviving to age of inclusion are likely healthier than individuals excluded from participation due to morbidity or mortality, both of which are likely related to the exposure and outcome.[303] This can also lead to depletion of susceptibles whereby individuals with poor sleep who are susceptible to disease are depleted in the study population.[304] These are challenges in any older cohort and likely lead to an underestimation of association. We also had limited power in dementia/CIND analyses and in ApoE-ε4 modification assessments due to small numbers of participants diagnosed with dementia/CIND and small sample sizes within strata. Finally, the study population was of predominately Mexican ancestry and results may not be generalizable to the Latinos overall or other sub-groups.

We also had several strengths. We explored sleep-cognitive and dementia association in an older Latino cohort (SALSA) with data collected over 10 years with rich sociocultural and clinical health measures, including repeated measures of global cognitive function and a

thorough multistage clinical dementia/CIND diagnosis. While our sleep measures were limited, we used two separate self-reported measures, restless sleep and overall fatigue, to capture more than one sleep dimension in association with cognitive outcomes. In incident dementia/CIND assessments, we accounted for the competing risk of death in our analyses with Fine and Gray's competing risk regression models.[235] We also accounted for the genetic contribution of ApoE-ε4 genotype by assessing whether it played a modifying role. Finally, we add to a body of literature exploring sleep and cognitive outcomes. While this association has been explored in other racial/ethnic populations, it has received limited attention among Latinos.[21-26,93,307,308]

6.3 Conclusions

Among older Latinos, overall fatigue was associated with worse cognitive performance at study onset, but rates of cognitive decline did not differ by fatigue status over time, suggesting that the differential cognitive performance by fatigue status may have been established before study onset. These associations should be explored among larger Latino populations that are followed for longer periods of time and beginning earlier in life. Future studies should also explore repeated sleep assessments for a better understanding of how sleep and cognition interact over time. If a reciprocal relationship is established over time and at earlier stages of adulthood, poor sleep may be an important target for cognitive prevention and intervention efforts among Latinos, and intervention tactics promoting healthy sleep may have long term cognitive benefits for the Latino population.

6.4 Main tables and figures

Table 12. Descriptive characteristics[a] of participants with sleep and cognition data, overall and by self-reported poor sleep measure: Sacramento Area Latino Study on Aging.

	Median (interquartile range) or N (%)		
	Overall (N=1716)	**Restless sleep (N=404)**	**Overall fatigue (N=496)**
	Sociodemographic and cultural characteristics		
Age	69.5 (65.0, 74.7)	70.2 (65.0, 75.1)	69.8 (64.9, 75.5)
Female sex (vs. male)	1001 (58.3)	269 (66.6)	338 (68.2)
US nativity (vs. non-US)	847 (49.4)	175 (43.3)	244 (49.2)
High education (vs. low)[b]	1206 (70.3)	321 (79.5)	364 (73.4)
Marriage/domestic partnership (vs. none)	694 (40.5)	174 (43.2)	227 (45.8)
Missing	1	1	0
Major lifetime occupation			
Non-manual	367 (21.6)	64 (16.0)	95 (19.3)
Manual	1016 (59.8)	239 (59.8)	267 (54.3)
Other[c]	315 (18.6)	97 (24.3)	130 (26.4)
Missing	18	4	4
Gross household income per month			
<$1000	746 (44.1)	223 (55.8)	266 (54.4)
$1000-$1999	542 (32.1)	119 (29.8)	130 (26.6)
≥$2000	403 (23.8)	58 (14.5)	93 (19.0)
Missing	25	4	7
Acculturation score	-0.67 (-2.14, 0.31)	-1.42 (-2.30, -0.05)	-1.08 (-2.31, 0.28)
English survey language (vs. Spanish)	739 (43.1)	128 (31.7)	204 (41.1)
		Health measures	
Insurance coverage (vs. none)	1554 (90.7)	369 (91.3)	464 (93.7)
Missing	2	0	1
Body mass index			
>25	297 (18.9)	68 (18.6)	80 (17.8)
25-29	605 (38.4)	137 (37.5)	167 (37.1)
≥30	675 (42.8)	160 (43.8)	203 (45.1)
Missing	139	39	46
Any alcohol consumption: yes (vs. no)	933 (54.4)	196 (48.5)	209 (42.1)
Smoking status			
Never	787 (45.9)	184 (45.5)	221 (44.7)
Former	730 (42.6)	168 (41.6)	223 (45.1)
Current	198 (11.6)	52 (12.9)	51 (10.3)
Missing	1	0	1
Any ApoE-ε4 gene: yes (vs. no)	221 (14.2)	54 (14.8)	63 (14.3)
Missing	155	40	56

	Median (interquartile range) or N (%)		
	Overall (N=1716)	**Restless sleep (N=404)**	**Overall fatigue (N=496)**
Good or better self-rated health (vs. worse than good)	840 (49.0)	256 (63.4)	325 (65.5)
Missing	3	0	0
High depressive symptoms (vs. low)			
Baseline	439 (25.6)	228 (56.4)	239 (48.2)
Ever	912 (53.2)	307 (76.0)	361 (72.8)
Hypertension (vs. none)			
Baseline	1163 (67.8)	270 (66.8)	367 (74.0)
Ever	1549 (90.3)	358 (88.6)	463 (93.4)
Diabetes (vs. none)			
Baseline	557 (32.5)	138 (34.2)	200 (40.3)
Ever	779 (45.4)	186 (46.0)	260 (52.4)
Mortality during study period: yes (vs. no)	592 (34.5)	156 (38.6)	210 (42.3)
		Sleep measures	
Restless sleep in past week (vs. none)	404 (23.5)	404 (100.0)	190 (38.3)
Overall fatigue in past month (vs. none)	496 (28.9)	190 (47.0)	496 (100.0)
		Cognitive measures	
3MSE (raw score)	90.0 (83.0, 94.0)	88 .0 (81.0, 93.0)	88.5 (80.0, 93.5)
Dementia diagnosis (vs. none)			
Baseline	29 (1.7)	9 (0.5)	9 (0.5)
Ever	137 (8.0)	42 (10.4)	47 (9.5)
CIND diagnosis (vs. none)			
Baseline	45 (2.6)	15 (0.9)	18 (1.0)
Ever	113 (6.6)	29 (7.2)	36 (7.3)
Dementia/CIND diagnosis (vs. none)			
Baseline	74 (4.3)	24 (5.9)	27 (5.4)
Ever	225 (13.1)	62 (15.4)	73 (14.7)
Age at dementia/CIND diagnosis (years)	75.4 (71.2, 80.8)	75.9 (71.1, 81.5)	75.3 (71.1, 81.6)

Abbreviations: SALSA, Sacramento Area Latino Study on Aging; ApoE-ε4, apolipoprotein E-ε4; 3MSE, Modified Mini-Mental State Exam; CIND, cognitive impairment, no dementia.

[a]Characteristics collected at baseline unless otherwise stated.

[b]Educational attainment: high ≥12 years; low <12 years.

[c]Includes participants categorized as unemployed or housewives.

Table 13. Change in errors on the Modified Mini-Mental State Exam (3MSE) from linear mixed models by poor sleep measure, overall and by apolipoprotein E-ε4 (ApoE-ε4) status: Sacramento Area Latino Study on Aging.

	β (standard error) log-transformed 3MSE errors			
	Restless sleep		**Overall fatigue**	
	Crude (N=1716)	Adjusted[a] (N=1337)	Crude (N=1716)	Adjusted[a] (N=1337)
			Overall	
Sleep measure	0.16 (0.05)	-0.00 (0.04)	0.18 (0.05)	0.09 (0.04)
Age	0.04 (0.00)	0.13 (0.01)	0.04 (0.00)	0.13 (0.01)
Sleep measure*Age	0.01 (0.01)	0.00 (0.01)	0.01 (0.01)	0.00 (0.00)
			ApoE-ε4 status	
			Not present	
Sleep measure	0.17 (0.05)	-0.01 (0.05)	0.17 (0.05)	0.08 (0.04)
Age	0.04 (0.00)	0.13 (0.01)	0.04 (0.00)	0.13 (0.01)
Sleep measure*Age	0.01 (0.01)	0.01 (0.01)	0.01 (0.01)	0.00 (0.01)
			Present	
Sleep measure	0.23 (0.14)	0.00 (0.13)	0.31 (0.13)	0.14 (0.12)
Age	0.05 (0.01)	0.16 (0.02)	0.04 (0.01)	0.15 (0.02)
Sleep measure*Age	-0.02 (0.02)	-0.02 (0.01)	0.00 (0.01)	0.01 (0.01)
Interaction *p*-value	0.74	0.66	0.32	0.29

Abbreviations: 3MSE, Modified Mini-Mental State Exam; ApoE-ε4, apolipoprotein E-ε4; SALSA, Sacramento Area Latino Study on Aging.

[a]Adjusted for age (continuous), sex, education, major lifetime occupation, family income, marital status, US acculturation status, any alcohol consumption, smoker status, depression, hypertension, diabetes, practice effects, survey language, and in overall models, ApoE-ε4 status.

Table 14. Hazard ratios for dementia/CIND by poor sleep measure, overall and by apolipoprotein E-ε4 (ApoE-ε4) status: Sacramento Area Latino Study on Aging.

	Hazard ratio (95% confidence interval)			
	Restless sleep		**Overall fatigue**	
	Crude (N=1642)	Adjusted[a] (N=1420)	Crude (N=1642)	Adjusted[a] (N=1420)
Overall	1.09 (0.75, 1.56)	0.87 (0.58, 1.30)	0.97 (0.69, 1.37)	0.86 (0.61, 1.23)
ApoE-ε4 genotype				
Not present	1.22 (0.81, 1.85)	0.94 (0.59, 1.49)	1.10 (0.74, 1.64)	0.91 (0.61, 1.35)
Present	0.69 (0.28, 1.69)	0.72 (0.29, 1.77)	0.81 (0.35, 1.88)	0.73 (0.32, 1.65)
Interaction *p*-value	0.30	0.35	0.52	0.38

Abbreviations: CIND, cognitive impairment with no dementia; ApoE-ε4, apolipoprotein E-ε4.

[a]Adjusted for age (continuous), sex, education, major lifetime occupation, family income, marital status, US acculturation status, any alcohol consumption, smoker status, depression, hypertension, diabetes, survey language, and in overall models, ApoE-ε4 status.

CHAPTER 7: DISCUSSION

This dissertation sought to gain a greater understanding of the cognitive disparity among Latinos in the US by examining the contribution of sociocultural factors to cognitive outcomes in an intergenerational cohort of Latinos in the Sacramento, California region. We additionally focused on poor sleep given its known associations with poor cognitive outcomes and a body of research that has suggested Latinos face higher proportions of poor sleep. We hypothesized that (1) high US acculturation in single-generations and across generations would be associated with worse sleep and cognitive outcomes; (2) that low SEP would exacerbate these harmful associations; and (3) that our findings would identify poor sleep as a potential pathway linking high US acculturation and poor cognitive outcomes.

First, we found that associations between US acculturation and poor sleep varied by generational cohort, the acculturation status of previous generations (i.e. intergenerational acculturation), and socioeconomic context. Consistent with our hypothesis, high intergenerational US acculturation was associated with shorter sleep durations among middle-age GEN2. Conversely, among older GEN1, high US acculturation in single generations and across generations was associated with better sleep outcomes (i.e. less restless and better sleep overall). However, when we explored these associations within varying socioeconomic context among GEN1, we found high intergenerational US acculturation either had null (e.g. restless sleep) or harmful (e.g. fatigue) sleep associations in higher SEP settings (i.e. high educational attainment or non-manual occupations). The harmful association correlated with the negative acculturation hypothesis and second generation findings, and also provided support for previous research

suggesting high US acculturation may be beneficial for health in low SEP settings. High US acculturation may be beneficial in low SEP settings due to multiple potential mechanisms. For example, more US acculturation can enhance the ability to access health and social services, which may be especially relevant at older age.[44]

Intergenerational findings among both GEN1 and GEN2 indicated upwardly mobile acculturation (i.e. the intermediate level where a parent had low acculturation and the subsequent generation had high acculturation) may not associate with sleep outcomes. Sleep associations were null for these intermediate groups, while associations were identified between measures of high intergenerational US acculturation and some sleep outcomes in both generations, though in opposite directions. Intermediate levels of intergenerational US acculturation are likely to be more bicultural in nature, and the positive and negative influences of each culture on sleep may counteract to ultimately result in no association. However, previous studies have found beneficial associations between some health outcomes and biculturalism.[46] Overall, our findings highlighted the importance of sociocultural pathways in patterning sleep. Future studies should explore whether the differential sleep associations by cohort are a function of SEP, age, or both.

Second, we examined associations between US acculturation, cognitive performance, and incident dementia/CIND among the larger GEN1 population. High US acculturation was associated with better cognitive performance at study onset, but not rate of cognitive decline over the 10-year period. These associations did not vary by level of educational attainment and were robust to language adjustment. We used educational cut points based on attainment of a high school degree, which aligns with previous cognitive literature, but further assessment of how associations between acculturation, cognition, and dementia vary within lower levels of educational attainment (i.e. less than a high school degree) may provide a greater understanding

of the contributing role of educational attainment to cognitive outcomes within this population. Still, the observed results may indicate that acculturation influences cognitive performance via factors separate from education and language use. In a sensitivity assessment, we explored whether language acculturation or other acculturative factors drove associations between US acculturation and cognitive outcomes, but results did not vary by either grouping of acculturative factors (language vs. practice and identity). This may indicate that a broad acculturative factor, such as community integration, that resonates with both language acculturation and practice and identity acculturation may drive the association. Enhanced community integration may operate on cognitive performance in multiple ways; for example, improved mental health, physical activity, or cardiovascular health are potential pathways that may explain the beneficial association of high US acculturation on cognitive performance in this population.

For dementia/CIND, we did not find associations with a multidimensional measure of high US acculturation. However, practice and identity US acculturation, a subset of acculturative measures that include social interactions and personality identity, was associated with a reduced risk of dementia/CIND overall and among participants with a higher education (≥12 years). Language acculturation was not associated with incident dementia/CIND. The observed benefit of higher education for dementia/CIND correlates with the literature and hypothesized advantages of a larger cognitive reserve and enhanced SEP stemming from more education. Advantages linked to both more education and high acculturation like strong social support may drive the joint reduction of dementia/CIND risk in this population.

The beneficial association between high practice and identity US acculturation and dementia/CIND observed in GEN1 conflicted with our negative acculturation hypothesis, but correlated with GEN1 findings of a beneficial association between high US acculturation and

sleep outcomes (i.e. aim 1 results). Our findings provide further support to previous research suggesting high US acculturation is beneficial to health in low SEP settings. Though we assessed these associations among "high" educational attainment, an indicator of higher SEP, education is low among GEN1 overall, so the consistent beneficial association of high US acculturation is not surprising across levels of educational attainment. Perhaps we would find a result for cognitive outcomes more consistent with our negative acculturation hypothesis among participants with non-manual occupations as we did for sleep outcomes. Further exploration of this within the same population would provide a greater understanding of how high US acculturation associates with cognitive performance and dementia in higher socioeconomic settings among older Latinos. Overall, our results point to the importance of sociocultural pathways in shaping cognitive outcomes among this population, and suggest that community integration and social support should be explored further as acculturative factors driving the association.

Third, among the older GEN1 Latino population, we examined the association between self-reported restless sleep and fatigue at study onset with cognitive performance and risk of dementia/CIND over the 10-year period. We ultimately decided this question would be best addressed with a methodological approach that accounts for the variation of sleep over time, but this approach is outside of the scope of this dissertation and will be pursued at a future date. However, briefly, with the proposed methodological approach, participants who reported overall fatigue had worse cognitive performance than those who did not report fatigue at study onset. Poor sleep measures were not associated with rate of cognitive decline or incident dementia/CIND. Due to small numbers, stratified analyses by ApoE-ε4 genotype were underpowered to detect significant effect modification and this should be explored further in a

larger Latino population to elucidate whether sleep may drive the disproportionate burden of poor cognitive outcomes among Latinos.

While we were unable to fully assess how sleep, cognitive decline, and dementia were associated in our study population, we were able to draw conclusions about how a high US acculturation, or cultural orientation, may shape sleep and cognitive outcomes. GEN1 participants were older Latinos of low SEP and we observed that high US acculturation had protective associations against poor sleep, poor cognitive performance, and dementia in this population. A positive link between sleep and cognitive outcomes has been well-explored in populations largely comprised of non-Latinos.[23,64,91,92] If the same associations were observed among Latino populations, improved sleep may be a connecting pathway between high US acculturation and improved cognitive outcomes given the many shared risk factors that are shaped by the acculturative process.

However, the positive acculturation association for both sleep and cognition may be driven by the low SEP of GEN1. We observed reversed acculturation-sleep associations among the middle-age GEN2 cohort of a higher SEP whereby high US acculturation was associated with worse sleep duration, though differing ages among the cohorts may also be a contributing factor. In GEN1, the beneficial association between high US acculturation and fatigue among non-manual occupations provides further support for the importance of SEP in shaping the influence of acculturation on health. When SEP is low, high US acculturation may enhance health via increased social support and community integration or greater knowledge and ability to access health and social services. These factors may be especially relevant in old age when chronic conditions are more prevalent. While this needs to be explored in other Latino

populations with more diverse socioeconomic profiles, we can conclude that the influence of acculturation on sleep and cognitive outcomes depends upon socioeconomic context.

Overall, our results highlight the importance of sociocultural pathways in shaping sleep and cognitive outcomes among Latinos. Future studies should consider the process of acculturation and immigration over generations, along with socioeconomic factors, in sleep and cognitive studies among Latinos in the US. Moreover, exploration of community integration and social support as acculturative factors that drive these associations through multiple health pathways (e.g. risk behaviors, mental health, and related chronic health conditions) may provide greater understanding of how acculturation shapes health.

Our results provide an understanding of how a broad cultural orientation works in conjunction with sociodemographic factors to shape sleep and cognitive disparities among Latinos. Our overall results were not consistent with the negative acculturation hypothesis, and the influence of acculturation on sleep and cognition instead was found to vary by socioeconomic factors, and sleep associations may vary by age group as well. Future studies in Latino populations should explore these same associations to elucidate the complex sociocultural pathways shaping sleep and cognition. If a deeper understanding of the sociocultural framework that shapes sleep and cognitive outcomes could be gained, future studies could build upon these findings by (1) identifying underlying mechanistic behaviors linking acculturation to these health outcomes for intervention targets (e.g. physical activity), and (2) developing efficacious prevention and intervention efforts aimed at reducing disparities that incorporate upstream sociocultural factors (e.g. enhancing community integration). Additionally, social policy measures developed to improve the broader socioeconomic environment may serve to improve sleep and cognitive disparities, as well as other related health behaviors and outcomes.

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