# The Association between Social Isolation and Memory Function in Middle-aged and Older Adults: A Cross-sectional Analysis of the Comprehensive Cohort of the Canadian Longitudinal Study on Aging

by

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## Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

## Abstract

**Background:** Social isolation is a psychosocial risk factor thought to be inversely associated with memory function, although only a small number of published studies exist in the field. These studies report mixed results due to variations in methods (e.g., study design, measures of social isolation that do not capture the full extent of the construct) or the inclusion of highly select samples of target populations. Given limitations of the published literature, this thesis investigated the cross-sectional association between social isolation and memory in a large, community-dwelling sample of Canadian adults aged between 45 and 85 years. The association was examined across the entire sample and in separate stratified analyses defined by age group and sex.

**Methods:** Baseline data from the Comprehensive Cohort of the Canadian Longitudinal Study on Aging (CLSA) were used to regress memory scores onto a composite Social Isolation Index (SII) that measured numbers of social contacts, frequencies of interaction with these contacts, frequencies of participation in social activities, marital status, and retirement status. The SII ranged from 0–5 and scores between 2-5 were classified as "socially isolated", while scores between 0-1 were classified as "not socially isolated". The dichotomous version of the SII was used in all analyses. Memory was measured using the immediate and delayed recall administrations of the Rey Auditory Verbal Learning Test (RAVLT); raw test scores were converted into z-scores ($\mu = 0$, $\sigma = 1$) and analyzed separately for each administration. Multivariable linear regression models controlled for a range of covariates, including age group, sex, education, income, presence of chronic conditions ($\geq 1$ versus 0), functional impairment, presence of depressive symptoms, smoking status, alcohol use, and functional social support (low versus high). Weight and strata variables were included in the models to account for the

CLSA's complex survey design. Full models adjusted for all covariates (except for those used for stratification purposes) were separately stratified by age group and sex to assess effect modification.

**Results:** Regression models showed small, inverse associations between social isolation and RAVLT I ($\hat{\beta}$ = -0.0019; 95% CI: -0.0469 to 0.043) and RAVLT II ($\hat{\beta}$ = -0.0010; 95% CI: -0.0496 to 0.0475) z-scores. However, the associations were weak and not statistically significant. Stratification by age group and sex did not show the presence of effect modification.

**Conclusion:** The results did not provide evidence for a cross-sectional association between social isolation and memory in the CLSA sample. These results may indicate the absence of an association in the population of middle-aged and older Canadian adults. The CLSA intentionally excluded cognitively impaired individuals from the study (recruitment bias) and individuals who were not socially isolated appeared to be more likely to participate in the study (volunteer bias). Taken together, these biases may have contributed to the weak and statistically non-significant associations. Longitudinal analyses may be needed to investigate the association between social isolation and memory in the CLSA, as more variability in the sample's degree of social isolation and memory can be expected as the participants age over time.

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## List of Abbreviations

| | |
|---|---|
| ADL | Activity of Daily Living |
| APOE | Apolipoprotein E |
| CES-D10 | Center for Epidemiological Studies Short Depression Scale |
| CI | Confidence Interval |
| CLSA | Canadian Longitudinal Study on Aging |
| DCS | Data Collection Site |
| ELSA | English Longitudinal Study on Aging |
| FSS | Functional Social Support |
| IADL | Instrumental Activity of Daily Living |
| LSNS | Lubben Social Network Scale |
| MMSE | Mini Mental State Examination |
| MOS-SSS | Medical Outcomes Study – Social Support Survey |
| NuAge | Quebec Longitudinal Study on Nutrition and Aging |
| OR | Odds Ratio |
| RAVLT | Rey Auditory Verbal Learning Test |
| RDD | Random Digit Dialing |
| SD | Standard Deviation |
| SII | Social Isolation Index |

# 1 Background

## 1.1 Healthy Aging

The World Health Organization defines healthy aging as the development and maintenance of levels of functional ability to enable wellbeing in older age.[1] An individual's physical and mental abilities (including memory function), and the characteristics of an individual's environment (including social isolation), are factors that affect one's functional ability. Understanding these factors is necessary to develop effective preventive or treatment interventions to promote healthy aging. The preservation of mental and physical capacities into old age can have substantial positive impacts for the health of aging populations.[2]

## 1.2 Cognitive Function

Cognition is a critical component of healthy aging and is commonly defined as the mental process involved in acquiring, storing, and using information. Cognition broadly encompasses abilities such as reasoning, problem-solving, memory, processing speed, and executive function. Intact cognition is important for the performance of activities of daily living (ADL) and instrumental activities of daily living (IADL), both of which are needed to maintain functional ability.[3] The Diagnostic and Statistical Manual of Mental Disorders (5$^{th}$ Edition) lists six domains of cognitive function: (1) language, (2) learning and memory, (3) social cognition, (4) complex attention, (5) executive function and (6) perceptual-motor function. These domains are collectively referred to as 'global cognitive function'.[4]

### *1.2.1 Memory*

Memory loss is detrimental to healthy aging because it is associated with substantial declines in quality of life and it is one of the defining symptoms of major neurocognitive

disorder (dementia).[5–7] Researchers have identified four distinct yet inter-linked memory systems: episodic memory, semantic memory, implicit memory, and working memory (see Appendix A for a full summary of these systems).[8] Aging is associated with substantial declines in the performance of cognitive tasks requiring explicit, conscious retrieval of information, which involves episodic memory.[9] Episodic memory serves to encode information and provide conscious recollection of past events and experiences.[9] Working memory, which pertains to the short-term storage and use of information, is another memory system subject to age-related changes over time.[163]

Episodic memory is particularly relevant to aging because it decreases linearly as people age and it is the first memory system to decline over time.[9] While the other memory systems may also decline with age, their trajectories of decline may not always be linear. Working memory may show small declines in early adulthood that generally increase later in life.[163]

Working memory and episodic memory are measured using task-based instruments such as the Rey Auditory Verbal Learning Test (RAVLT),[10,166,167] which requires persons to recall a list of words at multiple time points after first hearing the list (Section 3.2.1). A score of zero on the delayed recall test (RAVLT II) often reflects the underlying pathology of major neurocognitive disorder due to Alzheimer's disease (AD).[11,12] Examples of other tools used to measure episodic memory include the East Boston Memory Test (EBMT)[13] and the Wechsler Memory Scale (WMS).[14] The EBMT has the benefit of being brief and easy to administer compared to the WMS. However, further studies are required to examine the construct validity of the EBMT.[13]

### *1.2.2 Factors Influencing Cognitive Function and Memory*

#### 1.2.2.1 Non-Modifiable Factors

Age and biological sex are the two most important non-modifiable factors influencing memory. Increasing age has been shown to accelerate deficits in memory due to age-related structural and functional changes in the brain. Structural changes include declining volume of the temporal lobes,[15] changes in white and gray matter,[16] synaptic loss, and neuronal network dysfunction.[2] Functional changes include reduced resting-state functional connectivity of the hippocampus,[17] decreased cerebral blood flow,[18] and lower glucose metabolism in the parietal lobe of the brain.[19]

For biological sex, many studies have shown that females have greater dementia-related cognitive deficits than males. Researchers have identified several sex differences at the biological level that may help explain the variation in memory between females and males, including accelerated brain atrophy and an increased presence of apolipoprotein (APOE) ε4 allele in females compared to males. [20,21] Some of the effects of biological sex may be difficult to disentangle from the effects of age. Higher prevalence rates of global cognitive impairment in females are partly due to the fact that females generally live longer than males. The incidence of diseases with high mortality (e.g., cardiovascular diseases) tend to be higher in aging males, whereas aging females generally face higher incidences of low mortality diseases (e.g., musculoskeletal diseases).[22] Age in itself is a strong risk factor for cognitive impairment and major neurocognitive disorder.[23]

#### 1.2.2.2 Modifiable Factors

*Psychosocial factors* such as social isolation and depression have been studied in relation to cognitive function. Maintaining a socially active lifestyle that minimizes social isolation has

been found to be protective against cognitive decline.[24] Low levels of social isolation (assessed by engagement in social activities, frequency of interaction with social contacts, participation in voluntary/paid work, the number of people within social networks, marital status, and living arrangements) are associated with better memory outcomes.[25] Additionally, evidence points to the importance of depression in the onset of memory deficits. A meta-analysis reported that depression was inversely associated with cognitive function in participants aged 18 years or older, though the effects were small to moderate (Hedges' g = -0.36; 95% CI: -0.41 to -0.31).[26] However, this association was magnified in older age; a 20-year old depressed person was expected to score 0.14 SD below controls on cognitive measures, while a 70-year old depressed person was expected to score 0.49 SD below controls.[26]

*Lifestyle factors* associated with the onset of cognitive decline include physical inactivity, fatty diets, excessive alcohol consumption, and smoking. Regular physical activity and healthy diet are among the many modifiable factors that convey protective effects against cognitive decline.[27] In addition, a longitudinal study reported that small to moderate alcohol intake in older adults reduces the risk of cognitive decline.[28] However, the study found U-shaped associations between dosage of alcohol consumption and cognitive function, such that the protective effects of alcohol intake diminished following excessive consumption.[28] Current smoking increases the risk of cognitive decline, as does diabetes, mid-life obesity, and mid-life hypertension (all of which are associated with lifestyle factors).[27]

### 1.3 Social Support

Social support is a key psychosocial component of healthy aging. Two broad dimensions of social support exist, namely structural (objective) support and functional (subjective) support.[29–31] Structural support is quantitative in nature and refers to counts of the number of

people in one's social network, as well as the frequency of contact with these people.[29–31] Structural support also includes the frequency of participation in community-related events such as religious services, sports and cultural activities, and volunteer work.[32]

Functional support refers to the degree of help an individual believes or perceives will be available from members of their social network, when needed.[33] Various subtypes of functional social support exist, including emotional, tangible, informational, affectionate, and positive social interactions.[34] Emotional support is "the presence [receipt] of encouragement and comfort combined with the presence of interest and concern (p. 848)".[6] Tangible support, or instrumental support, is the provision of financial help, assistance with chores, or transportation.[35] Informational support is the provision of advice or information about strategies to cope with stress and solve problems.[35] Affectionate support involves displays of love and affection.[34] Lastly, positive social interaction is the presence of individuals to participate in enjoyable activities with.[34]

The literature does not always differentiate between structural and functional social support.[40,160] Many articles describe 'social support' without specifying the type of support being studied and utilize measurement instruments that blend together objective and subjective aspects of social support (e.g., Lubben Social Network Scale[36]).[37,38] Some broad-based indices of social support combine structural and functional assessments with measures of loneliness.[39]

Newall and Menec argue that structural and functional support are distinct concepts that should be measured separately.[40] They believe structural social support–which they call 'social isolation'–is the objective state of a *lack* of quantifiable social relationships, whereas functional social support is "what members of a social network *do* (p. 2673)" to help one another in times of need.[40]

Recent work with the Canadian Longitudinal Study on Aging (CLSA) has distinguished between structural and functional social support. For example, Menec et al. investigated the association between social isolation and psychological distress,[41] while Ohman, Yoo, and Rutter examined the association between functional social support and memory or executive function.[42–44] Kang and Oremus recently conducted a systematic review in preparation for longitudinal research into social isolation, loneliness, and memory.[45]

### 1.4 Social Isolation

Social isolation is a situation where someone has low numbers of social contacts (friends, family, etc.), infrequent interactions with these contacts, infrequent participation in social activities, lives alone, and is not married or in a common-law relationship. Menec et al. also include being retired versus employed in their definition of social isolation.[41] A detailed rationale for studying social isolation and its impact on memory is presented in Section 2.1 below.

Menec et al.'s conception of social isolation is based on the work of Steptoe and colleagues, who developed a similar measure for use in the English Longitudinal Study on Aging (ELSA). [41,46] Similarly, Choi et al.,[47] Zahodne et al.,[30] Dinapoli et al.,[48] and Yu et al.[49] have utilized composite social isolation indices similar to Menec et al.'s measure of social isolation (the quantitative operationalization of social isolation is explained in Section 3.2.2 below). These composites included combinations of questions about the size of the social network, frequency of contact with others, participation in social activities, living alone, marital status, and retirement status.

Social isolation and structural social support are opposites of the same objective measure of social relationships. An individual with low social isolation will have high structural social support, and vice versa. This is consistent with calls to eliminate the term 'structural social

support' from the literature and replace it with 'social isolation' (personal communication, Verena Menec, August 19, 2021).

### *1.4.1 Social Isolation and Health*

The absence of social isolation is an important component of successful aging. The presence of social isolation is associated with many chronic diseases that adversely affect healthy aging, including diabetes[50] and cardiovascular disease.[51] Additionally, social isolation is associated with lower reported well-being and quality of life,[24] higher risk of dementia,[52] increased risk of death, [53] and increased likelihood of psychological distress.[41] Social isolation is also associated with negative health behaviours such as reduced physical activity, inconsistent fruit and vegetable intake, and higher prevalence of smoking.[46] All of the aforementioned findings in this section are from longitudinal studies, wherein social isolation was measured variously as the number of members in a social network, less than monthly contact with family/friends/neighbours, lack of participation in social activities/organizations, living alone, or being retired.

### *1.4.2 Factors Influencing Social Isolation*

#### 1.4.2.1 Age

Age influences the trajectory of social isolation over time.[41,54–56] In a study by Menec et al., the prevalence of social isolation (measured as described in Section 3.2.2 below) increased with age.[41] The study analyzed CLSA's Comprehensive Cohort and found that the prevalence of social isolation across age groups was 3.2%, 5.1%, 6.3%, and 8.9% in those aged 45-54 years, 55-64 years, 65-74 years, and 75-85 years, respectively.[41]

Several possible reasons exist to explain the association between age and social isolation. Older adults are especially more susceptible to experiences or factors that can increase the

likelihood of social isolation.[54] For example, as adult children leave home and close family or friends pass away, the absolute number of people in an older individual's social network declines.[55,57]

Widowhood may be a particularly stressful life event that places older adults at higher risk for social isolation.[56–58] Older age is also often accompanied by chronic illness, which increases the risk for social isolation.[41,56,57] Further, the onset of functional impairment, cognitive impairment, and physical disabilities such as weakened eyesight and hearing impairment are barriers preventing older adults from interacting with members of their social networks.[41,56,57] Older adults may also rely on their work colleagues as an important source of social interaction, and retirement may be a factor associated with smaller social networks and decreases in social contacts.[56,58]

Age may also serve as an effect modifier of associations between social isolation and memory. For example, a longitudinal study found that the absence of social isolation (measured by marital status, volunteer activities, and contact with parents, children, and neighbours) protected against memory decline (measured by immediate and delayed word recall) only in individuals aged over 65 years.[5]

#### 1.4.2.2 Gender

Gender is an important variable influencing social isolation. In the absence of a spouse or significant other, men are at higher risk of social isolation because they typically do not create opportunities for social connection with other acquaintances, whereas women meet their social interaction needs through their female friends despite the absence of a partner.[41,59]

Longitudinal research reported that one component of social isolation–namely social participation in neighbourhood associations, hobby groups, local event groups, senior citizen

clubs, and volunteer groups–was associated with less cognitive decline on the Cognitive Performance Scale[60] in women only.[61] Similarly, another longitudinal study reported that higher frequencies of interaction with friends conveyed beneficial cognitive effects for women, but not men, with cognition being measured by the Short Portable Mental Status Questionnaire, the Barcelona Test, and the Established Populations for Epidemiologic Studies of the Elderly (EPESE) Short Story Recall.[62]

## 1.5 Theories/Mechanisms Linking Social Isolation and Cognitive Function

Researchers have identified various theoretical frameworks and mechanisms to explain the link between social isolation and cognitive function. Four different explanations will be discussed below: cognitive reserve theory, social control theory, use-it-or-lose-it theory, and the brain-derived neurotrophic factors mechanism.

### *1.5.1 Cognitive Reserve*

Cognitive reserve is the ability to maintain cognitive function despite the presence of age-related brain changes or Alzheimer's disease/dementia-related pathology.[63] Earlier life exposures, such as educational or occupational attainment, may contribute to a buildup of cognitive reserve. These exposures strengthen neural connections and enhance one's ability to counteract the adverse cognitive effects of age-related biological changes or disease pathology.[24,64]

Engaging in a socially active lifestyle has been shown to be associated with increases in cognitive reserve in later life.[24,65] Through communication and interaction with peers over the life course, social interaction delivers mental stimulation to build up cognitive reserve.[24,65] A longitudinal study found that the association between social isolation and cognitive function is moderated by cognitive reserve ($\hat{\beta}$ = 0.05, 95% CI: 0.10 to 0).[24] Social isolation was measured

using the Lubben Social Network Scale-6 (LSNS-6)[36] and cognitive function was measured using the Cambridge Cognitive Examination (CAMCOG).[66] Cognitive reserve was measured by an amalgam of years of education, occupational complexity, and engagement in cognitively stimulating activities (e.g., reading a book or playing games such as crosswords) at baseline.

### *1.5.2 Social Control Theory*

The Social Control Theory describes the ability of social networks to influence an individual's personal choices, including health behaviours.[68,69] Social control operates through two processes: (1) indirectly, when an individual avoids making health-compromising choices due to a self-imposed obligation to maintain relationships with others, or (2) when an individual's social network directly influences her or him to avoid health risks and adopt positive health behaviours. An example of the latter would be following the edicts of a religious community to abstain from certain behaviours, e.g., abstinence from tobacco consumption among Jehovah's Witnesses or alcohol consumption among Muslims.[69] Conversely, social control may also sway individuals to undertake negative health behaviours,[69] as observed when peer pressure among adolescents contributes to substance abuse.[69]

The existing literature on social control focuses on the effect of marital status on health behaviours. Spouses may persuade and influence each other's health choices.[70,71] A cross-sectional study of Korean middle-aged adults found that married individuals had a higher likelihood of adopting positive health behaviours than their single counterparts, e.g., lowering smoking and alcohol consumption, undergoing health screening, and eating regular breakfasts.[71]

Marital status may also play a protective role against the risk of developing dementia. A population-based longitudinal study found that the risks of cognitive impairment and dementia were higher in divorced and widowed individuals compared to married couples.[72] Persons who

were never married, widowed, or divorced had 45%, 39%, and 42% higher odds of memory impairment (measured by the National Health and Aging Trends Study cognitive tests)[73], respectively, compared to married persons.[74]

### *1.5.3 Use-It-Or-Lose-It Theory*

The use-it-or-lose-it theory claims that cognitively active lifestyles enhance brain activity, increase synaptic connections, and strengthen neural network structure;[51] in contrast, cognitive inactivity leads to cognitive impairment.[76] Engagement with social networks or participation in social activities requires the use of cognitive processes such as memory to recall past conversations, attention and reasoning to comprehend others' perspectives and make judgments about others' emotions, and problem-solving tactics to address experiences faced during inter-personal interactions.[77]

Similar to the cognitive reserve theory, the use-it-or-lose-it theory draws upon the importance of mentally stimulating activities for the maintenance of cognitive function, although the mechanism through which this occurs differs between the two theories. The cognitive reserve theory places an emphasis on the build-up of a pre-existing reserve of cognitive abilities accumulated throughout the life course, while the use-it-or-lose-it theory states that cognitive activity has a direct effect on the maintenence of neural structures. Both theories likely work together to exert a combined effect on the maintenance of cognitive function.

### *1.5.4 Brain-derived Neurotrophic Factors Mechanism*

One biological mechanism underlying the pathway linking social isolation and memory is the presence of brain-derived neurotrophic factors (BDNF), which have been shown to be protective against the risk of cognitive decline.[78]

Stress, physical activity and diet are some of the key factors influencing the upregulation of BDNF expression.[79] BDNF play an important role in mediating the neuroplastic changes related to memory processes in the brain.[78,79] Some of the processes by which BDNF supports memory storage include changes in spine morphology; a larger number, size, and complexity of dendritic spines; and enhanced neurogenesis.[78,79] BDNF are also supportive in memory formation and maintenance due to their essential role in the strengthening and consolidation of synapses.[78,79]

Animal studies have shown that social interaction may contribute to increasing levels of BDNF expression via epigenetic regulation.[78,80] Given the importance of BDNF in neuronal cell function, decreasing levels of BDNF have been shown to be associated with cognitive decline.[81] A study found that BDNF levels were significantly decreased by 34% and 62% in participants with mild cognitive impairment and Alzheimer's disease, respectively, compared to participants with no cognitive impairment.[81] In addition, a positive association was observed between BDNF levels and cognitive test scores, including the Mini Mental State Examination (MMSE) score and Global Cognitive Score.[81]

### 1.6 Social Isolation/Structural Social Support and Memory

The following section contains a summary of findings related to social isolation/structural social support and memory, and then includes a summary of the broader literature on social isolation/structural social support and cognitive function (see Section 1.7 below). See Appendix B for a description of the literature search strategy, Table B1 for the search syntax used in the literature review, and Figure B1 for the PRISMA flowchart. A summary of the included studies is shown in Appendix C, Table C1. For the purposes of the literature review, the thesis candidate

employed the original term ("social isolation" or "structural social support") used by authors to describe the exposure variables in their articles.

Out of 19 studies that explored the association between social isolation/structural social support and memory, one study was cross-sectional and 18 studies were longitudinal. The cross-sectional study analyzed data from 267 community-dwelling Appalachian individuals aged 70 to 94 years and found that greater social isolation (a composite measure derived by low frequency of social contact, lack of social participation, and being unmarried) was associated with poorer memory ($\hat{\beta}$ = 0.25, 95% CI: 0.11 to 0.39), with memory measured using the California Verbal Learning Test II and the Rey Osterrieth Complex Figure.[48]

Four longitudinal studies reported no statistically significant associations between social isolation/structural social support and memory, where the exposure variable was measured by a mix of less than monthly participation in social activities (including voluntary work, sport/social clubs, religious organizations, political/community organizations), network size, contact frequency, or a composite social isolation index assessing relationship status, volunteer activities, number of family members/friends, and contact frequency with family/friends/neighbours.[82–85] Measures of memory included the Telephone Interview for Cognitive Status (TICS),[83] the Rey Auditory Verbal Learning Test (RAVLT),[84] the Consortium to Establish a Registry for Alzheimer's Disease (CERAD),[85] and the revised Hopkins Verbal Learning Test (HVLT-R).[82] Sample sizes in these four studies were 203,[83] 1,966,[84] 2,533,[85] and 11,498 individuals,[82] respectively, all aged 50 years or older. Study locations included Alaska,[83] Netherlands,[84] the United States,[85] and Australia.[82]

Fourteen longitudinal studies reported statistically significant, inverse associations between social isolation and memory, or statistically significant, positive associations between

structural social support and memory.[5,30,49,86–96] Of the the six studies that measured social isolation/structural social support using a composite index (including marital status, volunteer activities, frequency of contact with family/friends/neighbours, membership in an organization/religious group/committee, and participation in social activities), higher levels of structural social support were significantly associated with slower rates of memory decline, while increasing social isolation was significantly associated with lower memory scores.[5,30,49,86,87,96] Memory was measured with the Selective Remind Test,[86] immediate and delayed word recall tests,[5,49,87] the CERAD list learning task,[30] and the California Verbal Learning Test (CVLT).[96] Samples sizes ranged from 855[86] to 16,638[5] participants aged 50 years or older, recruited from New York City,[86] a nationally representative population of American older adults,[5] the Health and Retirement Study (HRS),[30] the English Longitudinal Study of Aging (ELSA),[87] the China Health and Retirement Longitudinal Study (CHARLS),[49] and the Age, Gene/Environment Susceptibility-Reykjavik Study (AGES-Reykjavik).[96] Most studies had follow-up periods of 4 years[49,88,90,91] and 6 years,[5,30,86,94] while one study had a follow-up period of 5 years.[96] The longest lengths of follow-up among studies ranged from 8 years[93,95] to 10 years.[87,89] Despite variation in the lengths of follow-up periods, the longitudinal studies consistently reported statistically significant, inverse associations. Factors other than length of follow-up may have contributed to the findings. For example, the study with the shortest follow-up length of 4 years recruited individuals from the ELSA, which is a large representative sample of the English population, thereby allowing for the adjustment of 10 covariates to reduce the possible impact of residual confounding.[88]

Eight of the 14 longitudinal studies measured structural social support using single indicators (not composite measures), including social network size, frequency of contact with family/friends, or social engagement (participation in volunteer/sports/hobby groups, senior

citizen clubs, neighbourhood associations, religious organizations). Increasing network size, contact frequency, and social engagement were significantly associated with better episodic memory over time.[88–95] One longitudinal study (with an 8-year follow-up period) found that the type of social relationship had differential effects on results.[93] Low frequency of contact with friends was significantly associated with larger memory decline ($\hat{\beta}$ = 0.07, 95% CI: 0.05 to 0.09), while low frequency of contact with family was not significantly associated with memory decline ($\hat{\beta}$ = 0.01, 95% CI: -0.01 to 0.03).[93] Memory was measured using immediate and delayed word recall tests,[88,89,91,94,95] the East Boston Memory Test,[92] the Brief Test of Adult Cognition by Telephone,[90] and the CERAD list learning task.[93] Samples sizes ranged from 615[92] to 19,832[94] participants. Most samples contained persons aged 50 years or older, but one study included a sample size of individuals aged 25 to 74 years.[90] Studies were undertaken in the United States,[93,95] England,[88,90] China,[89,91] Europe,[94] and Israel.[94] One study specifically recruited African American adults.[92]

Differences in the magnitude of the association varied between the aforementioned 19 studies partly due to a lack of consistency in the definitions and measurement of social isolation/structural social support. Measures restricted to specific components of social isolation did not capture the totality of the concept. For example, some individuals may be unmarried or living alone, or they connect with family and friends on an infrequent basis, but they may have other forms of social contact, i.e., interaction with a formal caregiver. Many studies also included highly-select subgroups of the population (e.g., Native Americans,[83] Appalachian individuals[48]), thereby reducing the applicability of the results to other populations. Some studies adjusted for as few as 3[83] to 5[82] covariates, thereby leading to the possibility of residual confounding. Further, sex and gender differences were generally not tested across the studies.

## 1.7 Social Isolation/Structural Social Support and Cognitive Function

The remaining 35 studies of social isolation/structural social support retrieved in the literature search used global cognitive function as the measure of outcome: 14 were cross-sectional, 19 were longitudinal, and 2 were systematic reviews.

### *1.7.1 Cross-sectional Studies*

Twelve of the 14 cross-sectional studies showed statistically significant, inverse associations between social isolation and cognitive function or positive associations between structural social support and cognitive function.[47,62,101–110] The sample sizes ranged from 189[107] to 6,076 persons.[47] The locations of recruitment included Korea,[47,103] Germany,[101] the United States,[102] China,[104,110] Spain,[62,105,106] Europe,[107] Ireland,[108] and South Africa.[109] Generally, the studies included individuals aged 50 years or older, with the exception of three studies that recruited persons aged 45 years or older,[81] 75 years or older,[101] or 90 years or older.[47,62,104]

To measure social isolation, some studies used a composite social isolation index, which was based on not being married or not cohabiting with a partner, less than monthly contact with children, less than monthly contact with other immediate family or friends, and non-participation in organizations/religious groups/committees.[47,110] Other studies used low frequency of participation in social activities as the measure of social isolation, which included church or other religious gatherings, friendship organizations (senior citizen clubs, etc.), alumni associations, and volunteering.[62,101,102,105–109] A few studies measured social isolation using social contacts, where participants indicated the number of family/friends/neighbours they had contact with and how frequently they had contact with them.[103,104] Despite utilizing different measures of

social isolation, all of the aforementioned cross-sectional studies pointed to the same conclusion: there was an inverse association between social isolation and cognitive function. Measures of cognitive function in these 12 studies included the MMSE, the Short Portable Mental Status Questionnaire (Korean and Chinese versions), and the Structured Interview for the Diagnosis of Dementia of the Alzheimer Type (SIDAM).

A limitation of some of these 12 studies was that the average age of participants was approximately 80 years,[110] which could possibly lead to selection biases where participants were more likely to be socially isolated due to older age and more likely to be cognitively intact due to a healthy survivor effect.[54,111] In addition, some studies included limited subsamples of the population, such as rural dwellers only, where generalizability is unlikely to extend beyond the limited sample frame.[104]

The remaining two cross-sectional studies found no association between social isolation (measured by low participation in social activities and small social networks) and cognition (measured by a battery of 19 performance tests and the MMSE).[112,113] The sample sizes ranged from 838[113] to 1,643[112] participants who were recruited from Sweden[112] or the United States.[113] The authors of the Swedish study reported that participants were chosen through a simple random sample, but provided no other details.[112] Participants in the American study were recruited from subsidized housing facilities and continuous care retirement communities in metropolitan Chicago.[113] The small sample sizes may be one of the factors contributing to discrepancy in results.

### *1.7.2 Longitudinal Studies*

Three of the 19 longitudinal studies did not find any association between social isolation and cognitive decline.[114–116] In these studies, social isolation was measured by social network

size and cognition was measured by the Wechsler Adult Intelligence Scale-III UK,[114] an unnamed composite test of multiple cognitive domains (immediate and delayed verbal memory, attention, and executive function),[115] and the Short Portable Mental Status Questionnaire.[116] Sample sizes ranged from 213[115] to 4,603[116] participants who were aged 60 years or older. The areas of recruitment included Scotland,[114] the United States,[115] and Taiwan.[116] The lengths of follow-up ranged from 2[115] to 7 years.[116] Despite the large variation in lengths of follow-up, all of the longitudinal studies indicated a lack of statistically significant associations between social isolation and cognitive function. Factors other than length of follow-up alone may be important. For example, attrition was higher among participants with higher levels of social isolation and greater cognitive decline in the longitudinal study with the longest follow-up period (7 years).[116]

The remaining 16 longitudinal studies found that lower social isolation/greater structural social support was significantly associated with better cognitive function in late life.[61,117–131] The sample sizes ranged from 184 to 28,945 participants and recruitment took place in the United States, China, Korea, India, and Eastern Europe. Most studies included individuals aged 60 years or older, with one study recruiting individuals aged 45 years or older.[130] Cognitive function was assessed using the MMSE,[132] the Telephone Interview for Cognitive Status,[133] and a composite test of overall cognitive function (immediate word recall, animal naming task, letter cancellation task and delayed word recall). Some of the limitations of these studies included small sample sizes (e.g., as few as 184 participants),[93] selective subgroups of participants (e.g., residents of Narón Council, Spain[119] or largely African American participants),[122] and adjustment for small numbers of covariates (e.g., a study by Bae et al. controlled for only 2 covariates: age and education[123]). The lengths of follow-up ranged from 2[128] to 12 years[118] across studies. Despite many studies having shorter follow up-periods (ranging from 2 to 6 years),[61,117,122,125,127,130] their

findings consistently reported significant associations, similar to the results of studies with longer lengths of follow-up (ranging from 10 to 12 years).,[118,124,126,129,131] This may indicate the presence of other factors that affect the results. For example, the study with the shortest follow-up period of 2 years[128] had a larger sample size (n=8,291) than one of the studies with the longest length of follow-up of 12 years (n=5,678).[124]

### *1.7.3 Systematic Reviews*

Two systematic reviews reported that social isolation was associated with decreased cognitive function.[29,134] The first systematic review, by Kuiper et al., included 31 studies, of which 12 studies were featured in the literature review above.[29] Articles were included if they were peer-reviewed, quantitative, and used longitudinal study designs in general study populations. Findings showed that social isolation (measured by small social network size, including the number of children/family/friends seen at least once a month) was a stronger predictor of cognitive decline than functional social support.[29] The MMSE was the commonly used measure of cognitive function among the studies included in the review. A limitation of the review was that it examined overall cognitive function, rather than assessing separate subdomains of cognition.

The second systematic review, by Kelly et al., included 39 studies, of which 13 studies were described in the literature review above.[134] Articles were included in the review if they were peer-reviewed, observational studies or randomized controlled trials and included a sample of individuals aged 50 years or older without cognitive impairment. The systematic review reported that while the absence of social isolation (measured by large social networks and social activity) was associated with improved global cognition, only functional social support (also examined in Kelly et al.'s review) conveyed beneficial effects for episodic memory.[134] Global

cognition was measured using composite measures of cognitive function and episodic memory was measured using various tests, including the RAVLT and the California Verbal Learning Test. The measures of social networks included living arrangements, marital status, numbers of social ties or frequency of contact with friends and family; measures of social activity included engagement in facilitator-led group discussions, social interactions, field trips, travel or outings, visiting and receiving visitors, participation in voluntary activities, religious activities, membership in community groups or associations, or attending social groups. A possible reason for the discrepancy in findings between Kelly et al. and Kuiper et. al's systematic review is that the majority of studies in Kelly et al.'s systematic review included single indicators of social isolation, which do not fully represent the totality of social isolation.

## 1.8 Conclusion

Altogether, the literature suggests that social isolation is inversely associated with memory and cognitive function, whereas structural social support is positively associated with cognitive function. However, a preponderant number of studies included highly-select subgroups of the population and several studies utilized small sample sizes, thereby allowing for greater possibility of random error. As well, most studies focused on global cognitive function, rather than memory. Many studies also only controlled for three to five covariates (leading to possible residual confounding) and did not assess effect modification by age or sex. There was also a lack of consistency in the variables used to measure social isolation.

# 2 Study Rationale and Research Questions

## 2.1 Study Rationale

This thesis was undertaken to fill gaps in the literature regarding the association between social isolation and memory, as described below.

*Gap 1 – The existing literature largely focuses on global cognitive function.* The thesis candidate studied memory as the outcome variable using the RAVLT. Although brief cognitive screening tools can be informative about overall levels of global cognitive functioning, it is important to use domain-specific measurement tools in order to gain an in-depth understanding of clinically relevant areas of cognitive function.[142] As described in Section 1.2.1 above, memory is a crucial cognitive domain to study in aging populations because it decreases linearly as people age and is the one of the first functions to decline over time.

*Gap 2 – Many studies used only a single indicator to measure social isolation.* Social isolation in the thesis was measured using a wider set of variables, including number of social contacts (friends, family, etc.) and frequency of interaction with these individuals, participation in social activities, marital status, and retirement status.[41]

*Gap 3 – Few studies included middle-aged adults in their samples.* The inclusion of middle-aged and older adults in the thesis allowed for the examination of the association of interest across different age groups. This is essential because today's middle-aged adults will become tomorrow's older adults, prompting it necessary to assess how the association of interest differs across age groups.

*Gap 4 – Few studies explored effect modification by age or sex.* Social isolation and memory may be differentially impacted by age or sex; therefore, it is important to assess effect

modification. The large amount of collected data in the CLSA provided enough power to undertake subgroup analyses by age group and sex.

*Gap 5 – Most studies had small sample sizes and controlled for five covariates or less.* In this thesis, the availability of a large sample size and robust set of collected data allowed for the adjustment of 11 relevant covariates in regression analyses, thereby reducing the risk of residual confounding. Also, the large sample size permitted subgroup analyses by age group and sex (gaps 3 and 4 above).

By addressing these gaps in the literature, the thesis will add to the body of evidence on the association between social isolation and memory.

## 2.2 Research Questions

This thesis used data from the Comprehensive Cohort of the CLSA to examine the baseline association between social isolation and memory in community-dwelling persons aged between 45 and 85 years. The research questions were:

1. Is social isolation, measured using Menec et al.'s social isolation index,[135] associated with immediate and delayed recall memory, measured using the RAVLT[10]?
2. Are the findings from Question 1 above maintained after adjusting for sociodemographic, health-related, and lifestyle covariates, as well as functional social support?
3. Do age group and sex, examined separately, modify the association between social isolation and memory after adjusting for covariates?

# 3 Methods

## 3.1 Data Source: The Canadian Longitudinal Study on Aging

### *3.1.1 Background and Study Design*

The CLSA is a national, longitudinal study exploring the healthy aging effects of a multitude of biological, physical, psychosocial, and societal factors.[136] The CLSA recruited 51,338 women and men aged 45 to 85 years between 2011 and 2015. These persons are currently being followed for at least 20 years, with data collection occurring at three-year intervals. To date, baseline, three-year, and six-year follow-up data have been collected by researchers.

Despite the availability of follow-up data, this thesis utilized baseline data only because earlier work showed that follow-up periods longer than three years will be necessary to detect cognitive change in the CLSA[43] and six-year follow-up cognition data are not expected to be available until early- to mid-2023. Also, a high degree of missingness exists for RAVLT scores at the first follow-up and these data may not be missing at random. Participants with lower cognition scores at baseline are more likely to have missing data at follow-up[43] and methodological approaches to address this issue are still under consideration by the research team.

The CLSA is split into the Tracking and Comprehensive Cohorts. The Tracking Cohort (n = 21,241 at baseline) recruited participants across all 10 Canadian provinces and is collecting data via computer-assisted telephone interviews. The Comprehensive Cohort (n = 30,097 at baseline) recruited participants who were located within 25 to 50 kilometers of 11 data collection sites (DCS) in seven provinces. The Comprehensive Cohort obtains data through in-home interviews and in-person visits at the data collection sites.

The CLSA collects common alphanumeric data on demographic, social, physical/clinical, psychological, economic, and health services variables from both cohorts.[136] Comprehensive Cohort participants undergo additional clinical (e.g., spirometry, bone scan), physical (e.g., grip strength, blood pressure), and neurocognitive testing, and may optionally provide blood and urine samples.[137] This thesis utilized alphanumeric data from the CLSA's Comprehensive Cohort to avail the largest possible sample size for analyses (n = 30,097). Also, there are potential issues concerning the validity of combined analyses of both Tracking and Comprehensive Cohorts, due to the variation in methods used to collect data across the cohorts.[143] Further, the Comprehensive Cohort was utilized to remain consistent with previous and ongoing research.[42-44,138]

### *3.1.2 Thesis Sampling Frame and Eligibility Criteria*

The CLSA employed the Canadian Community Health Survey (CCHS) on Healthy Aging[139] exclusion criteria when recruiting participants into the Comprehensive Cohort. Participants were excluded if they met the following conditions: (1) residents of Canadian territories; (2) residents of federal First Nations reserves or provincial indigenous settlements; (3) full-time members of the Canadian Armed Forces; (4) individuals under institutionalized care (excluding persons residing in independent-living seniors' residences); (5) individuals who could not speak English or French; and (6) persons whom the recruitment interviewers judged to be cognitively impaired, with judgements based on whether individuals could answer questions about informed consent, reply to basic queries about themselves (e.g., age, birthdate), and whether they seemed to understand the nature of the recruitment interview.

The CLSA used three sampling frames for recruiting Comprehensive Cohort participants: provincial health registries, random digit dialing (RDD) of landline telephones, and the Québec Longitudinal Study on Nutrition and Aging (NuAge).[140] Ministries of Health sent letters on the

CLSA's behalf to persons listed in provincial health registries; the letters invited interested individuals to contact the CLSA directly about participating. Persons who contacted the CLSA received information about the purpose of the study and were screened for eligibility over the phone. A national polling firm carried out recruitment via RDD and screened potential participants for eligibility over the telephone. If these individuals fit the eligibility criteria and gave permission, then their contact information was passed on to CLSA for follow-up. NuAge participants gave the study investigators permission for their contact information to be passed along to the CLSA and subsequently were contacted by a CLSA representative via telephone to assess eligibility and answer questions regarding the study. Recruitment was stratified by age group, sex, and province of residence. During recruitment, additional strata were added for low versus not low education, with 'low' being defined as less than a high school education.

## 3.2 Measures

### *3.2.1 Cognitive Function*

All participants in the Comprehensive Cohort completed a neuropsychological assessment for memory, executive function, and psychomotor speed.[142] This thesis focused on memory as the outcome variable, which the CLSA measured using a modified version of the RAVLT.[10] The unmodified RAVLT measures episodic memory,[167] working memory,[166,168] immediate and delayed memory,[166,167] recall,[167] verbal learning,[167] retention,[142, 166,167] recognition,[166,167] and susceptibility to interference.[167] To respect the maximum amount of interview time allotted to the CLSA's cognition measures, CLSA investigators modified the RAVLT from its original form and reduced the number of recall administrations from five to two and eliminated an interference test.[143] Therefore, the CLSA's modified RAVLT may be limited in its measurement of susceptibility to interference and verbal learning. Further, the integrity of

the assessment of delayed recall may be affected. As such, the CLSA's modified RAVLT only measures working memory and episodic memory (personal communication, Megan O'Connell, December 15, 2022). The impact this may have on results is further described in Section 5.5. The RAVLT has good reliability and high sensitivity to early cognitive impairment, and is available in both English and French.[142] The CLSA's RAVLT is described in further detail in Appendix D.

The CLSA administered the RAVLT in two increments during DCS visits: (1) for immediate memory recall (RAVLT I), participants listened to a list of 15 recorded words and had 90 seconds to immediately recall as many of the words as possible; and (2) for delayed memory recall (RAVLT II), five minutes following RAVLT I, participants had to recall as many of the same 15 words as possible (without hearing the list again) within 60 seconds. For each administration, one point was assigned to each correctly recalled word or variant word. Variant words came from a list of permitted words sounding similar to the 15 original words. Zero points were assigned for incorrectly recalled words. To receive points for variant words, the same variant word had to be recalled at both administrations. The CLSA audio-recorded the RAVLT administrations and trained staff listened to the recordings and scored the tests. Staff assigned missing values to participants whose recordings were blank or garbled, or who denied permission to audio-record responses.

RAVLT z-scores ($\mu = 0$; $\sigma = 1$) for use in all analyses were computed separately for English- and French-speaking participants. Separate sets of z-scores were also calculated for RAVLT I and II because each administration assesses a different construct of memory. RAVLT I measures working memory, specifically the aspect of working memory that processes phonological information.[168] RAVLT II measures complex memory functions, such as the

retrieval of information.[167] As such, RAVLT I and II were treated as separate outcomes in the thesis. Participants who switched languages from English to French (or vice versa) while undertaking either test were excluded from the analyses.[144]

### *3.2.2 Social Isolation*

Scores for social isolation were computed using a composite Social Isolation Index (SII) devised by Menec et al. (see Table 1), which is optimal for the thesis because it was derived using the CLSA data.[41] The index contains five items in total, and one point is awarded for each of the following criteria that a participant meets: 1) both lives alone and is not married or in a common-law relationship; 2) has either gotten together with friends or neighbours less frequently than 'within the last month', or reported having no friends or neighbours; 3) has either gotten together with relatives/siblings less frequently than 'within the last month', or reported having no relatives or siblings; 4) has either gotten together with children less frequently than 'within the last month', or has no children; and 5) is both retired and participates in no more than one of eight social activities at least once a month or more often. These activities include family- or friendship-based activities, church or religious activities, sports or physical activities, and educational or cultural activities. The SII score ranges from 0 to 5, with higher scores reflecting greater social isolation.

Although social isolation lies on a continuum, the thesis followed Menec et al.'s guidance and dichotomized the SII for all analyses: participants with scores between 2-5 were classified as socially isolated (coded as 1) and those with scores between 0-1 were classified as not socially isolated (coded as 0).[41] The dichotomization of social isolation is commonly used to capture prevalence rates and helps identify whether socially isolated individuals are vulnerable to poor outcomes such as low memory function as a result of being socially isolated.[40]

In the CLSA's social network module, a contact with a member of one's social network is defined as an in-person interaction. Other forms of interaction (e.g., telephone, video chat) are not considered to be a 'contact'. Menec et al.'s cut-off score prevents persons who may have had other forms of interaction with members of their social network from being recognized as socially isolated unless they also met at least one other condition of the SII.[135] However, participants who are living with at least one other person and married or in a common-law relationship may still be recognized as socially isolated if they meet two other SII criteria, such as not having friends/neighbours and not getting together with relatives/siblings at least once a month. Menec et al. describe the 0-1/2-5 cut-off as a means of accounting for the "substitutions and trade-offs of social relationships".[31] Several other researchers have drawn upon this concept of substitutions and trade-offs in their operationalizations of social isolation.[135,145–147]

**Table 1: Social Isolation Index**

| CLSA Module | Questions | Responses |
|---|---|---|
| ***Social Networks*** | When did you last get together with any of your children who live outside of your household? | Within the last day or two<br>Within the last week or two<br>Within the past month<br>Within the past 6 months<br>Within the past year<br>More than 1 year ago |
| | When did you last get together with any of your siblings who live outside of your household? | |
| | When did you last get together with any of your close friends who live outside of your household? | |
| | When did you last get together with any of your neighbours? | |
| | How many people, not including yourself, currently live in your household? | |
| | How many people do you consider close friends? | Provide a number |
| | How many of your neighbours do you know? | |
| | How many children do you have? | |
| | How many, if any, living siblings do you have? | |
| | About how many living relatives do you have? | |
| ***Social Participation*** | In the past 12 months, how often did you participate in family or friendship-based activities outside the household? | At least once a day<br>At least once a week<br>At least once a month<br>At least once a year<br>Never |
| | Sports or physical activities that you do with other people | |
| | Educational and cultural activities | |
| | Church or religious activities such as services, committees or choirs | |
| | Service club or fraternal organizational activities | |
| | Neighbourhood, community or professional association activities | |
| | Volunteer or charity work | |
| | Any other recreational activities involving other people, including hobbies, gardening, poker, bridge, cards and other games | |
| ***Sociodemographic*** | What is your current marital/partner status? | Single, never married or never lived with a partner<br>Married/living with a partner in a common-law relationship<br>Widowed<br>Divorced<br>Separated |

| | | |
|---|---|---|
| ***Retirement Status*** | At this time, do you consider yourself to be completely retired, partly retired or not retired? | Completely retired<br>Partly retired<br>Not retired |

*Note:* This table is adapted from the Social Isolation Index derived by Menec et al.[135]

### *3.2.3 Covariates*

Eleven variables served as covariates in the regression analyses (see Table 2). In line with the CLSA's recommendations, all regression models (base/crude, multivariable) contained three covariates–sex, age group, and province–to account for the CLSA's complex survey design.[144] Please note, models stratified by age group did not include age group as a covariate and models stratified by sex did not include sex as a covariate.

Based on the literature search,[102,110,122,125,127,135] along with the work of previous thesis students,[42,44] eight additional covariates were included in multivariable regression models. These additional covariates were divided into four categories: (1) sociodemographic information (education, annual household income), (2) health-related factors (chronic conditions, functional impairment, depressive symptoms), (3) lifestyle behaviours (smoking status and alcohol use), and (4) functional social support.

#### 3.2.3.1 Sociodemographic Variables

Sex was recorded as male or female. Age (in years) was categorized into four groups: 44-54 years, 55-64 years, 65-74 years, and 75 years or older. Province of residence was recorded during recruitment. Education was categorized into four groups: less than high school, high school diploma, less than post-secondary education, and any post-secondary education. Annual household income in Canadian dollars was categorized into four groups: less than $20,000, from $20,000 to under $50,000, from $50,000 to under $100,000, from $100,000 to under $150,000, and $150,000 or above.

#### 3.2.3.2 Health Variables

The presence of chronic conditions was assessed dichotomously as no chronic conditions versus one or more chronic conditions (Megan O'Connell, personal communication). Eleven

chronic conditions related to cognition were combined: high blood pressure (or hypertension), diabetes (or borderline diabetes or high blood sugar), cancer, hypothyroidism (or under-active thyroid gland or myxedema), hyperthyroidism (or over-active thyroid gland or Grave's disease), chronic obstructive pulmonary disease (or emphysema or chronic bronchitis), kidney disease (or kidney failure), cardiac chronic conditions (heart disease/congestive heart failure, myocardial infarction/acute myocardial infarction/heart attack, angina/chest pain due to heart disease), stroke-related conditions, peripheral vascular disease, and asthma.

Functional impairment was assessed using measures of ADL and IADL from the Older Americans Resources and Services (OARS) Multidimensional Assessment Questionnaire.[148] The CLSA's derived variable called "Basic and Instrumental Activities of Daily Living Classification" was employed in this thesis. The variable combines ADL and IADL responses from the OARS questionnaire into a five-level scale, ranging from no functional impairment to total functional impairment.[149] In the thesis, functional impairment was dichotomized as 'no functional impairment' versus 'any level of functional impairment'.

The presence of severe depressive symptoms was measured using the Center for Epidemiologic Studies Short Depression Scale (CES-D10).[150] Scale scores ranged from 0 to 30 and a cut-off of 10 or more[139] was used in a dichotomous variable to indicate the presence of severe depressive symptoms.

#### 3.2.3.3 Lifestyle Variables

Smoking status was measured using a self-report questionnaire derived from the Canadian Health Measures Survey[151] (CHMS) and the Canadian Tobacco Use Monitoring Survey[152] (CTUMS). Participants were asked "Have you smoked 100 cigarettes in your life?" and "At the present time, do you smoke cigarettes?". Participants who answered "no" to both

questions were classified as never smokers. Participants who answered that they smoked at least 100 cigarettes in their lifetimes, but currently do not smoke cigarettes, were classified as former smokers. Participants who answered that they smoke cigarettes at the present time were classified as current smokers.

Alcohol status was measured using a 6-item questionnaire from the Centre for Addiction and Mental Health Monitor that asked about the frequency of alcohol consumption in the past 12 months.[153] Based on responses, the CLSA categorized participants as 'regular drinkers' if they consumed alcohol at least once a month and 'occasional drinkers' if they consumed alcohol less than once a month. Participants were categorized as 'never drinkers' if they reported never consuming any alcohol in the past 12 months.

#### 3.2.3.4 Functional Social Support

Functional social support was measured with the 19-item Medical Outcomes Study–Social Support Survey (MOS–SSS).[34] This survey measured four subtypes of functional social support: emotional/informational support, tangible support, affectionate support, and positive social interactions. Participants were asked about the level of support they perceived would be available when needed, with questions asking about topics such as availability of help with daily chores in case of sickness, presence of someone to confide in, or presence of someone who shows the participant love and affection. Each question contained five response options ranging from 1 (none of the time) to 5 (all of the time). Overall functional social support scores were obtained by averaging the scores across all 19 items; these scores were dichotomized for inclusion in regression models, with average scores between 1 and 3 indicating low functional social support (coded as 0) and average scores between 4 and 5 indicating high functional social support (coded as 1).[44]

**Table 2: Description of Covariates**

| | Covariate | Measurement |
|---|---|---|
| ***Sociodemographic*** | Sex | Male |
| | | Female |
| | Age | 45-54 years |
| | | 55-64 years |
| | | 65-74 years |
| | | 75 years or older |
| | Education | Less than high school |
| | | High school diploma |
| | | Some post-secondary education |
| | | Post-secondary degree/diploma |
| | Province of residence | Each of the seven provinces with a data collection site |
| | Total annual household income (in Canadian dollars) | Less than $20,000 |
| | | From $20,000 to under $50,000 |
| | | From $50,000 to under $100,000 |
| | | From $100,000 to under $150,000 |
| | | From $150,000 or more |
| ***Health*** | Chronic conditions | 0 (absence of any conditions) |
| | | 1+ (presence of one or more conditions) |
| | Functional impairment | 0 (no functional impairment) |
| | | 1+ (any level of functional impairment) |
| | Depressive symptoms | < 10 (not severe) |
| | | $\geq$ 10 (severe) |
| ***Lifestyle*** | Smoking status | 0 (never smoker) |
| | | 1 (former smoker) |
| | | 2 (current smoker) |
| | Alcohol use | 0 (never drinker) |
| | | 1 (occasional drinker) |
| | | 2 (regular drinker) |
| ***Functional social support*** | Overall functional social support | $\leq$ 3 (low) |
| | | > 3 (high) |

## 3.3 Data Analyses

### *3.3.1 Descriptive Analysis*

Weighted descriptive analyses were performed for all variables using the CLSA's trimmed weights and geographical strata variable. Frequencies and percentages were used to report data for categorical variables, both overall and broken down by whether participants were socially isolated or not. Absolute standardized differences were used for comparing effect sizes between socially isolated and non-socially isolated participants. Bivariate associations were reported between each covariate and memory, i.e., memory was the dependent variable in a set of simple linear regression models each containing one covariate as the sole independent variable.

### *3.3.2 Regression Analysis*

Multivariable linear regression was used to model the relationship between the dichotomized SII and RAVLT I/II z-scores, with the SII considered as the exposure and the z-scores as the outcomes. The RAVLT I and RAVLT II z-scores were treated as separate outcomes and regressed separately onto the SII, resulting in two base/crude regression models.

Each base/crude regression model was referred to as 'Model 1', which also contained age group, sex, and province of residence. The sociodemographic, health, lifestyle, and functional social support covariates were added to each Model 1 in chunks. This resulted in 4 additional models for RAVLT I and 4 additional models for RAVLT II: Model 2 (Model 1 + sociodemographic), Model 3 (Model 2 + health), Model 4 (Model 3 + lifestyle), and Model 5 (Model 4 + functional social support).

The two full regression models with all four covariate chunks (Model 5) were stratified separately by age group and sex to assess effect modification, thereby yielding four stratified

models for age group and two stratified models for sex. All of the regression models included the CLSA's analytical weight and geographical strata variables. A summary of the analytical strategy for the regression models is presented in Appendix E.

Assessment of multicollinearity and model fit included the examination of variance inflation factors (≥ 10 suggested possible multicollinearity), observed versus predicted plots, and residual plots (see Appendices F and G). The level of statistical significance in all analyses was set at $\alpha = 0.05$. SAS v9.4 (The SAS Institute, Cary, NC) was utilized to conduct all descriptive and regression analyses and R v4.1.0 (The R Project for Statistical Computing, Vienna, Austria) was employed to generate all graphs.

### *3.3.3 Missing Data Analysis*

A complete case analysis approach was taken to manage missing data in this thesis. Unadjusted binary logistic regression models were used to explore the possible impact of missing data. The SII was regressed on a dichotomous RAVLT I 'missingness' variable (1 = missing data on RAVLT I, 0 = no missing data on RAVLT I) and the same regression was repeated for RAVLT II. The resulting regression models generated odds ratios that represented the odds of being socially isolated among participants with missing versus complete RAVLT I or II z-scores.

In the next evaluation of missing data, RAVLT I and II were separately regressed on a dichotomous SII 'missingness' variable (1 = missing data on SII, 0 = no missing data on SII. The resulting regression coefficients represented the change in RAVLT I or II z-scores for participants with missing versus complete SII data.

# 4 Results

## 4.1 Derivation of Analytical Sample

The analytical sample for the thesis was derived from the CLSA's baseline Comprehensive Cohort of 30,097 participants. Participants who did not undergo the memory tests at a data collection site were excluded from the analytical sample to avoid potential challenges relating to differences in the testing environment, as well as to.be consistent with previous cross-sectional analyses.[44,154] Participants with missing data on the exposure, outcome, or any covariate were also excluded from analyses (complete case approach). The analytical sample consisted of 24,531 participants (Figure 1).

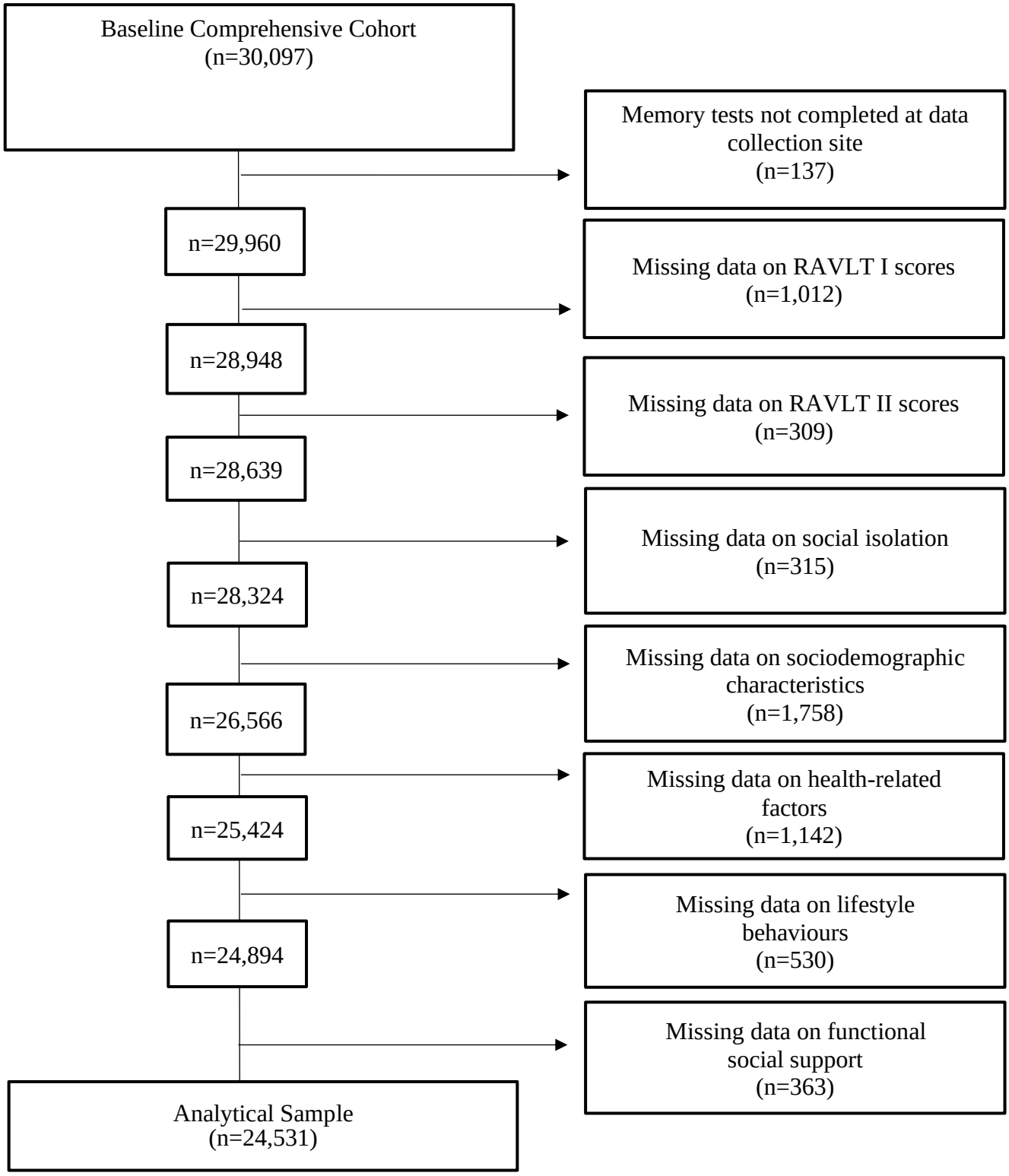


**Figure 1: Derivation of Analytical Sample**

*Note:* Approximately 0.02% (n=583) of participants had missing RAVLT I or II scores due to blank or garbled audio recordings, or due to lack of permission to audio-record responses.

## 4.2 Descriptive Analyses

Figures 2, 3, and 4 show the weighted distributions for the SII, RAVLT I z-scores, and RAVLT II z-scores for the analytical sample. Approximately 6% (n=175,294) of the weighted sample reported being socially isolated, and 94% (n=2,581,422) of the weighted sample reported being non-socially isolated (Figure 2). Mean weighted RAVLT I and II z-scores were -0.31 (95% CI: -0.32 to -0.29) and -0.24 (95% CI: -0.26 to -0.22), respectively (Figures 3 and 4). Minimum and maximum weighted RAVLT I z-scores were -2.98 and 3.31, respectively. Minimum and maximum weighted RAVLT II z-scores were -1.96 and 3.81, respectively (Figures 3 and 4). Table 3 shows the weighted frequencies and percentages for each covariate. Table 3 also reports absolute standardized differences comparing covariates between socially isolated and non-socially isolated participants. Table 4 shows the bivariate associations between each covariate and memory, as well as between SII and memory.

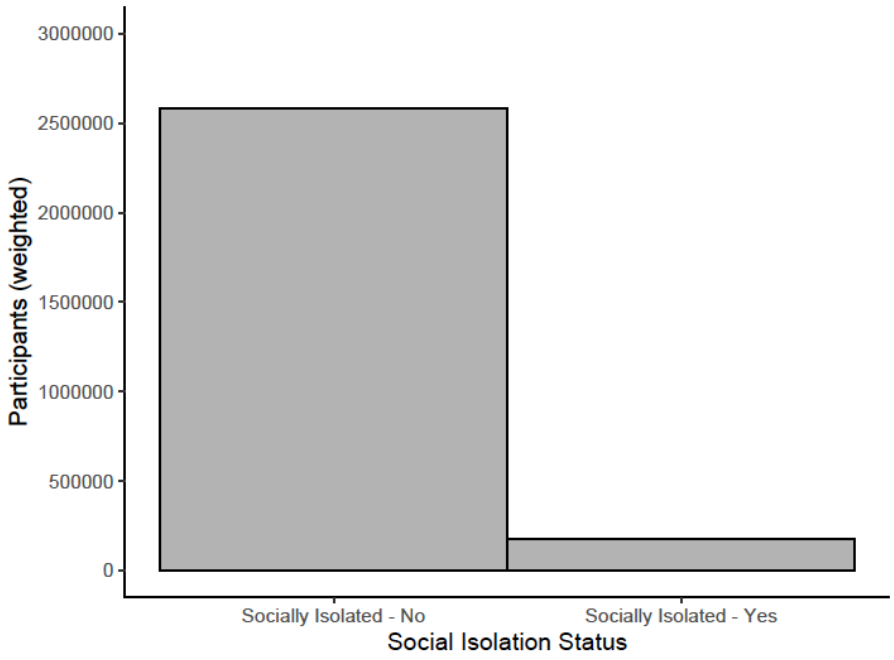


**Figure 2: Distribution of Baseline Social Isolation Index (Dichotomized) – Weighted Analytical Sample, Comprehensive Cohort–Canadian Longitudinal Study on Aging**

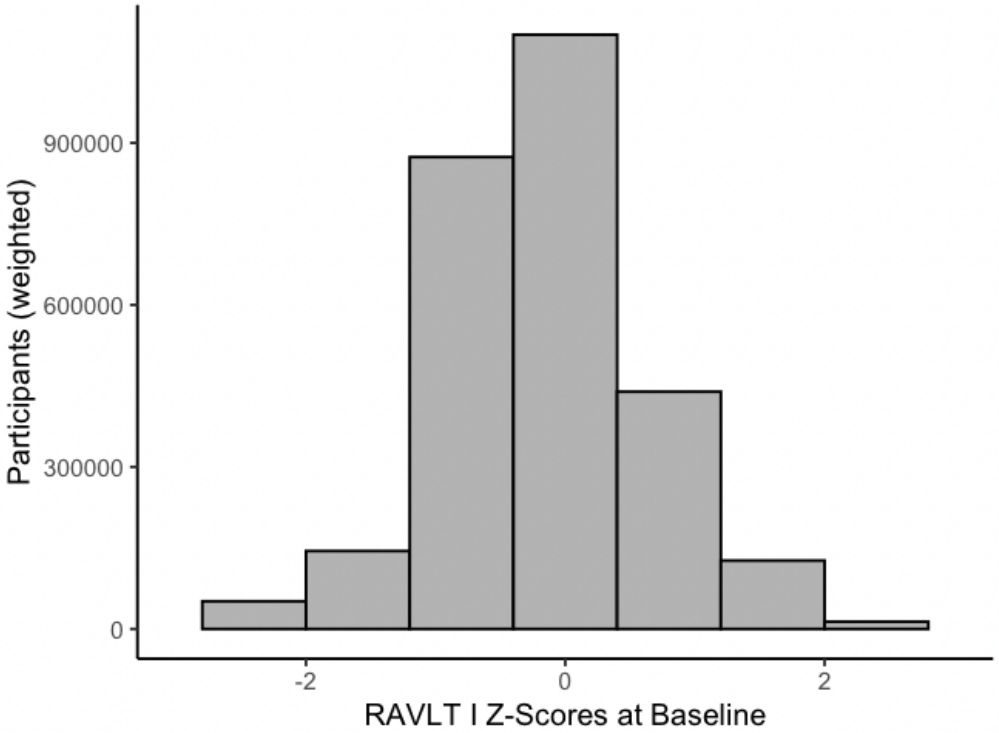


**Figure 3: Distribution of Baseline RAVLT I Z-scores – Weighted Analytical Sample, Comprehensive Cohort–Canadian Longitudinal Study on Aging**

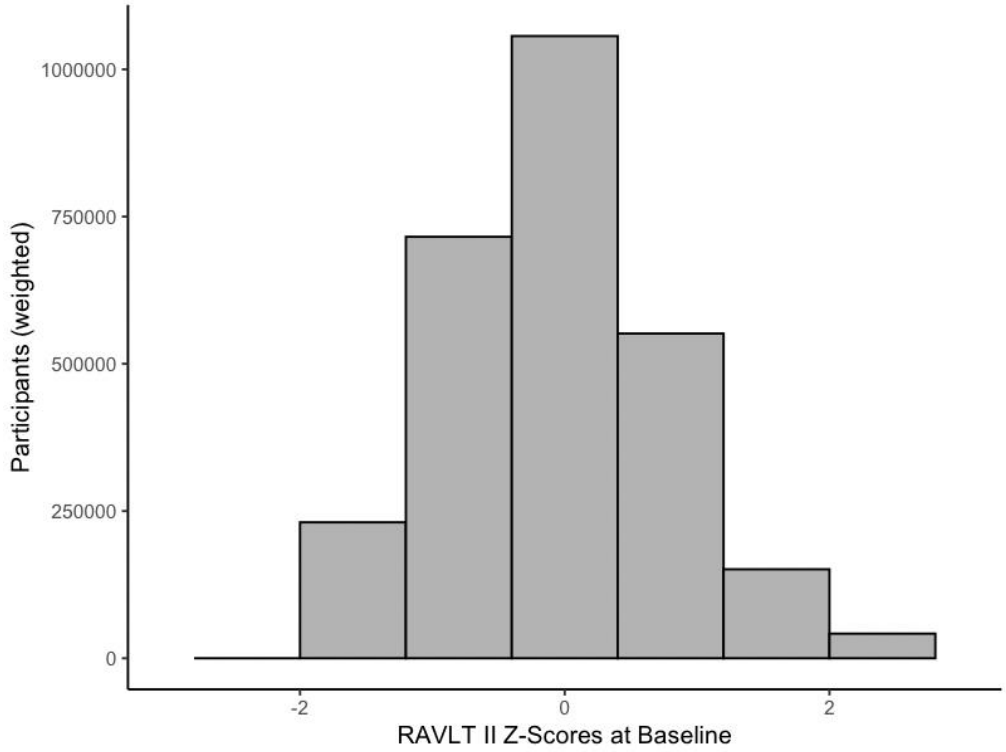


**Figure 4: Distribution of Baseline RAVLT II Z-scores – Weighted Analytical Sample, Comprehensive Cohort–Canadian Longitudinal Study on Aging**

### *4.2.1 Bivariate Associations with Social Isolation*

A larger proportion of those who were socially isolated were males (57.0% versus 50.3%; standardized difference = 0.10), 65 years or older (65-74 years: 23.4% versus 16.5%; standardized difference = 0.33; ≥ 75 years: 12.0% versus 9.3%; standardized difference = 0.28), and from British Columbia (38.4% versus 29.6%; standardized difference = 0.19) compared to those who were not socially isolated (Table 3). These standardized differences were equal to or greater than 0.10, suggesting a meaningful difference across groups. A greater proportion of those who were socially isolated reported some post-secondary education (8.4% versus 6.5%; standardized difference = 0.07) and the lowest annual household income (<$19,999) (7.3% versus 3.9%; standardized difference = 0.15), compared to those who were not socially isolated. With the exception of the lowest annual household income, the standardized differences for the education and income categories were less than 0.10, suggesting a lack of meaningful difference.

A greater proportion of those who were socially isolated reported at least one chronic condition (65.4% versus 61.2%; standardized difference = 0.09), any level of functional impairment (7.6% versus 6.2%; standardized difference = 0.06), and the presence of severe depressive symptoms (18.4% versus 14.3%; standardized difference = 0.11) compared to those who were not socially isolated. Although the standardized difference for depressive symptoms suggested meaningful difference, the standardized differences across chronic conditions and functional status categories were less than 0.10, indicating a lack of meaningful difference across groups.

A higher proportion of those who were socially isolated were current smokers (12.4% versus 9.1%; standardized difference = 0.11), never drinkers (13.3% versus 10.1%; standardized difference = 0.10), and occasional drinkers (12.4% versus 10.8%; standardized difference = 0.05)

compared to those who were not socially isolated. Although the standardized difference for occasional drinkers was less than 0.10, indicating a lack of meaningful difference, the standardized differences for current smokers, never drinkers, and regular drinkers were equal to or greater than 0.10, suggesting a meaningful difference across groups. A larger proportion of those who were socially isolated reported low functional social support compared to those who were not socially isolated (10.9% versus 4.6%). In contrast, a larger proportion of those were not socially isolated reported high functional social support compared to those who were socially isolated (95.4% versus 89.1%). The standardized differences for both low and high functional social support were 0.24, denoting a meaningful difference.

**Table 3: Distribution of Sociodemographic, Health, and Lifestyle Covariates by Social Isolation – Weighted Analytical Sample, Comprehensive Cohort–Canadian Longitudinal Study on Aging**

| Covariates | Total[1] (n=2,756,716) | Not Socially Isolated[2] (n=2,581,422) | Socially Isolated[3] (n=175,294) | Standardized Differences |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | |
| ***Sociodemographics*** | | | | |
| *Sex* | | | | |
| Female | 1,358,325 (49.3) | 1,283,001 (49.7) | 75,324 (43.0) | 0.13 |
| Male | 1,398,391 (50.7) | 1,298,421 (50.3) | 99,970 (57.0) | 0.10 |
| *Age Group (years)* | | | | |
| 45-54 years | 1,195,421(43.4) | 1,134,314 (43.9) | 61,107 (34.9) | 0.13 |
| 55-64 years | 834,583 (30.3) | 782,413 (30.3) | 52,170 (29.8) | 0.01 |
| 65-74 years | 465,779 (16.9) | 424,806 (16.5) | 40,973 (23.4) | 0.33 |
| ≥ 75 years | 260,934 (9.5) | 239,889 (9.3) | 21,045 (12.0) | 0.28 |
| *Province* | | | | |
| Alberta | 311,829 (11.3) | 293,606 (11.4) | 18,223 (10.4) | 0.03 |
| British Columbia | 831,927 (30.2) | 764,638 (29.6) | 67,289 (38.4) | 0.19 |
| Manitoba | 203,634 (7.4) | 192,888 (7.5) | 10,746 (6.1) | 0.06 |
| Newfoundland and Labrador | 58,949 (2.1) | 55,483 (2.2) | 3,466 (2.0) | 0.01 |
| Nova Scotia | 92,628 (3.4) | 86,554 (3.4) | 6,074 (3.5) | 0.01 |
| Ontario | 382,090 (13.9) | 361,359 (14.0) | 20,731 (11.8) | 0.07 |
| Québec | 875,659 (31.8) | 826,894 (32.0) | 48,765 (27.8) | 0.09 |
| *Education* | | | | |
| Less than secondary school | 122,482 (4.4) | 114,171 (4.4) | 8,311 (4.7) | 0.01 |
| Secondary school graduation | 238,862 (8.7) | 227,101 (8.8) | 11,761 (6.7) | 0.08 |
| Some post-secondary | 181,733 (6.6) | 166,995 (6.5) | 14,738 (8.4) | 0.07 |
| Post-secondary diploma | 2,213,638 (80.3) | 2,073,153 (80.3) | 140,485 (80.1) | 0.01 |
| *Annual Household Income* | | | | |
| < $19,999 | 113,795 (4.1) | 100,948 (3.9) | 12,847 (7.3) | 0.15 |
| $20,000 – 49,999 | 495,165 (18.0) | 462,537 (17.9) | 32,628 (18.6) | 0.02 |
| $50,000 – 99,999 | 923,102 (33.5) | 865,482 (33.5) | 57,620 (32.9) | 0.01 |
| $100,000 – 149,999 | 622,196 (22.6) | 583,766 (22.6) | 38,430 (21.9) | 0.02 |
| ≥ $150,000 | 602,458 (21.9) | 568,689 (22.0) | 33,769 (19.3) | 0.07 |

**Table 3 (Cont'd): Distribution of Sociodemographic, Health, and Lifestyle Covariates by Social Isolation – Weighted Analytical Sample, Comprehensive Cohort–Canadian Longitudinal Study on Aging**

| Covariates | Total[1] (n=2,756,716) | Not Socially Isolated[2] (n=2,581,422) | Socially Isolated[3] (n=175,294) | Standardized Differences |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | |
| *Presence of Chronic Conditions* | | | | |
| At least one chronic condition | 1,695,316 (61.5) | 1,580,604 (61.2) | 114,712 (65.4) | 0.09 |
| No chronic conditions | 1,061,401 (38.5) | 1,000,818 (38.8) | 60,583 (34.6) | 0.09 |
| *Functional Status* | | | | |
| No functional impairment | 2,559,669 (92.9) | 2,400,945 (93.0) | 158,724 (90.6) | 0.09 |
| Any level of functional impairment | 173,062 (6.3) | 159,773 (6.2) | 13,289 (7.6) | 0.06 |
| *Depressive Symptoms* | | | | |
| Not severe | 2,354,939 (85.4) | 2,211,918 (85.7) | 143,021 (81.6) | 0.11 |
| Severe | 401,778 (14.6) | 369,504 (14.3) | 32,274 (18.4) | 0.11 |
| ***Lifestyle*** | | | | |
| *Smoking Status* | | | | |
| Never smoker | 1,349,796 (49.0) | 1,270,427 (49.2) | 79,369 (45.3) | 0.08 |
| Former smoker | 1,150,962 (41.8) | 1,076,739 (41.7) | 74,223 (42.3) | 0.01 |
| Current smoker | 255,957 (9.3) | 234,255 (9.1) | 21,702 (12.4) | 0.11 |
| *Alcohol Use* | | | | |
| No drinker | 283,160 (10.3) | 259,823 (10.1) | 23,337 (13.3) | 0.10 |
| Occasional drinker | 300,048 (10.9) | 278,303 (10.8) | 21,745 (12.4) | 0.05 |
| Regular drinker | 2,173,508 (78.8) | 2,043,295 (79.2) | 130,213 (74.3) | 0.12 |
| ***Functional Social Support*** | | | | |
| Low | 138,237 (5.0) | 119,137 (4.6) | 19,100 (10.9) | 0.24 |
| High | 2,618,478 (95.0) | 2,462,284 (95.4) | 156,194 (89.1) | 0.24 |

*Notes:* Data are presented as column percentages.

[1] Unweighted n=24,531

[2] Unweighted n=22,862

[3] Unweighted n=1,669

### *4.2.2 Bivariate Associations with Memory*

Social isolation was statistically significantly associated with lower RAVLT I and II z-scores, with the magnitude of effect for both outcomes being approximately equal (Table 4). Compared to males, females had significantly higher RAVLT I and II z-scores. As age increased, RAVLT I and II z-scores decreased in a dose-response manner. With Ontario as the reference group, residence in British Columbia was statistically significantly associated with higher RAVLT I z-scores, while living in Manitoba, Nova Scotia, and Québec was associated with lower RAVLT I z-scores. For RAVLT II, living in Alberta, British Columbia, Newfoundland and Labrador, and Québec was statistically significantly associated with higher z-scores compared to living in Ontario. Levels of education were statistically significantly, and positively, associated with higher RAVLT I and II z-scores in a dose-response manner, with the reference category being 'less than secondary school'. As annual household income levels decreased, RAVLT I and II z-scores also decreased in a dose-response manner relative to the reference category of greater than $150,000.

The presence of at least one chronic condition versus no chronic conditions, reporting any level of functional impairment versus no level of impairment, and the presence of severe versus not severe depressive symptoms were all statistically significantly associated with lower RAVLT I and II z-scores.

Compared to never smokers, former smokers and current smokers had statistically significantly lower RAVLT I and II z-scores. Regular and occasional use of alcohol were statistically significantly associated with increased RAVLT II z-scores, compared to non-users. For alcohol use and RAVLT I z-scores, the associations were also positive yet only statistically

significant for regular users. Low functional social support was significantly associated with decreases in RAVLT I and II z-scores, compared to high functional social support.

**Table 4: Bivariate Associations between Independent Variables and Memory – Weighted Analytical Sample, Comprehensive Cohort–Canadian Longitudinal Study on Aging**

| Variables | Memory | |
|---|---|---|
| | **RAVLT I Z-score** | **RAVLT II Z-score** |
| | $\hat{\beta}$ (95% CI) | $\hat{\beta}$ (95% CI) |
| ***Exposure*** | | |
| *Social Isolation Status* (Ref: Not socially isolated) | | |
| Socially isolated | **-0.0917 (-0.1409, -0.0426)** | **-0.0973 (-0.1494, -0.045)** |
| ***Sociodemographics*** | | |
| *Sex* (Ref: Male) | | |
| Female | **0.3336 (0.3104, 0.3568)** | **0.3878 (0.3631, 0.4126)** |
| *Age group (years)* (Ref: 45-54 years) | | |
| 55-64 years | **-0.1685 (-0.1962, -0.1408)** | **-0.2215 (-0.2510, -0.1919)** |
| 65-74 years | **-0.3893 (-0.4192, -0.3594)** | **-0.4508 (-0.4828, -0.4189)** |
| 75 years and older | **-0.7979 (-0.8307, -0.7651)** | **-0.8525 (-0.8869, -0.8181)** |
| *Province of residence* (Ref: Ontario) | | |
| Alberta | 0.0228 (-0.0257, 0.0712) | **0.1153 (0.0636, 0.1669)** |
| British Columbia | **0.0782 (0.0427, 0.1138)** | **0.1643 (0.1247, 0.2039)** |
| Manitoba | **-0.0965 (-0.1394, -0.0536)** | 0.0173 (-0.0284, 0.0630) |
| Newfoundland and Labrador | -0.0020 (-0.0496, 0.0456) | **0.06800 (0.0145, 0.1215)** |
| Nova Scotia | **-0.1215 (-0.1659, -0.0771)** | 0.0055 (-0.0418, 0.0529) |
| Québec | **-0.1143 (-0.1502, -0.0784)** | **0.0458 (0.0067, 0.0849)** |
| *Education* (Ref: Less than secondary school) | | |
| Secondary school graduation | **0.3982 (0.3390, 0.4574)** | **0.3329 (0.2719, 0.3939)** |
| Some post-secondary education | **0.5112 (0.4487, 0.5737)** | **0.4406 (0.3763, 0.5050)** |
| Post-secondary degree/diploma | **0.6662 (0.6180, 0.7143)** | **0.6074 (0.5590, 0.6558)** |

**Table 4 (Cont'd): Bivariate Associations between Independent Variables and Memory –Weighted Analytical Sample, Comprehensive Cohort–Canadian Longitudinal Study on Aging**

| Variables | Memory | |
|---|---|---|
| | **RAVLT I Z-score** | **RAVLT II Z-score** |
| *Annual household income* (Ref: ≥$150,000) | | |
| <$20,000 | **-0.5542 (-0.6156, -0.4929)** | **-0.4311 (-0.4942, -0.3681)** |
| ≥$20,000 and <$50,000 | **-0.4493 (-0.4853, -0.4133)** | **-0.3748 (-0.4134, -0.3362)** |
| ≥$50,000 and <$100,000 | **-0.2400 (-0.2723, -0.2077)** | **-0.1864 (-0.2218, -0.1509)** |
| ≥$100,000 and <$150,000 | **-0.1017 (-0.1380, -0.0654)** | **-0.0428 (-0.0824, -0.0031)** |
| ***Health*** | | |
| *Presence of chronic conditions* (Ref: No chronic conditions) | | |
| At least one chronic condition | **-0.1597 (-0.1843, -0.1351)** | **-0.1694 (-0.1958, -0.1430)** |
| *Functional impairment* (Ref: No functional impairment) | | |
| Any level of functional impairment | **-0.2369 (-0.2792, -0.1946)** | **-0.2528 (-0.2962, -0.2094)** |
| *Depressive symptoms* (Ref: Not severe depressive symptoms) | | |
| Severe depressive symptoms | **-0.0887 (-0.1230, -0.0545)** | **-0.0706 (-0.1067, -0.0345)** |
| ***Lifestyle*** | | |
| *Smoking status* (Ref: Never smoker) | | |
| Former smoker | **-0.1652 (-0.1897, -0.1406)** | **-0.1485 (-0.1749, -0.1221)** |
| Current smoker | **-0.1954 (-0.2375, -0.1533)** | **-0.1545 (-0.1990, -0.1100)** |
| *Alcohol use* (Ref: Non-user) | | |
| Occasional user | 0.0465 (-0.0043, 0.0973) | **0.0913 (0.0380, 0.1447)** |
| Regular user | **0.1779 (0.1386, 0.2173)** | **0.1870 (0.1454, 0.2286)** |
| ***Overall functional social support*** | | |
| (Ref: High) | | |
| Low | **-0.2598 (-0.3109, -0.2087)** | **-0.2366 (-0.2913, -0.18193)** |

*Notes:* p < 0.05 in **bolded** font.

Ref = reference category; $\hat{\hat{\beta}}$ = regression coefficient value; CI = confidence interval.

## 4.3 Multivariable Regression Analyses

### *4.3.1 Research Question 1*

*Is social isolation, measured using Menec et al.'s social isolation index, associated with immediate and delayed recall memory, measured using the RAVLT?*

The base models (Model 1s) showed small, inverse associations between the SII and RAVLT I and II (Tables 5 and 6). This meant persons who were socially isolated had lower z-scores, on average, than persons who were not isolated. However, the regression coefficients were weak and not statistically significant. Although the regression coefficients suggested inverse associations between the SII and RAVLT I and II, the 95% confidence intervals contained the null value of 0, and since the true value could lie anywhere in between the confidence interval, the possibility of null or small and positive associations could not be ruled out.

### *4.3.2 Research Question 2*

*Are the findings from Question 1 above maintained after adjusting for sociodemographic, health-related, and lifestyle covariates, as well as functional social support?*

The strength of the inverse association between the SII and RAVLT I and II decreased sequentially following the addition of each set of covariates to the base models (Models 2 to 5 in Tables 5 and 6). The association between social isolation and RAVLT I and II remained statistically nonsignificant in all the adjusted models, again suggesting the possibility of no association or a small and positive association.

Regression diagnostics for the base models (Model 1s) suggested evidence of good model fit, as shown by the random scatter of points in the residual plots. The adjusted models (Models 2 to 5) indicated a lack of model fit, based on the detectable pattern of points in the residual plots

(see Appendices F and G). As such, the regression coefficients reported in Tables 5 and 6 may not be an accurate representation of the true association between social isolation and memory. See Section 5.5 for for a discussion of the poor model fit.

### *4.3.3 Research Question 3*

*Do age group and sex, examined separately, modify the associations between social isolation and memory?*

Full models, adjusted for all covariates (Model 5s), were stratified by age group and sex to assess effect modification. The models stratified by age group excluded age group as a covariate; likewise, the models stratified by sex excluded sex as a covariate. The directions of association between the SII and RAVLT I and II varied across age groups (Tables 7 and 8); however, the regression coefficients were close to zero and statistically nonsignificant. The associations between social isolation and RAVLT I and II were negative for males and positive for females; however, the regression coefficients were also close to zero and statistically nonsignificant. The 95% confidence intervals for the age group-stratified models encompassed the regression coefficients for the unstratified, fully-adjusted associations between SII and RAVLT I ($\hat{\beta}$ = -0.0019) and SII and RAVLT II ($\hat{\beta}$ = -0.0010) (Figures 5-6). The same observation was noted for the sex-stratified models (Figures 5- 6). These findings indicated a lack of evidence to suggest effect modification by age group and sex.[155]

**Table 5: Multivariable Linear Regression Analysis of the Associations between Social Isolation Index and RAVLT I Z-score – Weighted Analytical Sample, Comprehensive Cohort–Canadian Longitudinal Study on Aging**

| | **Model 1** $\hat{\beta}$ (95% CI) | **Model 2** $\hat{\beta}$ (95% CI) | **Model 3** $\hat{\beta}$ (95% CI) | **Model 4** $\hat{\beta}$ (95% CI) | **Model 5** $\hat{\beta}$ (95% CI) |
|---|---|---|---|---|---|
| ***Exposure*** | | | | | |
| *Social Isolation Status* (Ref: Not socially isolated) | | | | | |
| Socially isolated | -0.0231 (-0.0701, 0.0238) | -0.0167 (-0.0620, 0.0285) | -0.0120 (-0.0572, 0.0332) | -0.0052 (-0.0501, 0.0396) | -0.0019 (-0.0469, 0.0431) |
| ***Sociodemographics*** | | | | | |
| *Sex* (Ref: Male) | | | | | |
| Female | **0.3486 (0.3263, 0.3708)** | **0.3807 (0.3585, 0.4029)** | **0.3880 (0.3657, 0.4103)** | **0.3875 (0.3651, 0.4099)** | **0.3861 (0.3637, 0.4085)** |
| *Age group (years)* (Ref: 45-54 years) | | | | | |
| 55-64 years | **-0.1645 (-0.1915, -0.1375)** | **-0.1259 (-0.1528, -0.0990)** | **-0.1227 (-0.1498, -0.0957)** | **-0.1213 (-0.1484, -0.0943)** | **-0.1213 (-0.1484, -0.0942)** |
| 65-74 years | **-0.4032 (-0.4322, -0.3742)** | **-0.3080 (-0.3380, -0.2779)** | **-0.3043 (-0.3350, -0.2735)** | **-0.3090 (-0.3399, -0.2781)** | **-0.3098 (-0.3407, -0.2790)** |
| 75 years and older | **-0.8026 (-0.8345, -0.7707)** | **-0.6600 (-0.6937, -0.6262)** | **-0.6457 (-0.6808, -0.6105)** | **-0.6538 (-0.6892, -0.6184)** | **-0.6538 (-0.6892, -0.6184)** |
| *Province of residence* (Ref: Ontario) | | | | | |
| Alberta | -0.0074 (-0.0536, 0.0389) | -0.0283 (-0.0741, 0.0176) | -0.0310 (-0.0769, 0.0149) | -0.0296 (-0.0754, 0.0163) | -0.0295 (-0.0754, 0.0164) |
| British Columbia | **0.0704 (0.0365, 0.1043)** | **0.0799 (0.0464, 0.1133)** | **0.07812 (0.0448, 0.1116)** | **0.0803 (0.0469, 0.1136)** | **0.0798 (0.0465, 0.1132)** |
| Manitoba | **-0.0829 (-0.1238, -0.0419)** | **-0.0549 (-0.0952, -0.0147)** | **-0.0557 (-0.0959, -0.0155)** | **-0.0540 (-0.0941, -0.0139)** | **-0.0536 (-0.0937, -0.0136)** |
| Newfoundland and Labrador | -0.0308 (-0.0766, 0.0151) | -0.0271 (-0.0722, 0.0181) | -0.0293 (-0.0744, 0.0158) | -0.0217 (-0.0666, 0.0232) | -0.0228 (-0.0677, 0.0221) |
| Nova Scotia | **-0.1546 (-0.1964, -0.1128)** | **-0.1293 (-0.1707, -0.0879)** | **-0.1298 (-0.1711, -0.0885)** | **-0.1239 (-0.1653, -0.0826)** | **-0.1257 (-0.1671, -0.0843)** |
| Québec | **-0.1051 (-0.1392, -0.0710)** | **-0.0358 (-0.0703, -0.0014)** | **-0.0375 (-0.0719, -0.0031)** | **-0.0398 (-0.0742, -0.0053)** | **-0.0408 (-0.0753, -0.0064)** |

| | | | | |
|---|---|---|---|---|
| *Education* | | | | |
| (Ref: Less than secondary school) | | | | |
| Secondary school graduation | **0.2030** | **0.1961** | **0.1863** | **0.1851** |
| | **(0.1455, 0.2604)** | **(0.1386, 0.2535)** | **(0.1291, 0.2434)** | **(0.1280, 0.2423)** |
| Some post-secondary education | **0.2997** | **0.2955** | **0.2826** | **0.2828** |
| | **(0.2387, 0.3607)** | **(0.2346, 0.3565)** | **(0.2217, 0.3435)** | **(0.2218, 0.3437)** |
| Post-secondary degree/diploma | **0.3916** | **0.3841** | **0.3592** | **0.3592** |
| | **(0.3424, 0.4408)** | **(0.3349, 0.4334)** | **(0.3102, 0.4083)** | **(0.3101, 0.4083)** |
| *Annual household income* | | | | |
| (Ref: ≥$150,000) | | | | |
| <$20,000 | **-0.3893** | **-0.3532** | **-0.3021** | **-0.2885** |
| | **(-0.4523, -0.3264)** | **(-0.4161, -0.2902)** | **(-0.3651, -0.2392)** | **(-0.3525, -0.2245)** |
| ≥$20,000 and <$50,000 | **-0.2573** | **-0.2401** | **-0.2076** | **-0.2020** |
| | **(-0.2955, -0.2190)** | **(-0.2786, -0.2015)** | **(-0.2466, -0.1685)** | **(-0.2412, -0.1628)** |
| ≥$50,000 and <$100,000 | **-0.1378** | **-0.1304** | **-0.1126** | **-0.1106** |
| | **(-0.1704, -0.1052)** | **(-0.1631, -0.0978)** | **(-0.1454, -0.0798)** | **(-0.1434, -0.0777)** |
| ≥$100,000 and <$150,000 | **-0.0676** | **-0.0645** | **-0.0551** | **-0.0543** |
| | **(-0.1028, -0.0324)** | **(-0.0996, -0.0293)** | **(-0.0902, -0.0199)** | **(-0.0894, -0.0191)** |
| ***Health*** | | | | |
| *Presence of chronic conditions* | | | | |
| (Ref: No chronic conditions) | | | | |
| At least one chronic condition | | -0.0230 | -0.0171 | -0.0170 |
| | | (-0.0474, 0.0013) | (-0.0414, 0.0073) | (-0.0413, 0.0074) |
| *Functional impairment* | | | | |
| (Ref: No functional impairment) | | | | |
| Any level of functional impairment | | **-0.0830** | **-0.0709** | **-0.0697** |
| | | **(-0.1224, -0.0437)** | **(-0.1104, -0.0313)** | **(-0.1093, -0.0302)** |
| *Depressive symptoms* | | | | |
| (Ref: Not severe depressive symptoms) | | | | |
| Severe depressive symptoms | | **-0.0581** | **-0.0465** | **-0.0393** |
| | | **(-0.0905, -0.0257)** | **(-0.0789, -0.0142)** | **(-0.0723, -0.0063)** |

| | | | | | |
|---|---|---|---|---|---|
| ***Lifestyle*** | | | | | |
| *Smoking status* | | | | | |
| (Ref: Never smoker) | | | | | |
| Former smoker | | | | **-0.0667** | **-0.0665** |
| | | | | **(-0.0900, -0.0433)** | **(-0.0899, -0.0432)** |
| Current smoker | | | | **-0.1157** | **-0.1135** |
| | | | | **(-0.1563, -0.0751)** | **(-0.1542, -0.0728)** |
| *Alcohol use* | | | | | |
| (Ref: Non-user) | | | | | |
| Occasional user | | | | **0.0198** | 0.0194 |
| | | | | **(-0.0278, 0.0674)** | (-0.0282, 0.0670) |
| Regular user | | | | **0.1127** | **0.1113** |
| | | | | **(0.0757, 0.1496)** | **(0.0743, 0.1483)** |
| ***Overall functional social support*** | | | | | |
| (Ref: High) | | | | | |
| Low | | | | | **-0.0724** |
| | | | | | **(-0.1223, -0.0224)** |
| **R-Square** | 0.1287 | 0.1567 | 0.1587 | 0.1629 | 0.1632 |
| **Adjusted R-Square** | 0.1283 | 0.1561 | 0.1579 | 0.1620 | 0.1622 |

*Notes:* $p < 0.05$ in **bolded** font.

Ref = reference category; $\hat{\beta}$ = regression coefficient value; CI = confidence interval.

**Table 6: Multivariable Linear Regression Analysis of the Associations between Social Isolation Index and RAVLT II Z-score – Weighted Analytical Sample, Comprehensive Cohort–Canadian Longitudinal Study on Aging**

| | **Model 1** $\hat{\beta}$ (95% CI) | **Model 2** $\hat{\beta}$ (95% CI) | **Model 3** $\hat{\beta}$ (95% CI) | **Model 4** $\hat{\beta}$ (95% CI) | **Model 5** $\hat{\beta}$ (95% CI) |
|---|---|---|---|---|---|
| ***Exposure*** | | | | | |
| *Social Isolation Status* (Ref: Not socially isolated) | | | | | |
| Socially isolated | -0.0192 (-0.0690, 0.0305) | -0.0152 (-0.0639, 0.0336) | -0.0104 (-0.0591, 0.0382) | -0.0041 (-0.0525, 0.0444) | -0.0010 (-0.0496, 0.0475) |
| ***Sociodemographics*** | | | | | |
| *Sex* (Ref: Male) | | | | | |
| Female | **0.4032 (0.3795, 0.4269)** | **0.4296 (0.4057, 0.4534)** | **0.4381 (0.4141, 0.4620)** | **0.4380 (0.4140, 0.4620)** | **0.4367 (0.4127, 0.4608)** |
| *Age group (years)* (Ref: 45-54 years) | | | | | |
| 55-64 years | **-0.2159 (-0.2446, -0.1872)** | **-0.1852 (-0.2139, -0.1565)** | **-0.1817 (-0.2107, -0.1528)** | **-0.1815 (-0.2104, -0.1525)** | **-0.1815 (-0.2104, -0.1525)** |
| 65-74 years | **-0.4643 (-0.4953, -0.4334)** | **-0.3882 (-0.4202, -0.3562)** | **-0.3837 (-0.4166, -0.3509)** | **-0.3894 (-0.4224, -0.3564)** | **-0.3901 (-0.4231, -0.3571)** |
| 75 years and older | **-0.8632 (-0.8967, -0.8297)** | **-0.7451 (-0.7803, -0.7099)** | **-0.7284 (-0.7652, -0.6915)** | **-0.7364 (-0.7736, -0.6992)** | **-0.7364 (-0.7736, -0.6992)** |
| *Province of residence* (Ref: Ontario) | | | | | |
| Alberta | **0.0819 (0.0326, 0.1312)** | **0.0669 (0.0177, 0.1160)** | **0.0639 (0.0147, 0.1131)** | **0.0654 (0.0161, 0.1146)** | **0.0654 (0.0162, 0.1147)** |
| British Columbia | **0.1547 (0.1171, 0.1924)** | **0.1586 (0.1212, 0.1960)** | **0.1565 (0.1192, 0.1939)** | **0.1600 (0.1227, 0.1973)** | **0.1596 (0.1223, 0.1969)** |
| Manitoba | 0.0314 | **0.0521** | **0.0512** | **0.0530** | **0.0533** |

| | | | | | |
|---|---|---|---|---|---|
| | (-0.0119, 0.0746) | **(0.0092, 0.0950)** | **(0.0084, 0.0940)** | **(0.0104, 0.0957)** | **(0.0107, 0.0960)** |
| Newfoundland and Labrador | 0.0352<br>(-0.0162, 0.0865) | 0.0335<br>(-0.0175, 0.0846) | 0.0303<br>(-0.0207, 0.0813) | 0.0355<br>(-0.0154, 0.0863) | 0.0345<br>(-0.016, 0.0853) |
| Nova Scotia | -0.0327<br>(-0.0772, 0.0118) | -0.0152<br>(-0.0594, 0.0291) | -0.0155<br>(-0.0597, 0.0287) | -0.01080<br>(-0.0549, 0.0334) | -0.0124<br>(-0.0566, 0.0318) |
| Québec | **0.0546**<br>**(0.0175, 0.0917)** | **0.1092**<br>**(0.0718, 0.1466)** | **0.1072**<br>**(0.0698, 0.1446)** | **0.1027**<br>**(0.0652, 0.1401)** | **0.1017**<br>**(0.0643, 0.1392)** |
| *Education*<br>(Ref: Less than secondary school) | | | | | |
| Secondary school graduation | | **0.1479**<br>**(0.0892, 0.2066)** | **0.1405**<br>**(0.0817, 0.1992)** | **0.1321**<br>**(0.0735, 0.1908)** | **0.1311**<br>**(0.0724, 0.1897)** |
| Some post-secondary education | | **0.2638**<br>**(0.2019, 0.3258)** | **0.2595**<br>**(0.1975, 0.3214)** | **0.2475**<br>**(0.1854, 0.3095)** | **0.2476**<br>**(0.1855, 0.3097)** |
| Post-secondary degree/diploma | | **0.3568**<br>**(0.3084, 0.4053)** | **0.3488**<br>**(0.3002, 0.3973)** | **0.3277**<br>**(0.2790, 0.3764)** | **0.3277**<br>**(0.2790, 0.3764)** |
| *Annual household income*<br>(Ref: ≥$150,000) | | | | | |
| <$20,000 | | **-0.2810**<br>**(-0.3448, -0.2171)** | **-0.2418**<br>**(-0.3061, -0.1775)** | **-0.1933**<br>**(-0.2583, -0.1283)** | **-0.1809**<br>**(-0.2466, -0.1153)** |
| ≥$20,000 and <$50,000 | | **-0.1826**<br>**(-0.2230, -0.1422)** | **-0.1640**<br>**(-0.2047, -0.1234)** | **-0.1336**<br>**(-0.1748, -0.0925)** | **-0.1286**<br>**(-0.1699, -0.0873)** |
| ≥$50,000 and <$100,000 | | **-0.0790**<br>**(-0.1145, -0.0435)** | **-0.0711**<br>**(-0.1067, -0.0355)** | **-0.0552**<br>**(-0.0909, -0.0194)** | **-0.0533**<br>**(-0.0890, -0.0175)** |
| ≥$100,000 and <$150,000 | | -0.0094<br>(-0.0478, 0.0289) | -0.0061<br>(-0.0445, 0.0324) | 0.0020<br>(-0.0364, 0.0405) | 0.0028<br>(-0.0357, 0.0413) |
| ***Health***<br>*Presence of chronic conditions*<br>(Ref: No chronic conditions) | | | | | |
| At least one chronic condition | | | -0.0232<br>(-0.0493, 0.0030) | -0.0183<br>(-0.0445, 0.0078) | -0.0182<br>(-0.0444, 0.0079) |

| | | | | | |
|---|---|---|---|---|---|
| *Functional impairment*<br>(Ref: No functional impairment) | | | | | |
| Any level of functional impairment | | | **-0.1162**<br>**(-0.1566, -0.0757)** | **-0.1048**<br>**(-0.1452, -0.0644)** | **-0.1036**<br>**(-0.1439, -0.0633)** |
| *Depressive symptoms*<br>(Ref: Not severe depressive symptoms) | | | | | |
| Severe depressive symptoms | | | **-0.0609**<br>**(-0.0953, -0.0266)** | **-0.0504**<br>**(-0.0846, -0.0162)** | **-0.0438**<br>**(-0.0787, -0.0089)** |
| ***Lifestyle*** | | | | | |
| *Smoking status*<br>(Ref: Never smoker) | | | | | |
| Former smoker | | | | **-0.0473**<br>**(-0.0723, -0.0223)** | **-0.0472**<br>**(-0.072, -0.0222)** |
| Current smoker | | | | **-0.0939**<br>**(-0.1365, -0.0512)** | **-0.0919**<br>**(-0.1346, -0.0492)** |
| *Alcohol use*<br>(Ref: Non-user) | | | | | |
| Occasional user | | | | **0.0508**<br>**(0.0010, 0.1007)** | **0.0505**<br>**(0.0006, 0.1003)** |
| Regular user | | | | **0.12919**<br>**(0.0895, 0.1689)** | **0.1279**<br>**(0.0882, 0.1677)** |
| ***Overall functional social support***<br>(Ref: High) | | | | | |
| Low | | | | | **-0.0656**<br>**(-0.1186, -0.0126)** |
| **R-Square** | 0.1374 | 0.1564 | 0.1583 | 0.1615 | 0.1617 |
| **Adjusted R-Square** | 0.1370 | 0.1558 | 0.1575 | 0.1605 | 0.1607 |

*Notes:* $p < 0.05$ in **bolded** font.

Ref = reference category; $\hat{\beta}$ = regression coefficient value; CI = confidence interval

**Table 7: Association between Social Isolation Index and RAVLT I Z-score Stratified by Age Group and Sex**

| | 45-54 years $\hat{\beta}$ (95% CI) | 55-64 years $\hat{\beta}$ (95% CI) | 65-74 years $\hat{\beta}$ (95% CI) | ≥ 75 years $\hat{\beta}$ (95% CI) | Male $\hat{\beta}$ (95% CI) | Female $\hat{\beta}$ (95% CI) |
|---|---|---|---|---|---|---|
| Socially Isolated (Ref: Not Socially Isolated) | 0.0146 (-0.0798, 0.1090) | -0.0508 (-0.1238, 0.0223) | 0.0233 (-0.0539, 0.1005) | 0.0608 (-0.0242, 0.1458) | -0.0003 (-0.0566, 0.0561) | 0.0008 (-0.0719, 0.0736) |

*Notes:* p < 0.05 in **bolded** font; adjusted for sociodemographic, health, lifestyle, and functional social support.
Ref = reference category; $\hat{\beta}$ = regression coefficient value; CI = confidence interval.

**Table 8: Association between Social Isolation Index and RAVLT II Z-score Stratified by Age Group and Sex**

| | 45-54 years $\hat{\beta}$ (95% CI) | 55-64 years $\hat{\beta}$ (95% CI) | 65-74 years $\hat{\beta}$ (95% CI) | ≥ 75 years $\hat{\beta}$ (95% CI) | Male $\hat{\beta}$ (95% CI) | Female $\hat{\beta}$ (95% CI) |
|---|---|---|---|---|---|---|
| Socially Isolated (Ref: Not Socially Isolated) | -0.0323 (-0.1386, 0.0739) | -0.0043 (-0.0782, 0.0696) | 0.0436 (-0.0395, 0.1267) | 0.0464 (-0.0429, 0.1357) | -0.0010 (-0.0625, 0.0605) | 0.0050 (-0.0731, 0.0831) |

*Notes:* p < 0.05 in **bolded** font; Adjusted for sociodemographic, health, lifestyle, and functional social support.
Ref = reference category; $\hat{\beta}$ = regression coefficient value; CI = confidence interval.

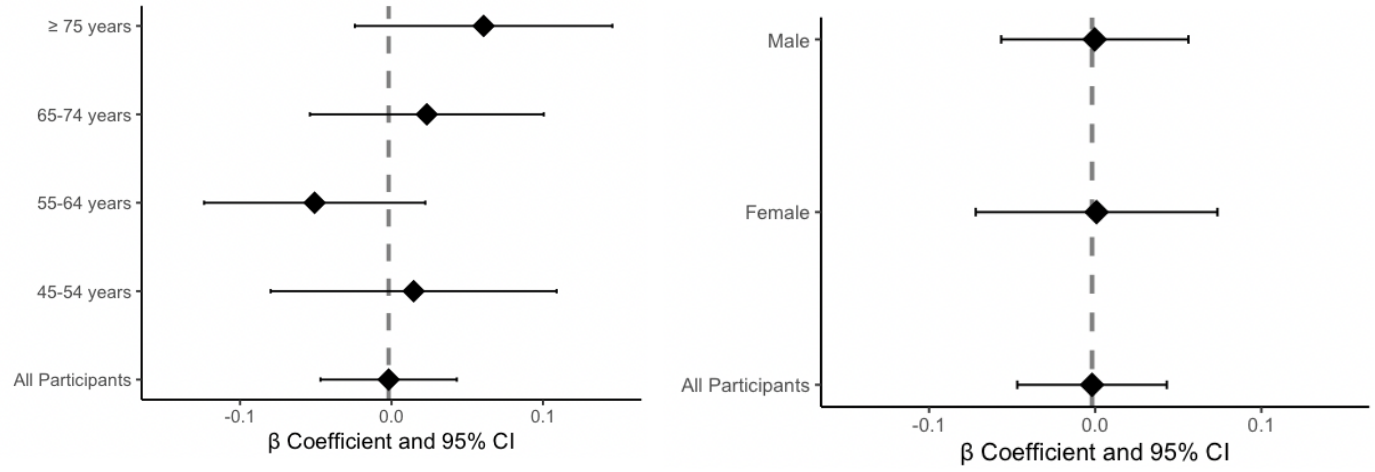


**Figure 5: Forest Plots showing the Association between Social Isolation Index and RAVLT I Z-score Stratified by Age and Sex**

*Notes:* adjusted for sociodemographic, health, lifestyle, and functional social support;
vertical line represents the unstratified association between social isolation and RAVLT I in the full model (Model 5);
$\hat{\beta}$ = regression coefficient value; CI = confidence interval.

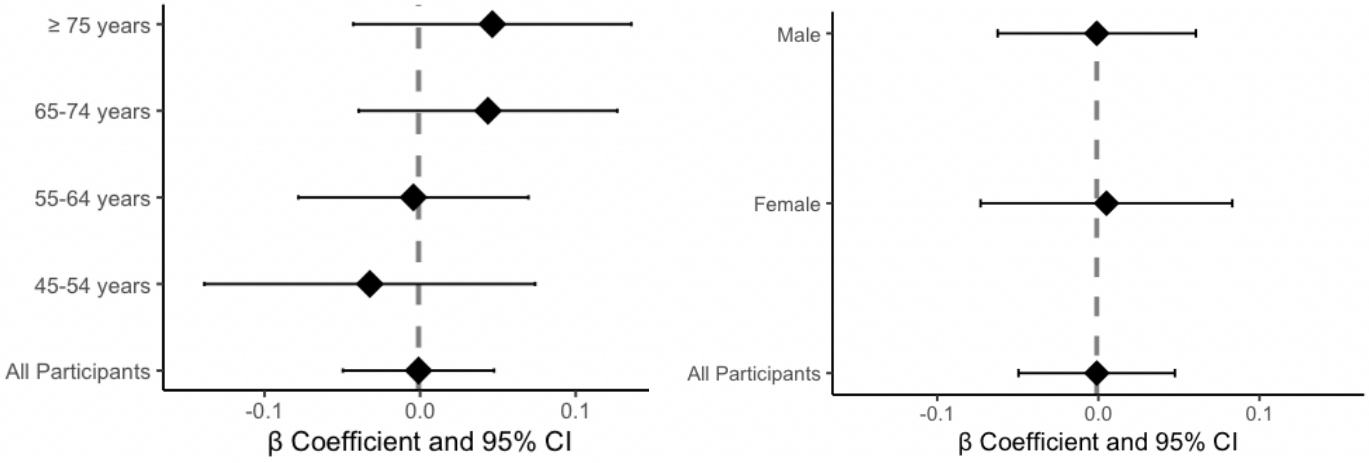


**Figure 6: Forest Plots showing the Association between Social Isolation Index and RAVLT II Z-score Stratified by Age and Sex**

*Notes:* adjusted for sociodemographic, health, lifestyle, and functional social support;
vertical line represents the unstratified association between social isolation and RAVLT II in the full model (Model 5);
$\hat{\beta}$ = regression coefficient value; CI = confidence interval.

## 4.4 Missing Data Analyses

On average, participants with missing SII scores had lower RAVLT I and II z-scores than participants with complete SII scores (Table 9). These associations were statistically significant.

**Table 9: Comparison of RAVLT I and II Z-scores among Participants with Missing versus Complete Social Isolation Index Scores**

| | ***Outcome*** | |
|---|---|---|
| | RAVLT I Z-score | RAVLT II Z-score |
| | $\hat{\beta}$ (95% CI) | $\hat{\beta}$ (95% CI) |
| ***Exposure*** | | |
| *Social Isolation Index Scores* (Ref: Compete Social Isolation Index Scores) | | |
| Missing Social Isolation Index Scores | **-0.2751 (-0.3784, -0.1719)** | **-0.2240 (-0.3319, -0.1161)** |

*Notes:* $p < 0.05$ in **bolded** font; Regression coefficients represent the change in RAVLT z-score for participants with missing versus complete social isolation index scores.
Ref = reference category; $\hat{\beta}$ = regression coefficient value; CI = confidence interval.

On average, participants with missing RAVLT I z-scores had a 12% increase in odds of being socially isolated, while participants with missing RAVLT II z-scores had a 19% increase in odds of being socially isolated, compared to those with no missing scores. However, these odds ratios were not statistically significant, meaning one cannot draw firm conclusions about the relation between missing RAVLT I or II z-scores and social isolation (Table 10).

**Table 10: Comparison of Social Isolation among Participants with Missing versus Complete RAVLT I and II Z-scores**

| | ***Outcome*** |
|---|---|
| | Socially Isolated |
| | OR (95% CI) |
| ***Exposure*** | |
| Missing versus Complete RAVLT I Z-scores | 1.12 (0.867, 1.448) |
| Missing versus Complete RAVLT II Z-scores | 1.19 (0.952, 1.497) |

*Notes:* Odds ratios represent the odds of being socially isolated for participants with missing versus complete RAVLT I and II z-scores.
OR = odds ratio; CI = confidence interval.

# 5 Discussion

## 5.1 Summary of Study Findings

This thesis investigated the association between baseline social isolation and memory, while controlling for sociodemographic characteristics, health-related factors, lifestyle behaviours, and functional social support. Analyses were separately stratified by age group and sex to assess effect modification. The base models showed small, inverse associations between the SII and RAVLT I and II, though the associations were weak and not statistically significant. After adjusting for sociodemographic, health-related, and lifestyle covariates, as well as functional social support, the regression coefficients for social isolation remained inversely associated and statistically nonsignificant. Given the absence of statistical significance, the possibility could not be ruled out that the true direction of association between SII and RAVLT I/II was positive or perhaps even null. A lack of evidence existed for effect modification by age group or sex.

## 5.2 Discussion of Unstratified Results

The thesis findings did not fully support the bulk of the literature on the association between social isolation and memory in middle- and older-aged adults. The existing literature generally found strong, inverse and statistically significant associations between social isolation and memory. In contrast, the associations in the thesis were small and statistically nonsignificant. However, given the very low proportion of socially isolated individuals in the sample, the thesis findings may not be entirely inconsistent with the literature, as the sample simply did not contain many at-risk individuals. The difference in findings between this thesis and the existing literature may be attributed to several factors: self-selection of non-socially isolated persons into the CLSA, exclusion of cognitively impaired persons from the CLSA, a younger analytical sample

in the thesis compared to other published studies, the cross-sectional study design of the thesis, the adjustment for a large number of covariates in this thesis compared to the literature, and the utilization of a more robust measure of social isolation in this thesis compared to other indices used in the literature.

Individuals who were not socially isolated may have been more likely to self-select themselves into the CLSA. Participants in the Comprehensive Cohort were required to undergo testing via in-home interviews and assessments completed at CLSA data collection sites. This level of in-person commitment may have inadvertently deterred or prevented socially isolated persons from participating in the study.

Similar to this thesis, Joyce et al. reported only 2% of participants being socially isolated (measured by monthly participation in voluntary/charity work, a sport/social/other club, a religious organization, or a political/community organization) in a longitudinal study of 11,498 community-dwelling Australians aged 70 years or older, followed over 4.7 years.[82] Joyce et al.'s findings showed no statistically significant association between social isolation and cognitive decline (hazard ratio [HR] = 1.00, $p = 0.99$), possibly due to the non-socially isolated nature of the analytical sample. Similarly, Shankar et al. reported that only 4.8% of their participants were socially isolated (measured by marital status, less than monthly contact with children/family/friends, and participation in organizations/religious groups/sports clubs/committees) in a longitudinal study of 8,630 individuals aged 50 years or older, followed for 4 years in the ELSA.[88] Shankar et al. found inverse associations between social isolation and memory, with similar and small magnitudes of effect for immediate and delayed recall (immediate recall: $\hat{\beta}$ = -0.14, 95% CI: -0.71 to 0.43); delayed recall: $\hat{\beta}$ = -0.14, 95% CI: -0.22 to -0.06). Consistent with Joyce et al.[82] and Shankar et. al.'s[88] findings, Gow et al.[114] reported a lack

of a significant association in a cross-sectional study of a largely non-socially isolated study sample. The study consisted of 1,091 individuals born in 1936 (aged 70 years old at the time of study publication) and reported a mean structural social support score of 6.6 ± 0.88 (range: 0 – 7),[114] with structural social support measured by marital status, living arrangements, and contact with family/friends. Higher scores indicated increased structural social support, which may be regarded as low social isolation. The study did not find a significant association between structural social support and cognitive function ($\eta_p^2 = 0.001$, $p = 0.430$), where $\eta_p^2$ represented the proportion of variance in the outcome accounted for by structural social support. Conversely, Pan and Chee[91] reported statistically significant associations in a longitudinal study of a predominantly socially isolated study population. The study contained 2,650 individuals aged 45 years or older, followed over 4 years in CHARLS. Social isolation was measured by the frequency and number of social activities. Approximately 60% of the sample reported infrequent social participation and the mean number of social activities was 1.40 (range: 1 - 7), with lower scores indicating increased social isolation. The findings showed a significant association between the frequency of social participation and memory ($\hat{\beta} = 0.26$, $p < 0.05$), as well as a significant association between the number of social activities and memory ($\hat{\beta} = 0.18$, $p < 0.05$).[91]

The second explanation for differences between the results of this thesis and other studies concerns the exclusion of persons with cognitive impairment from the CLSA at baseline. This likely biased enrolment toward persons who were more cognitively intact compared to the average individual in the population. As a result, most participants' memory scores were concentrated in a narrow range, regardless of whether they were socially isolated or not, thereby leading to an inability to adequately examine the impact of social isolation on memory.

An additional reason for the discrepancy between the thesis findings and the results of other studies relates to sample age. On average, the analytical sample in this thesis was younger than most of the other samples studied in the literature. The descriptive analyses indicated that over 73% of the analytical sample was under the age of 65 years. In contrast, 31 out of 54 studies included in the literature review had analytical samples comprising individuals aged 65 years or older. In general, younger individuals show less age-related cognitive impairment.[9] When combined with the exclusion of cognitively impaired individuals during recruitment, exposure to social isolation in this predominantly younger, cognitively healthy sample was not accompanied by variations in memory score that were large enough to detect strong associations between social isolation and memory. As such, the results of this thesis reflect middle- and older-aged adults, rather than only older adults.

The cross-sectional study design employed in this thesis may have also influenced the results. In longitudinal research, where the sample moves through time, more participants can be expected to experience memory decline and perhaps become socially isolated over time. This may enhance the ability to find associations between social isolation and memory that may not be detectable in samples that are cognitively healthy and socially non-isolated at a single given point in time. The optimal nature of longitudinal research in the area is exemplified by the fact that 18 of the 19 studies examining the association between social isolation and memory in the literature review utilized longitudinal study designs. The 18 studies that longitudinally assessed the association between social isolation and memory reported statistically significant, inverse associations. The one cross-sectional study examining the association between social isolation and memory found statistically significant inverse associations, as well. Although one cannot definitively conclude whether longitudinal studies were more likely to report inverse, statistically

significant associations compared to cross-sectional studies, it is important to note that longitudinal studies with relevant follow-up periods may be the most appropriate study design in terms of fitting with biological plausibility. Assessment of social isolation in a cognitively healthy sample at baseline, followed by the assessment of cognitive function over a long follow-up period, may allow researchers to study the effect of social isolation on the natural progression of cognitive decline over time. In cross-sectional studies, or longitudinal studies with short follow-up periods, it may be more challenging to determine whether associations are consistent with proposed underlying biological mechanisms because these mechanisms involve the notion of changes over time.

Another reason for divergent results between the thesis and existing literature relates to the fact that a robust set of 11 covariates were adjusted for in this thesis. Many published studies controlled for fewer covariates, with 29 out of 54 studies in the literature review adjusting for less than 10 covariates. Unadjusted confounding in these earlier studies may have created strong and inverse associations when, in truth, the relation between social isolation and memory is weak or non-existent. Province or region of residence and functional social support were some of the key covariates that the majority of studies did not adjust for, but were controlled for in this thesis. Through the minimization of residual confounding in the thesis, the regression coefficients reported in Tables 5 to 8 may be closer representations of the true relation.

Lastly, the utilization of a more multifaceted measure of social isolation in this thesis compared to other measurement tools used in the literature may be another reason for conflicting results. Unlike other research[61,62,82,90–95,101–103,105–109,114,117,126,127,129–131] which measured social isolation using single indicators, the SII used in this thesis is a composite measure which captures the totality of social isolation. The use of a more multifaceted measure of social

isolation in this thesis may have led to a more accurate measure of the number of individuals who were socially isolated in the sample. For example, individuals who lived alone were not classified as socially isolated unless they were unmarried/not in a common-law relationship and also reported small social networks and low levels of participation in social activities. The richness of the measure of social isolation used in this thesis prevented participants from being labelled as socially isolated if they only met one of the criteria for isolation. As such, the results of this thesis may be a more accurate representation of the true association between social isolation and memory.

### 5.3 Discussion of Results Stratified by Age Group and Sex

The results of this thesis did not show evidence for effect modification by age group or sex. This may be explained by the largely non-socially isolated and cognitively normal analytical sample, which characterized CLSA participants regardless of age group or sex.

The published literature shows mixed results regarding effect modification by age group. In a longitudinal study of 16,638 community dwelling individuals, Ertel et al. did not find an association between structural social support and memory decline among individuals below the age of 65 years ($\hat{\beta}$ = 0.00; 95% CI: -0.01 to 0.01); however, higher structural social support was positively associated with memory function among those aged 65 years or older ($\hat{\beta}$ = 0.04; 95% CI: 0.03 to 0.05).[5] Meanwhile, a cross-sectional analysis of 5,059 individuals aged 40 years or over in rural South Africa found a significantly stronger association between overall social contact and cognition among those aged 60 years or older compared to middle-aged adults: a one-SD increase in social contact (measured by number of communication events per month) was associated with 0.50 (95% CI: 0.36 to 0.68) times the risk of cognitive impairment in 40 to 59 year old adults, versus 0.79 (95% CI: 0.67 to 0.93) in adults aged 60 years or older.[109]

In contrast, the evidence for effect modification by sex is inconclusive, which aligns with the results of this thesis. Numerous studies did not provide strong evidence for effect modification by sex. Ertel et al. found the regression coefficients for the association between structural social support and cognition to be equal between men and women ($\hat{\beta}$ = 0.03; 95% CI: 0.02 to 0.04), indicating a lack of evidence for effect modification by sex.[5] In a longitudinal analysis of 964 Spanish individuals aged 65 years or older, Zunzunegi et al. found that higher scores on a social integration index (measured by membership in a community association, at least monthly attendance at religious services, and visits to community centers for older adults) were associated with a decreased probability of cognitive decline (measured using a scale of items extracted from the Short Portable Mental Status Questionnaire, the Barcelona Test, and the EPESE short story recall) among both men (OR = 0.68; 95% CI: 0.45 to 1.04) and women (OR = 0.73; 95% CI: 0.47 to 1.13), although the wide and non-significant confidence intervals did not provide evidence for effect modification.[62]

Further, Li and Dong cross-sectionally analyzed a sample of 3,157 Chinese-Americans aged 60 years or older and found that social network size (number of people in one's network) was positively associated with episodic memory (measured by the East Boston Memory Test),[67] in both men ($\hat{\beta}$ = 0.06; 95% CI: 0.03 to 0.10) and women ($\hat{\beta}$ = 0.05; 95% CI: 0.02 to 0.08).[156] The study also found that frequency of contact (measured by the average frequency that a participant talked with network members within the past year) was positively associated with episodic memory among both men ($\hat{\beta}$ = 0.05; 95% CI: -0.01 to 0.12) and women ($\hat{\beta}$ = 0.03; 95% CI: -0.02 to 0.09).[156] In a longitudinal study of 3,729 Korean individuals aged 55 years or older,[103] Lee et al. found that monthly engagement in social activities among participants with low cognitive function scores at baseline (measured by the Korean MMSE) was protective

against cognitive decline for both women (OR= 0.61; 95% CI: 0.46 to 0.82) and men (OR = 0.69; 95% CI: 0.44 to 1.06). Due to the closeness of the effect sizes between men and women, and the width of the confidence intervals, in Li and Dong and Lee et al.'s studies, insufficient evidence existed to indicate the presence of effect modification by sex.

A few studies report large differences in point estimates between men and women, although the 95% confidence intervals may be too wide to detect effect modification by sex. Read et al.'s[87] longitudinal analysis of 11,233 individuals aged 60 years or over from the ELSA found the directions of association between social isolation (defined as a combination of not being married/not cohabiting with a partner, less than monthly contact with family and friends, and lack of participation in organizations, sports clubs, or committees) and memory (measured with a word list recall) were negative for both males and females, with the strength of association being stronger for males ($\hat{\beta}$ = -0.33; 95% CI: -0.48 to -0.04), than females ($\hat{\beta}$ = -0.08; 95% CI: -0.39 to 0.23). On the other hand, Joyce et al. found a positive association between social isolation and memory only for women ($\hat{\beta}$ = -0.78; 95% CI: -1.33 to -0.22), whereas the association was close to the null for men ($\hat{\beta}$ = 0.02; 95% CI: -0.44 to 0.48).[82]

Although Read et al.[87] report point estimates of the regression coefficients that are far apart, their findings do not provide strong evidence for effect modification because the 95% CI for females is wide enough that the beta coefficient for females could equal or exceed the beta coefficient for males. The results by Joyce et al.[82] also do not provide strong support for effect modification, despite the large difference in point estimates, because the 95% CI are wide enough to include the possibility that the effects across males and females are equivalent, or the inverse effect among males is stronger than the inverse effect among females.

## 5.4 Strengths

The first strength of this study is the inclusion of 45- to 85- year-old adults recruited from seven Canadian provinces. This allowed for the exploration of the association of interest across different age groups and a wide geographical area. The existing literature is generally focused on older adults recruited from narrow geographical areas such as specific cities or regions.

The second strength is the large sample size, which reduced the possibility of underpowered analyses, allowed for adjustment by a range of important covariates, and facilitated subgroup analyses by age group and sex. Third, the comprehensiveness of data captured in the CLSA enabled the thesis candidate to control for a robust set of covariates, thereby helping to minimize residual confounding. This included controlling for functional social support, which had not been explored as a covariate in any published study of social isolation and memory to date.

The fourth strength of the thesis is the use of Menec et al.'s[135] SII to measure the exposure variable. The SII is based on the perspective that multiple aspects of social engagement must be absent to produce social isolation.[157] The absence of any one aspect would be insufficient to lead to social isolation. Since other research[61,62,82,90–95,101–103,105–109,114,117,126,127,129–131] utilized measures of social isolation based on limited aspects of social isolation (e.g., only frequency of participation in social activities), the SII used in this thesis was a more robust and valid measure of the construct. Therefore, the thesis results may provide a more valid assessment of the true association between social isolation and memory than many of the published studies.

## 5.5 Limitations

Some limitations to this thesis should be noted. First, participants in the analytical sample tended to be healthier, more educated, and reported higher household incomes compared to the

average individual in the population. As such, the findings of this thesis may not be generalizable to all persons aged 45 years or over. Second, as described in Section 5.2 above, recruitment and volunteer biases may have led to underestimates of the association between social isolation and memory.

Third, a high degree of missing data existed for memory and other key variables of interest. Missing data analyses indicated that participants with missing SII scores had significantly lower RAVLT I and II z-scores than participants with complete SII scores. Further, participants with missing RAVLT I and II z-scores had an increased odds of being socially isolated, though the associations were not statistically significant. The complete case approach taken in this thesis may have led to the exclusion of persons with lower RAVLT I/II z-scores (poorer memory) and persons at higher risk of social isolation, thereby magnifying the direction of bias resulting from the recruitment and volunteer biases. In essence, missing data led the analytical sample to further overrepresent a cognitively healthy, non-socially isolated subset of the target population, which could have attenuated any inverse associations between social isolation and memory, should they have existed in the target population.

Fourth, the thesis candidate elected not to do a longitudinal analysis based on previous research showing minimal changes in memory scores over a three year follow-up period.[43] Since the analyses were based on cross-sectional data, this thesis could not establish temporality and reverse causality bias is possible. For example, individuals with reduced memory function may lower their degree of social engagement because they find it difficult or embarrassing to maintain social connectivity in the face of cognitive impairment.[101,109,169]

Fifth, the regression diagnostics for the adjusted models indicated a lack of model fit based on the patterns of the residuals. As such, these models may not capture the true association

between social isolation and memory, leading to inaccurate estimates of model parameters. Data transformation was considered as a possible method of handling poor model fit. However, data transformations may alter the underlying associations in the data and muddle the interpretation of the regression coefficients. Additionally, data transformations would not solve the challenges posed by selection bias or missing data. Ultimately, the thesis candidate opted to recognize the poor model fit as a limitation of the data and acknowledge its impact on the results.

As described in Section 3.2.1, the CLSA investigators modified the RAVLT from its original form and reduced the number of recall administrations from five to two and eliminated an interference test.[143] Therefore, the recall from the first trial of the delayed recall test (the only recall trial used in CLSA) may actually reflect working memory and there is no encoding of information occurring, which is required for consolidation. The CLSA's modifications to the RAVLT reduce the comparability of the results of this thesis to studies which utilize the original version of the RAVLT (personal communication, Megan O'Connell, December 15, 2022).

## 5.6 Implications for Policy and Practice

One important use of research results is to inform policy and practice. Several social-focused interventions have been proposed to manage or prevent cognitive decline, including befriending interventions (e.g., pet or dance therapy sessions delivered in group formats at community centres) or communication technology interventions (e.g., virtual book or poetry readings).[158] However, most of these interventions are multi-pronged in nature and it is difficult to identify a specific component directed primarily toward reducing social isolation without also affecting functional social support (personal communication, Verena Menec, September 6, 2022).

Conceptually, an intervention focused on growing a person's social network would target social isolation. An example of such a program would be a community health centre that enables older adults with cognitive impairment to have dance or pet therapy in group sessions (personal communication, Verena Menec, September 6, 2022). Based on the inconclusive findings of this thesis, one cannot assess whether socially-focused interventions would preserve memory or reduce rates of memory decline, nor can one judge whether such interventions would convey additional protective effects for specific age or sex groups. However, the findings in relation to key factors (e.g., sociodemographic, health-related, or lifestyle variables) associated with social isolation and memory may aid policy makers in the identification of individuals most vulnerable to social isolation or poor memory. Males, individuals aged 65 years or older, and those reporting the lowest annual household income tended to be more socially isolated and had lower RAVLT I and II z-scores, indicating that resources should be targeted toward these individuals. Additional research using longitudinal CLSA data would be required to inform policy and practice in the area of social isolation and memory.

# 6 Conclusion

This thesis found inverse associations between social isolation and RAVLT I and II. However, these associations were weak and statistically nonsignificant, and the results did not rule out the possibility of null or positive associations. A lack of evidence existed for effect modification by age group or sex.

The findings of the thesis did not agree with much of the existing literature, which found social isolation to be a risk factor for memory or cognitive impairment. Whether the thesis results were 'biased' or closer to the true association in the population than previous research is a matter of debate. The strengths and weaknesses of the thesis seemed to exert opposing forces on the extent to which the results could be judged as 'valid'. For instance, the population-level sample, multi-pronged SII, and robust covariate set could lead one to believe the small effect sizes were more accurate estimates of the true association than what was observed in previous studies. Conversely, the presence of selection bias (recruitment and volunteer bias) and missing data could have attenuated true associations. Finally, despite the large sample size available for analysis, the study may have still been underpowered to detect the very small point estimated regression coefficients obtained in the regression models. Longitudinal data may improve the ability to evaluate the association between social isolation and memory in the CLSA. Over time, additional participants will become socially isolated and some will experience decreased memory function. These changes will hopefully lead to a more heterogenous analytical sample that will provide a better indication of whether persons who are socially isolated have lower memory scores, on average. These data may also generate a stronger evidence base from which to explore whether social engagement programs are a worthwhile use of resources, since public

funding of these programs would be predicated on the fact that reducing social isolation benefits memory.

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## Appendix A. Summary of Memory Systems

**Table A1: Summary of Memory Systems**

| | Description | Example |
|---|---|---|
| Episodic memory | The ability to consciously recollect past events and experiences.[159] | Remembering what one ate for dinner the night before.[159] |
| Semantic memory | Storage of concepts and facts, commonly referred to as long-term memory.[8,159] | Being aware that a dog has four legs.[8] |
| Implicit memory | Recollection of past events or the ability to perform a task without conscious retrieval of information.[8] | Knowing how to ride a bicycle.[8] |
| Working memory | The processes involved in temporary storage and manipulation of information.[8] | Being able to subtract one dollar from a bill total.[8] |

## Appendix B. Literature Search Strategy

A systematic search of the literature was developed with the help of a public health librarian and undertaken by the thesis candidate. The literature search for English-language studies was performed using PubMed and PsycINFO in February 2021, with the date range for the search running from database inception to the month of the search. An updated literature search using the original search strategies was performed in October 2022. Articles were included if the exposure variable was social isolation/structural social support and the outcome variable was memory or global cognitive function. Filters were applied across the PubMed and PsycINFO databases to include peer-reviewed journal articles only and exclude animal studies and age groups 0-39 years. Articles were also excluded if the study population contained caregivers or individuals with dementia. Articles were screened at title, abstract, and full-text levels. The relevant data were extracted into tables, which included year of publication, author, title, study design, description of participants, measures of exposure and outcome, key findings, and covariates (see Appendix C).

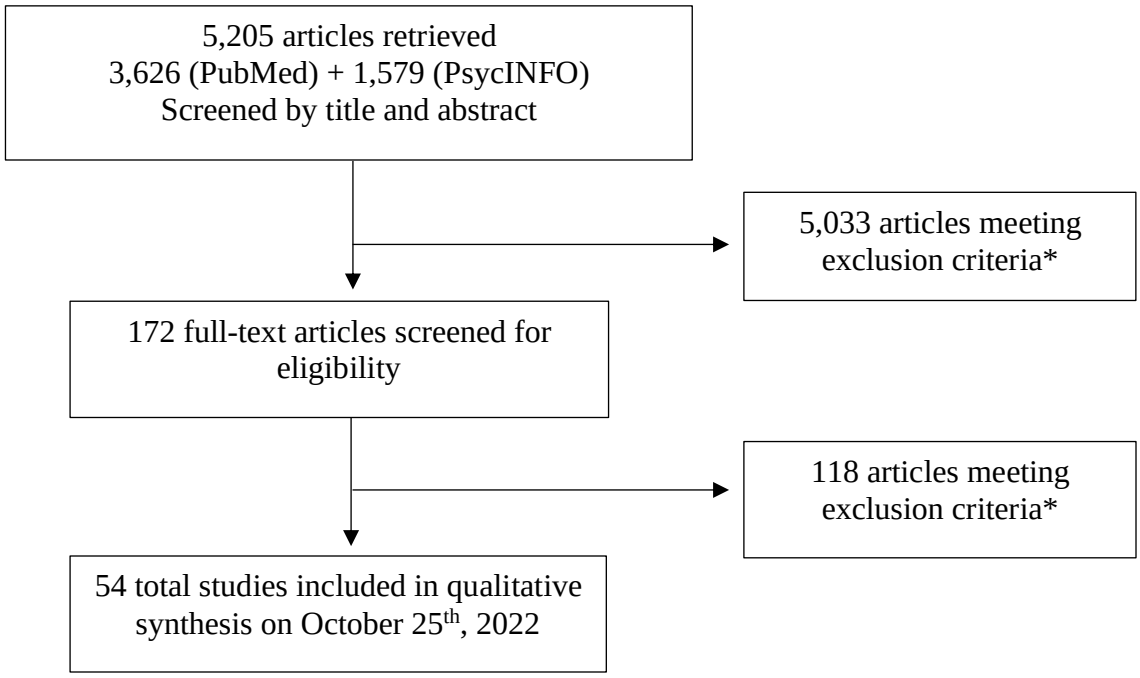
Fifty-four relevant studies were retrieved from the literature search. Of these 54 studies, 19 studies pertained directly to social isolation/structural social support and memory, and 35 studies pertained to social isolation/structural social support and cognitive function. The relevant articles included 37 longitudinal studies, 15 cross-sectional studies, and 2 systematic reviews. Most studies were comprised of participants aged 60 years or over, with some studies including individuals aged 50 years or over. Articles pertaining to functional social support, as well as articles that blended structural and functional social support into a single measure, were not addressed in this thesis because they were not directly pertinent to the main exposure of social isolation.

**Table B1: Search Syntax used in the Literature Review**

| PubMed | PsycINFO |
|---|---|
| (social isolation[mesh] OR social environment[mesh] OR social integration[mesh] OR social network[tiab] OR social relationship*[tiab] OR social cohesion[tiab] OR community network*[tiab] OR social activity*[tiab] OR social engagement[tiab] OR social ties[tiab] OR social participation[tiab] OR structural social support[tiab] OR structural support[tiab]) AND (memory[mesh] OR dementia[mesh] OR cognition[tiab] OR cognitive decline[tiab] OR cognitive function[tiab] OR memory[tiab] OR dementia*[tiab] OR cognitive impairment[tiab]) | (Abstract: social isolation* OR Abstract: social integration* OR Abstract: social network* OR OR Abstract: social activity* OR Abstract: social engagement* OR Abstract: social relationship* OR Abstract: social environment* OR Abstract: social ties OR Abstract: social participation OR Abstract: structural social support OR Abstract: structural support) AND (Abstract: cognition OR Abstract: memory OR Abstract: dementia OR Abstract: cognitive function OR Abstract: cognitive decline OR Abstract: cognitive impairment) |

| Filters applied: | Excluded: |
|---|---|
| 1. Journal articles<br>2. Humans<br>3. English<br>4. Age group: 45 years or older | 1. Age group: 0 to 39 years<br>2. Population: animals<br>3. Filtered: peer-reviewed journals only |

**Figure B1. PRISMA Flowchart**




*Exclusion criteria:

1. Study populations include non-humans, caregivers, or populations with dementia
2. Article is not available in English
3. Memory or cognitive function is not included as the outcome variable
4. Exposure variable includes loneliness or functional social support aspects

**Appendix C. Summary of the Literature on the Association between Social Isolation and Cognitive Function**
**Table C1: Summary of Literature**

| First Author | Study Design | Study Population | Measures of exposure (social isolation) | Measures of outcome (memory function) | Key findings | Covariates |
|---|---|---|---|---|---|---|
| Bae, S. (2020) | Longitudinal | 5678 adults aged 60 years or older, living in 17 regions across Korea | Social activities: frequency of participation in religious activities, social gatherings, leisure, cultural, or sports, reunions, volunteering, and political/civic organizations | Cognitive function: Korean version of the MMSE | "With regard to different types of social club, attending social gatherings was the strongest predictor of cognitive function, with greater attendance associated with better cognitive function ($\hat{\beta}$ = 0.254, $p < 0.001$). Likewise, attending or participating in leisure, cultural, and sports activities ($\hat{\beta}$ = 0.191, $p < 0.001$) and religious activities ($\hat{\beta}$ = 0.226, $p < 0.001$) were associated with better cognitive function." (Bae, S., 2020, p. 658). | |
| Bae, S. (2021) | Longitudinal | 5549 people aged 60 years or older (mean age = 70.27; SD = 7.26) in Korea | Social activities: frequency of participation in social gatherings, leisure, cultural, or sports, family or school reunions, and volunteering | Cognitive function: Korean version of the MMSE | Social activity was positively associated with cognitive function ($\hat{\beta}$ = 1.040, t = 17.710, $p < 0.001$). | Age, education |

| | | | | | | |
|---|---|---|---|---|---|---|
| Barnes et al. (2004) | Longitudinal | 6,102 non-Hispanic African Americans and whites, aged 65 years or older | Social networks: number of children/ relatives/ friends seen at least once a month.<br><br>Social engagement: four items related to social and productive activity. | Cognitive function: East Boston Story (2 tests; episodic memory), perceptual speed (symbol digit modalities test); global cognition: MMSE | "Higher number of social networks and level of social engagement were positively correlated with initial level of cognitive function (networks estimate = 0.003, engagement estimate = 0.060, both $p < 0.001$). Both resources were also associated with a reduced rate of cognitive decline." (Barnes et al., 2004, p. 2322). | Socioeconomic status, cognitive activity, physical activity, depressive symptoms, and chronic medical conditions |
| Béland et al. (2005) | Cross-sectional | 1,571 community-dwelling people aged 65 or older living in Leganés, Spain | Structural social support: social networks, social engagement | Cognitive function: the Leganés Cognitive Test | "Rate of change in cognitive function was associated with social integration only. At high levels of social integration, cognitive function remained stable over time, while with low levels of social integration, cognitive function declined at an accelerating rate as participants aged." (Béland et al., 2005, p. 325). | Gender, education, depressive symptoms, chronic conditions, functional limitations |
| Belessiotis-Richards et al. (2021) | Cross-sectional | Individuals from 3 cross-sectional datasets:<br>a) The 10/66 Dementia Research Group (aged 65 years or | Social isolation: less than monthly contact with relatives/friends/ neighbors, attendance at | Cognitive function: a cognitive index consisting of 3 tasks: verbal fluency in 1 minute, 10-word | "Socially isolated participants had a lower mean z-score than those who were not isolated in LASI and SAGE (−0.36 to −0.15 compared to −0.16 to 0.21) but not in 10/66 (Table 4). After full adjustment, socially isolated | Socioeconomic factors, age, and sex |

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|---|---|---|---|---|---|---|
| | | older, n=2004, across urban and rural India)<br>b) The Longitudinal Aging Study in India (aged 65 years or older, n=386, across urban and rural India)<br>c) The Study of Global AGEing (aged 65 years or older, n=2441, across 6 states in India) | clubs/societies, attendance of social activities outside the home | learning, and 10-word delayed recall test<br><br>Secondary: dementia diagnosis | participants performed worse on cognitive testing across all three datasets." (Belessiotis-Richards et al., 2021, p. 9). | |
| Bourassa et al. (2017) | Longitudinal | 19,832 individuals from Europe and Israel (mean age = 64; SD = 10.01) | Social engagement: participation in recreational and social activities that involve interaction with other individuals | Cognitive function: a composite of 3 cognitive tasks of verbal fluency, immediate and delayed word recall<br><br>Memory: immediate and delayed word recall from the 10-word | "Lower social participation predicted a steeper decline in memory; a one SD unit decrease in participants' within-occasion social participation (accounting for mood symptoms, physical activity, and physical health) resulted in a change of 0.21 of a SD in the slope of memory." (Bourassa et al., 2017, p. 143). | Depressive symptoms, physical activity, physical health |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | delayed recall test | | |
| Choi et al. (2016) | Longitudinal | 6076 individuals aged 45 years or older from the Korean Longitudinal Study of Aging | Social participation: consistent participation, consistent non-participation, participation to non-participation, and non-participation to participation | Cognitive function: Korean version of the MMSE | "Promotion of participation in religious organizations, friendship organizations, and family/school reunions (only for older persons) may help preserve cognitive function in individuals aged 45 years or older in Korea." (Choi et al., 2016, pp. 912-9) | Age, sex, marital status, education, employment status, number of chronic diseases, physical activity, region |
| Christelis et al. (2020) | Longitudinal | Individuals from The Survey of Health, Ageing, and Retirement in Europe (SHARE) dataset (aged 50 years or older, across 20 European countries) | Social participation: participation in voluntary/ charity work, an educational/ training course, a sport/social/ other club, and a political/ community-related organization | Cognitive function: recall capacity (measured via the RAVLT), fluency (measured via the Woodcock Johnson III (WJ III) Test of Cognitive Abilities), and numeracy (based on the WJ III Test of Achievement) | "Being socially active has a strong positive effect on cognition, with point estimates amounting to 0.67–0.84 SDs for all four cognitive scores when engaging in two or more activities compared to none." (Christelis et al., 2020, p. 7). | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Dickinson et al. (2011) | Longitudinal | 101 non-depressed older adults from the Center for Aging Subject Registry in the US; 112 depressed adults, from the NCODE study (aged 60 years or older) | Duke social support index: instrumental social support, social interactions, subjective social support, and non-family social network; Depression; stressful life events | Cognition: immediate and delayed verbal memory, attention/ executive functions | "There was a consistent pattern of decreased social interaction and instrumental social support predicting decline in cognitive performance while controlling for covariates; Subjective social support and social network size did not appear to be associated with changes in cognition." (Dickinson et al., 2011, pp. 1267-1274). | Age, sex, education, physical health, depression |
| DiNapoli et al. (2014) | Cross-sectional | 267 Appalachian older adults (mean = 78.5; range = 70–94 years). | LSNS-6: divided into dimensions of social disconnectedness and perceived isolation.<br><br>Social disconnected-ness: size of the participant's active social network.<br><br>Perceived isolation: perceived support network | Overall cognitive function, memory, executive functioning, attention, and language abilities | "Results indicated a significant positive association between all predictor variables (e.g., social isolation, social disconnectedness, and perceived isolation) and outcome variables; Perceived isolation accounted for nearly double the amount of variance in overall cognitive functioning than social disconnectedness (10.2% vs. 5.7%)." (DiNapoli et al., 2014, pp. 161-179). | Age, sex, education, marital status, income, race, vascular risk factors, depressive symptoms |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | and perceived confidence in network | | | |
| Ertel et al. (2008) | Longitudinal | 16,638 community-dwelling individuals, aged 50 years or older | Social integration: marital status, volunteer activities, and contact with parents, children, and neighbors | Memory: immediate and delayed word recall | "Respondents with high social integration and low social integration had similar memory scores at baseline (1998) but diverged over successive assessments. Compared with respondents with low social integration, respondents with high social integration in 1998 had slower rates of memory decline over time. Social integration was protective against memory decline. For those younger than 65 years, however, social integration was associated with memory score at baseline but not with memory decline over time." (Ertel et al., 2008, pp. 1215-1220). | Age, gender, race, education, household income, household wealth, prevalent health conditions, mobility, large muscle index, ADL, fine motor skills, IADL, and depressive symptoms |
| Evans et al. (2018) | Longitudinal | Individuals aged 65 years or older, across two locations in Wales, (Gwynedd and Ynys Mon, and Neath Port Talbot). 3593 individuals from baseline and | Social Isolation: Lubben Social Network Scale-6, number of relatives/friends the participant sees or hears from at least once a month, could call on for | Cognitive function: Cambridge Cognitive Examination | "Social isolation was associated with cognitive function at baseline and two-year follow-up. Findings suggest that maintaining a socially active lifestyle in later life may enhance cognitive reserve and benefit cognitive function." (Evans et al., 2018, p. e0201008). | Age, gender, education, sensory problems (hearing and eyesight), ability to complete daily tasks alone |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | 2,236 individuals from follow-up | help, and can speak with about private matters | | | |
| Evans et al. (2019) | Systematic review and meta-analysis | Community-dwelling individuals aged 50 years or older | Social isolation: social network/contact and/or social engagement/ activity | Cognitive function, decline, or change using a standardized measure of global cognitive function, memory, or executive function | "Low levels of social isolation characterized by high engagement in social activity and large social networks were associated with better late-life cognitive function (r = 0.054, 95% CI: 0.043 to 0.065)." (Evans et al., 2018, pp. S119-S144). | |
| Fan et al. (2021) | Longitudinal | 3314 Chinese adults aged 65–110 years from the Chinese Longitudinal Healthy Longevity Survey (CLHLS) | Social relationships: divided into 3 categories – social activities, social networks, and social support | Cognitive decline: the Chinese version of the MMSE | There was an inverse association between social activities ($\hat{\beta}$ = −0.29, p = 0.02) and cognitive decline. There was also an inverse association between social networks ($\hat{\beta}$ = −0.48, p < 0.001) and cognitive decline. | Age, sex, education, residence, exercise, drinking, smoking, activities of daily living, chronic diseases, depression, and baseline cognitive function |
| Fankhauser et al. (2017) | Cross-sectional | 118 individuals (aged 60 years or older) | Size of the social network, frequency of | Cognitive function: MMSE | "Network size was significantly associated with the cognitive status (mini mental status | Depression, ADL, education, frequency of |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | contact, satisfaction with the social network and social support | | examination; $\hat{\beta}$ = 0.15, p < 0.05) and with odds of cognitive impairment (odds ratio [OR]: 0.96, 95% confidence interval [CI]: 0.93–0.99).” (Fankhauser et al., 2017, p. 125). | participation in physical/ cognitive/ creative social activities |
| Glei et al. (2005) | Longitudinal | 2,387 individuals (aged 60 years or older) | Social network: marital status, social ties, frequency of social contact, participation in social activities | Cognitive function: Short Portable Mental Status Questionnaire | “Participation in social activities is significantly associated with reduced risk of cognitive impairment, yet, no evidence of a relationship between the participants’ social networks and cognition. These findings suggest that the extent of participation in social activities may be a more important predictor of cognitive performance than various aspects of respondents’ social networks.” (Glei et al., 2005, pp. 864-871). | Age, sex, education, occupational status, satisfaction with current economic situation, functional status, depressive symptoms |
| Goldberg et al. (2021) | Longitudinal | 855 individuals from a stratified random sample of 50% of all Medicare beneficiaries, aged 65 years or older, in Manhattan, New York City | Social isolation: 24 items, including not going to club/center, lack of contact with friends, if ill might go unnoticed for 24h, health interferes with participation | Cognitive function: the Neuropsychologi-cal Test Battery; cognitive decline was measured using the Selective Reminding Verbal List Learning Test | “Both restriction and isolation (HR = 1.78, 95% CI [1.17, 2.70], p = 0.007) were associated with episodic memory and incident dementia, individuals with high scores on Isolation performed 2.66 times worse on memory (Figure 1 and Supplement Table 3, β = −2.66, 95% CI [−3.72, −1.59], P < .001) and the effect did not change over time | Age, sex, education |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | social/leisure activities | | (Isolation × Time, p = 0.11)." (Goldberg et al., 2021, p. 1207). | |
| Golden et al. (2009) | Cross-sectional | 334 community-dwelling individuals aged 65 years or older; recruited from the registers of five Dublin urban general practices | Social activities: 4 questions regarding visiting and/or being visited by friends and/or relatives | Cognitive function: MMSE | Social engagement was associated with cognitive impairment (OR = 0.68, p < 0.001). | Age, gender |
| Gow et al. (2013) | Cross-sectional | 1,091 individuals, aged 70 years, all born in 1936 | Social support: marital status, living arrangement, social contact (volume), level of support received, satisfaction with social support | Cognition: WAIS-III UK, Wechsler Memory Scale-III UK, tests of reaction time and inspection time | "Participants who were unmarried or who lived alone performed more poorly on all the cognitive measures though the differences were significant only for marital status and general cognitive ability and processing speed. Receiving more social support was associated with better cognitive performance (there was no association with memory)." (Gow et al., 2013, pp. 464-463). | Social class (occupation), depressive symptoms |
| Gow et al. (2016) | Longitudinal | 802 individuals from Glostrup 1914 Cohort (Copenhagen) | Social resources: marital status, living arrangements, frequency of telephone contact, loneliness, instrumental | Cognitive ability: Wechsler Adult Intelligence Scale | "Cognitive benefits were reported in terms of being married, not living alone, and reduced feelings of loneliness. Lack of association between social contact/support and cognitive ability. Interventions need to be more than simply increasing contact but may need to target the psychological underpinning of | Sex, education, social class |

| | | | | | | |
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| | | | support, support to others | | what makes older people experience loneliness." (Gow et al., 2016, pp. 480-486). | |
| Griffin et al. (2020) | Longitudinal data analysis | 6654 individuals aged 65 years or older from the Health and Retirement Study (HRS) | Objective social isolation: contact with social network, partner status | Cognitive function: modified version of the Telephone Interview for Cognitive Status | "Loneliness ($\hat{\beta}$ = −.34, 95% confidence interval [CI] = [−0.56, −0.11), and cynical hostility ($\hat{\beta}$ = −.14, 95% CI = [−0.24, −0.04) correlated with lower cognitive function, but none predicted change in cognitive function. Objective social isolation was associated with lower cognitive function ($\hat{\beta}$ = −.27, 95% CI = [−0.41, −0.12]) and steeper decline in cognitive function ($\hat{\beta}$ = −.09, 95% CI = [−0.16, −0.01])." (Griffin et al., 2020, pp. 52-60). | Age, education, sex, SES, race, health status, and functional limitations |
| Gurung et al. (2003) | Longitudinal | 439 individuals aged 70 to 79 years at baseline participating in the MacArthur Successful Aging Study (MSAS) in the US | Emotional and instrumental support: questionnaire Psychosocial variables: self-efficacy, social ties, mastery, depression (Hopkins Symptom Checklist) | Cognitive function: Boston Naming Test, delayed Recognition Span Test, Wechsler Adult Intelligence Scale-Revised, somatization (Hopkins Symptom Checklist) | "The men's social support increased over time for all types of support from all sources. The women's social support increased over time for all types of support from their children and friends and relatives but not from their spouses. Women experienced greater increases in negative behaviors from their spouses over time than did men." (Gurung et al., 2003, pp. 487-496). | Age, sex, income, physical functioning, and somatization |

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| Harling et al. (2020) | Cross-sectional | Individuals aged 40 years or older in the Agincourt Health and Demographic Surveillance System in Mpumalanga province, South Africa | Frequency of social activity, social network size, social support | Cognitive function: orientation in time, episodic memory (immediate and delayed recall tests) and ability to count forward from one to 20 and complete a number pattern | "In age and gender-adjusted regressions, a one-SD increase in social contact communication per month (38 additional events) was associated with 0.58 (95% confidence interval (CI): 0.48, 0.69) times the risk of having cognitive impairment." (Harling et al., 2020, p. 6). | Age, gender, country of origin, education, self reported literacy, self rated childhood health, fathers occupation, marital status, employment status, household wealth |
| Holtzman et al. (2004) | Longitudinal | 354 community-dwelling adults aged 50 years or older in Baltimore, Maryland | Frequency of participation in social activities: church or other religious gatherings, friendship organizations, alumni associations, and volunteering | Cognitive function: MMSE | "The longitudinal models showed that interactions in larger social networks at Wave 1 related to better maintenance of MMSE at Wave 3 and reduced odds of decline from the population-based median cutoff score (at minimum) to a lower quartile score." (Holtzman et al., 2004, p. 282) | Cerebro-vascular disease or risk, age, education, depressive symptomatol-ogy at testing, race, gender, physical disability, and alcohol use disorder |
| Hülür et al. (2021) | Longitudinal | 19,297 individuals from the Health and Retirement Study (mean age at baseline = 66 | Structural social support: contact frequency with children, relatives, and friends | Episodic memory: immediate and delayed free-recall test | Increased social contact was positively associated with memory function ($\gamma = 0.79$; SE = 0.03; $p < 0.01$). The association was non-significant in models containing control variables. | Age, gender, education, functional health, and depressive symptoms |

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| | | years, SD = 10, range = 50–104) | | | | |
| James et al. (2011) | Cross-sectional | 1138 individuals aged 65 years or older recruited from approximately 40 retirement and subsidized housing facilities in the Chicago metropolitan area (mean age = 79.6; SD = 7.5) | Social isolation: marital status, monthly contact with children/other immediate family/friends, participation in organizations/ religious groups/ committees. | Global cognitive function and 5 cognitive domains: episodic, semantic, working memory, perceptual speed, visuospatial ability | Increased social activity was associated with 0.47 times lower risk of decline in global cognitive function ($p < 0.001$). The association was similar for the other cognitive domains. | Age, sex, education, race, social network size, depression, chronic conditions, disability, neuroticism, extraversion, cognitive activity, and physical activity |
| Kang et al. (2016) | Systematic review and meta-analysis | 42 peer- reviewed articles with participants (aged 2-6 or 65 years or older) | Social engagement: frequency of social activities. | Overall cognition, diagnosis of dementia, and specific domains of cognition (semantic and working memory, perceptual speed, and visuospatial memory) | "Findings collectively indicate that (a) greater social engagement is associated with higher levels of cognition in older adulthood, and the impact of social engagement on cognition may be more evident in at-risk populations; (b) the positive influence on cognition is largely consistent in both ends of the life span; (c) the relationship between social engagement and cognition is similar across different study designs." (Kang et al., 2016, pp. 1639-1659). | |

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| Kelly et al. (2017) | Systematic review | 3 RCTs, 34 observational studies, 2 genetic studies | Social activities, social networks, social support, and composite measures of social relationships (CMSR) | Cognitive function: episodic memory, semantic memory, overall memory ability, working memory, verbal fluency, reasoning, attention, processing speed, visuospatial abilities, overall executive functioning, and global cognition | "Social activity was associated with global cognition and overall executive functioning, working memory, visuospatial abilities and processing speed, but not episodic memory, verbal fluency, reasoning, or attention. social networks was associated with global cognition, but not episodic memory, attention or processing speed social support was associated with global cognition and episodic memory but not attention or processing speed. CMSR was associated with episodic memory and verbal fluency but not global cognition.<br><br>Functional SS is a better predictor of health outcomes than structural SS." (Kelly et al., 2017, p. 259). |
| Kuiper et al. (2016). | Systematic review and meta-analysis | | Structural social support: low social activity and small social network size | Cognition: incident cognitive impairment, cognitive decline, global cognitive decline, perceptual speed, semantic memory | "Poor functional social relationships were associated with cognitive decline [OR: 1.15 (95% CI: 1.00-1.32)]. However, results were heterogeneous (Q = 21; p = 0.00; $I^2$ = 66%). poor structural social relationships are associated with cognitive decline [OR: 1.08 (95% CI: 1.05-1.11), but results were also heterogenous. With regard to the type of social |

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| | | | | | relationship measurement, they found a stronger association between a small social network and cognitive decline." (Kuiper et al., 2016, pp. 1169-1206). | |
| Lara et al. (2019) | Longitudinal | A Spanish nationally representative sample of 1691 adults aged 50 years or older | Social isolation: marital status, monthly contact with children/ immediate family/friends, participation in organizations, religious groups, or committees | Cognition: immediate recall, delayed recall, verbal fluency, forward digit span, backward digit span, and a composite cognitive score | "Higher social isolation was associated with lower scores in the composite cognitive score, verbal fluency, and forward digit span ($\hat{\beta}$= −0.06 to $\hat{\beta}$ = −0.85; p < .05). However, no effect of social isolation on the remaining cognitive tests was found." (Lara et al., 2019, pp. 1613-1622). | Age, sex, education, physical activity, alcohol use, ADL, depression, stroke, diabetes |
| Lee et al. (2020) | Longitudinal | 501 adults aged 60 years or older in South Korea | Social activity: 7 social activities were investigated for social participation | Cognitive function: MMSE | Social activity was positively associated with cognitive function only in women. | Age, education, medical comorbidities, activity level, depressive symptoms |
| Li et al. (2018) | Cross-sectional | 3,157 American Chinese older adults, aged 60 years or older in Chicago | Social network: network size, volume of contact, proportion kin, proportion female, proportion co-resident, and | Cognitive function: Chinese-MMSE | "Unit increases in network size, volume of contact, proportion kin, proportion co-resident were associated with higher level of global cognition.<br>Similar trends were observed in episodic memory, working memory, executive function and C-MMSE. Social network has differential impact on female | |

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| | | | emotional closeness. | | versus male older adults." (Li & Dong, 2018, pp. 246-256). | |
| Menec et al. (2019) | Cross-sectional | 48,330 individuals aged 45-85 in the CLSA | Social isolation: dichotomized social isolation index using five questions (marital status, living arrangement, latest social contact, retirement status, social participation in 8 defined activities in the past year) | | "Factors that predict social isolation and loneliness differ for women and men. Being older, male, having low income, functional impairment, and more chronic conditions, and higher education were associated with increased odds of being socially isolated. Being younger, male, living alone, having low education, low income, functional impairment, and more chronic conditions increased the odds of being lonely. Living in a city was related to social isolation because cities are more likely to have socio-economically deprived neighborhoods." (Menec et al., 2019, p. e0211143). | Age , sex, education, household income, functional status, chronic conditions |
| Millán-Calenti et al. (2013) | Cross-sectional | 600 community-dwelling residents of Narón Council (A Coruña, Spain), aged 65 years or older | Social support: the extent of contact with others, the satisfaction with contacts, and the availability of help when needed | Cognitive status: the MMSE | "A lower extent of contact was related to COG (OR: 2.26). Fair satisfaction with contacts was related to DEP (OR: 2.88) and COG-DEP (OR: 4.22). A low level of satisfaction with contacts was an important predictor for DEP (OR: 7.99) and COG-DEP (OR: 7.88). Therefore, different dimensions of social support were independently correlated with | Age, gender, education, functional status, comorbidities |

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| | | | | | different aspects of mental health. Quantitative aspects of social support were significantly linked to the presence of cognitive impairment." (Millán-Calenti et al., 2013, pp. 199-214). | |
| Oremus et al. (2019) | Cross-sectional | 21,241 individuals aged between 45-85 years from the Tracking Cohort of the CLSA | Social support availability: the MOS-SSS | Cognitive function: RAVLT | "The proportion of participants with low global cognitive function was often greater among persons who reported low global SSA. The proportion of persons with high cognitive function was greater in participants with high SSA." (Oremus et al., 2019, pp. 1084-1089). | |
| Oremus et al. (2020) | Cross-sectional | 21,241 individuals aged between 45-85 years from the Tracking Cohort of the CLSA | Social support availability: the MOS-SSS | Memory: RAVLT | "Higher SSA (four subscales and overall) was associated with better memory.<br><br>Age group did not modify any of the associations between SSA and memory but was an independent and statistically significant predictor of memory. Both immediate and delayed recall were most associated with overall SSA and emotional/informational support." (Oremus et al., 2020, p. 103962). | Age, sex, education, province, marital status, home ownership, living arrangement, household income, rural/urban residence, smoking status, average alcohol consumption, ADL, IADL, |

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| | | | | | | chronic health conditions |
| Park et al. (2017) | Longitudinal | 11,036 community-dwelling older individuals aged 65 or older | Social engagement: engagement with social network and volunteering.<br><br>Social network: contact frequency with nieghbours/ people nearby<br><br>Volunteering: time spent in past year doing volunteer work for religious, educational, health-related or other charitable organizations | Cognitive function: Telephone Interview for Cognitive Status (TICS) | "Patterns of association between social engagement and cognitive function trajectory emerged differentially. Changes in social network engagement were significantly associated with three trajectory groups after controlling for the baseline of social engagement: those who became more engaged were more likely to be high-to-moderate cognitive function (RRR = 1.24). Those who became less engaged over time were less likely to be in the stable-high group (RRR = 0.78). Social engagement in old age may serve as a potential protective resource." (Park et al., 2017, p. 393). | |

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| Poey et al. (2017) | Cross-sectional | 779 individuals aged 70 years or older in the Aging, Demographics, and Memory Study (ADAMS) module of the Health and Retirement Study (HRS) in the US | Family network size, social engagement (volunteering, giving help, paid work), perceived social support availability, loneliness (CES-D8) | Dementia: diagnosis; genetic risk: APE e4 allele | "A richer social environment is associated with less risk of cognitive decline and presence of the APOE e4 allele was related to poorer cognitive health.<br><br>The e4 allele and being less socially engaged were independently associated with a greater risk of Alzheimer's disease.<br><br>Living arrangements, perceived social support, and loneliness were found to moderate the relationship between APOE e4 allele and cognitive function." (Poey et al., 2017, pp. 1031-1040). | Cognitive status, sex, depressive symptoms, |
| Rafnsson et al. (2020) | Longitudinal | 6,677 individuals from the English Longitudinal Study of Ageing | Social isolation: the extent of contact with children, family apart from spouse and children (e.g., cousins), friends, and marital status | Dementia: physician diagnosis of dementia or Alzheimer's disease;<br><br>Augmented dementia assessment: memory (immediate and delayed recall), | "In multivariable analyses, loneliness was positively and independently related to increased risk of developing dementia, whereas being married and having more close relationships were each independently associated with a reduced dementia risk. By contrast, social isolation defined as extent of contact with family and friends was not related to development of dementia. Our findings suggest that structural | Household income, education, marital status, physician diagnoses of coronary heart disease (CHD), cancer, stroke, diabetes, and hypertension, mobility |

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| | | | | and time orientation. | aspects of social activity such as the frequency of contacts outside the marital relationship are less important than perceptions of closeness." (Rafnsson et al., 2020, pp. 114-124). | |
| Read et al. (2020) | Longitudinal | 6,123 women and 5,110 men aged 50+ from the ELSA | Social isolation: living status, contact with children/other family members/friends, and membership in any organizations, religious groups or committees | Memory: word list recall test | "Social isolation increased and memory decreased over time. Among men an initially high level of social isolation was associated with a somewhat greater decrease in memory. Among women a greater increase in social isolation predicted a greater decrease in memory and a larger change in social isolation was associated with further larger changes in isolation, although when social isolation reached a higher level it subsequently decreased." (Read et al., 2020, pp. 367-376). | Age, education, wealth, home ownership, smoking, physical activity, long-term illness, depressive symptoms, working or doing voluntary work |
| Rodriguez et al. (2018) | Longitudinal | 1,015 individuals aged 75 years or older from the LEILA study in Leipzig, Germany | Social network: locally integrated network, the family-dependent network, the local self-contained network, the | Cognitive function: SIDAM | "A better cognitive status was associated with a smaller likelihood of having a restricted social network.<br><br>The risk of dementia over the follow- up period was significantly higher among individuals with restricted than with integrated social networks." | Age, sex, marital status, form of residency, education, smoking status, medical history |

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| | | | wider community-focused network, and private-restricted network | | (Rodriguez et al., 2018, pp. 163-170.) | |
| Schwartz et al. (2019) | Cross-sectional | Adults aged 50 years or older in Israel as part of the Survey of Ageing, Retirement and Health (SHARE) | Contact frequency: the average score of the contact with the social network members, and it was re-coded such that higher scores meant more frequent contact | Cognitive function: cognitive tests of immediate recall, delayed recall and fluency | "The results indicated a significant total direct effect (path C) of contact frequency on cognitive performance ($\hat{\beta}$ = 0.11, t (1348) = 3.71, p = 0.001, 95% CI = 0.05, 0.17; Adjusted $R^2$ = 0.32). The indirect effect was also significant, indicating that frequent contact with the social network was related to improved cognition also through reduced depressive symptoms. Contact frequency is important for cognitive health in the second half of life, and it operates both directly and by decreasing depressive symptoms." (Schwartz et al., 2019, pp. 1008-1016). | Age, education, gender, marital status, social activities and physical health |
| Seeman et al. (2001) | Longitudinal study | 1,189 adults aged 70-79 years in three regions in US | Quantitative SS: Marital status, number of close ties with children, number of close | Cognitive function (6 domains): language (Boston Naming Test), | "Better cognitive function was correlated with being unmarried and reporting greater conflicts/demands from social network (but unmarried participants were more women | Age, education, ethnicity, income, number of chronic conditions, pulmonary |

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| | | | friends and relatives, participation in religious or other groups.<br><br>Qualitative SS: Frequency of receiving emotional and instrumental support, frequency of negative interactions, frequency of providing support to others | abstraction (Wechsler Adult Intelligence Scale-revised), spatial ability, delayed spatial recognition, incidental recall of confrontation naming items, delayed recall of a story. | than men).<br><br>For men and women, social ties and support demonstrated generally similar patterns of association.<br><br>Big difference was in marital status – for men, being married was associated with larger network size and greater emotional/instrumental support. For women, being married was associated with fewer other close ties, less group memberships, and less emotional support.<br><br>No evidence for any mediational effects of covariates. Qualitative SS more important than quantitative SS." (Seeman et al., 2001, pp. 243-255). | function, depressive symptoms, self-efficacy beliefs, frequency of leisure and work related activity, frequency of strenuous activities conducted on a regular basis |
| Seeman et al. (2011) | Longitudinal | 7108 adults aged 25-74 years | Social engagement: frequency of social contacts, extent of social support and social conflict | Cognitive function: Brief Test of Adult Cognition by Telephone (BTACT) | "Significant positive association between social contacts and support and executive function and episodic memory, independent of all covariates. Higher social contacts and support were associated with better executive functioning. Higher social conflict was associated with poorer executive functioning. | Age, gender, education, race, health status, health behaviors |

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| | | | | | Social conflict was significantly and negatively associated with executive function but not episodic memory. Over time, decline in social contact was associated with poorer executive function and episodic memory. SS-cognition association was stronger among younger than older adults (may be due to attrition and survivor bias)." (Seeman et al., 2011, pp. 141-152). | |
| Shankar et al. (2013) | Longitudinal | Prospective cohort (ELSA) with a 4-year follow-up | Social isolation: marital status, frequency of social contact, social participation | Cognitive function (verbal fluency, immediate and delayed recall) | "Loneliness and isolation are associated with poorer cognitive function among older adults. Education moderated the association between isolation and delayed recall as well between loneliness and delayed recall." (Shankar et al., 2013, pp. 161-170). | Age, sex, education, wealth, marital status, working status, depression, CVD, diabetes, smoking, physical activity |
| Sharifian et al. (2019) | Cross-sectional | 548 older adults aged 60-93 years from the Washington Heights-Inwood Columbia Aging Project | Social networks: the number of living children, relatives other than children, and friends that participants felt close with. | Cognition: The neuropsychological battery including four cognitive domains: episodic memory, language, visuospatial and | "Analyses revealed that networks with a greater proportion of friends were associated with better global cognition than networks with a greater proportion of family. Additionally, larger social network size was only associated with better global cognition among individuals who had a | Age, sex, education, ethnicity/race, marital status, and physical illness burden. |

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| | | | | speed/executive functioning. | greater proportion of friends in their networks." (Sharifian et al., 2019, pp. 956-963). | |
| Sörman et al. (2015) | Longitudinal | 1,715 participants aged 65 years or older | Social relationships: living status, having close friend(s), frequency of in-person contact with friends and acquaintances, frequency of contact with friends and acquaintances through other ways (i.e. phone) | Dementia: diagnosis | "The variable visiting/visits from friends was associated with reduced risk of all-cause dementia. Further, a higher value on the relationships index (sum of all variables) was associated with reduced risk of all-cause dementia and AD. using a single-question assessment of stress and a checklist measure of selected depressive symptoms has obvious limitations." (Sörman et al., 2015, pp. 1391-1399). | Age, gender, years of education, and MMSE scores, alcohol use, smoking status, obesity, cardiovascular risk factors, perceived general stress, depressive symptoms |
| Tomioka et al. (2018) | Longitudinal cohort | Community-dwelling older adults aged 65 or older | Social participation: participation in neighborhood associations, hobby groups, local event groups, senior citizen clubs, and volunteer groups | Cognitive decline: Cognitive Performance Scale | "Greater social group participation prevents CD in women, while the beneficial effect of each type of SP on cognition differs between genders." (Tomioka et al., 2018, pp. 799-806). | Age, family, body mass index, pensions, comorbidities, medications, alcohol, smoking, depression, self-rated health, and instrumental activities of daily living |

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| Wang et al. (2017) | Cross-sectional | 981 community-dwelling individuals aged 6 years or older in Daqing City | Social isolation: Lubben Social Network Scale-6 | Cognitive function: MoCA (Montreal Cognitive Assessment) - Changsha version | "Participants with high LSNS-6 scores presented better cognition. Social isolation was significantly associated with domains of visuo-spatial constructional executive functions, naming, language, and delayed memory, but not with concentration, orientation or abstraction." (Wang et al., 2017, p. 472). | |
| Yu et al. (2020) | Longitudinal | 7761 participants (mean age=60.97, SD=7.31) | Social isolation: marital status, contact with children, participation in social activities over the last month | Cognitive function: episodic memory (immediate word recall), orientation, visuospatial ability, numeric ability | "Social isolation is associated with cognitive decline in Chinese older adults, and the relationships are independent of loneliness." (Yu et al., 2020, pp. 1-2421). | Age, gender, education, residence, smoking, drinking, ADLs, chronic diseases, depressive symptoms |
| Zahodne et al. (2019) | Longitudinal | 10,390 participants from the Health and Retirement Study (mean age = 69, SD = 9.53) | Structural aspects of social relations were assessed via marital status, social network size, and contact frequency.<br><br>Quality of social relations was assessed to | Memory: Episodic memory functioning was assessed every two years with a variant of the Consortium to Establish a Registry for Alzheimer's Disease | "Both structure and quality of social relations were associated with initial memory level, such that being married/partnered, reporting more frequent contact with children and friends, reporting less support from family members other than partners and children, and reporting less strain across relationship types were each independently associated with better initial memory. In | Age, gender, race, mental and physical health, chronic conditions, self-rated health |

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| | | | examine positive and negative dimensions via social support and social strain, respectively. | (CERAD) list learning task | contrast, only structure was associated with subsequent memory decline. Specifically, being married/partnered and reporting more frequent contact with friends were each independently associated with slower memory decline." (Zahodne et al., 2019, pp. 751-765). | |
| Zamora-Macorra et al. (2016) | Cross-sectional | 2211 participants from the SAGE study; city/metropolitan area, urban/rural, housing, and households with people aged 50 and older | Social support levels: social network index, social cohesion index, and trust index | Cognitive function: memory, verbal fluency, immediate and delayed memory; using the Memory Wechsler Scale and the CERAD neuro-psychology battery | "For respondents ages 71–80 y/o, there was an inverse relationship with cognitive impairment for those with medium (OR 0.23, p = 0.020) and high (OR 0.07, p = 0.000) SSL in comparison with low SSL. While social support helped to improve cognitive function in older adults aged 71–80, this same association was not observed in adults of other ages. Those younger than 70 y/o may not need such a strong support network as a result of being more self-sufficient. After 80, social networks were not enough to help diminish the negative impact of cognitive impairment. There was a window of opportunity for those aged 71–80 years old, as they appeared to benefit the most by the presence | Sex (men/women), age, marital status (with partner/without partner), place of residency (urban/rural), education (years of, classified as elementary, secondary (middle school), high school and college or university), and household members (number and socioeconomic status) |

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| | | | | | of social support." (Zamora-Macorra et al., 2016, pp. 113-118). | |
| Zhou et al. (2018) | Longitudinal | Participants from a large nationally representative survey (the CLHLS), including adults aged 65 years or older | Social engagement: marital status, living arrangement, availability of help, availability of a confidant, participation in social activities; | Dementia: diagnosis | "Participants with consistently high or increased SE had a lower risk of dementia than those with consistently low SE ((OR = 0.14, 95% CI = 0.06–0.28 and OR = 0.33, 95% CI = 0.23–0.48, respectively). Higher SE can reduce the risk of dementia. Furthermore, consistently high or increasing SE is associated with a lower risk of dementia." (Zhou et al., 2018, pp. 1551-1557). | Age, literacy, type of residence, engagement in physical labor, smoking, drinking, exercise, health status |
| Zunzunegui et al. (2003) | Longitudinal | 964 individuals (65+) in Leganes, Spain | Social networks (size and frequency), social integration (frequency and membership), and social engagement (frequency) | Cognitive function: orientation and memory (Short Portable Mental Status Questionnaire, the Barcelona Test, the EPESE short story recall) | "Social networks, social integration, and social engagement are associated with cognitive decline controlling for age, baseline cognitive function, education, cardiovascular morbidity, depression, and functional limitations. Formal participation in social activities has protective effects against cognitive decline. The influence of social relations on cognitive function is to some extent different for gender. Engagement with friends was protective in women but not in men." | Age, education, depressive symptoms, blood pressure, functional limitations |

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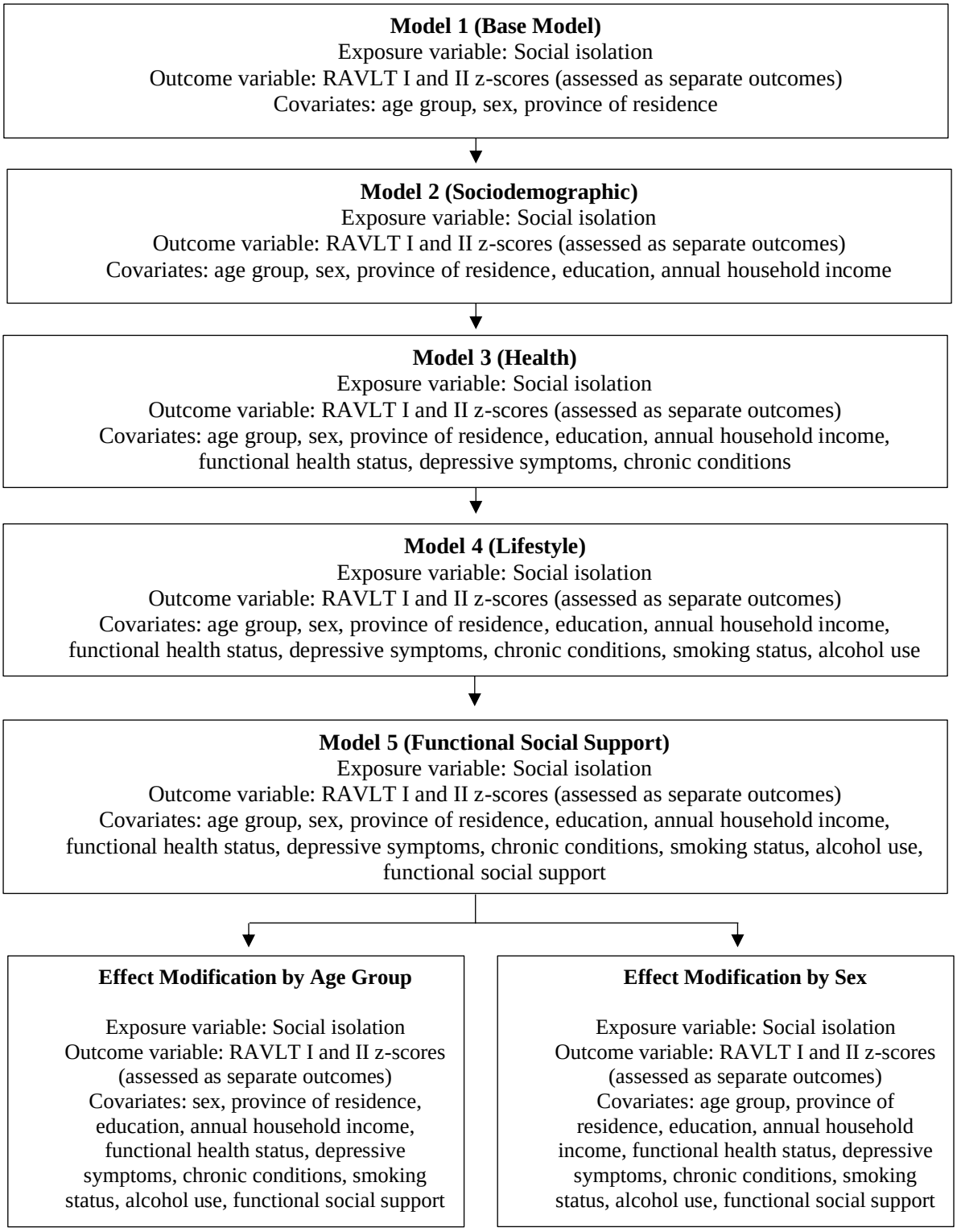
| | (Zunzunegui et al., 2003, pp. S93-S100). |

## Appendix D. List of Words Used in the Rey Auditory Verbal Learning Test (RAVLT)[142]

**Table D1: List of Words Used in the Rey Auditory Verbal Learning Test (RAVLT)**

| ENGLISH | FRENCH |
|---|---|
| Drum | Tambour |
| Curtain | Rideau |
| Bell | Cloche |
| Coffee | Café |
| School | Ecole |
| Parent | Parent |
| Moon | Lune |
| Garden | Jardin |
| Hat | Chapeau |
| Farmer | Fermier |
| Nose | Nez |
| Turkey | Dinde |
| Color | Couleur |
| House | Maison |
| River | Rivière |

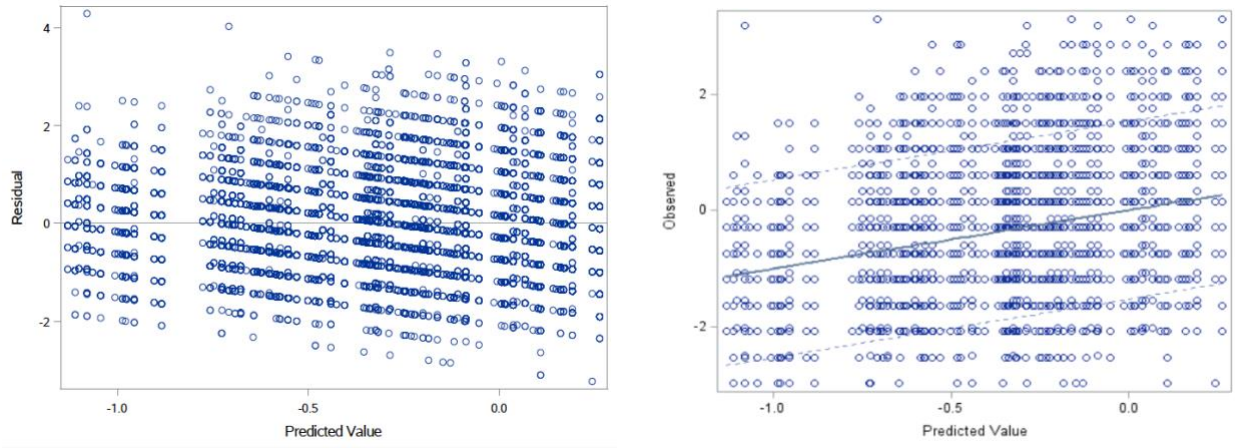
## Appendix E. Analytical Plan
## Table E1: Analytical Plan



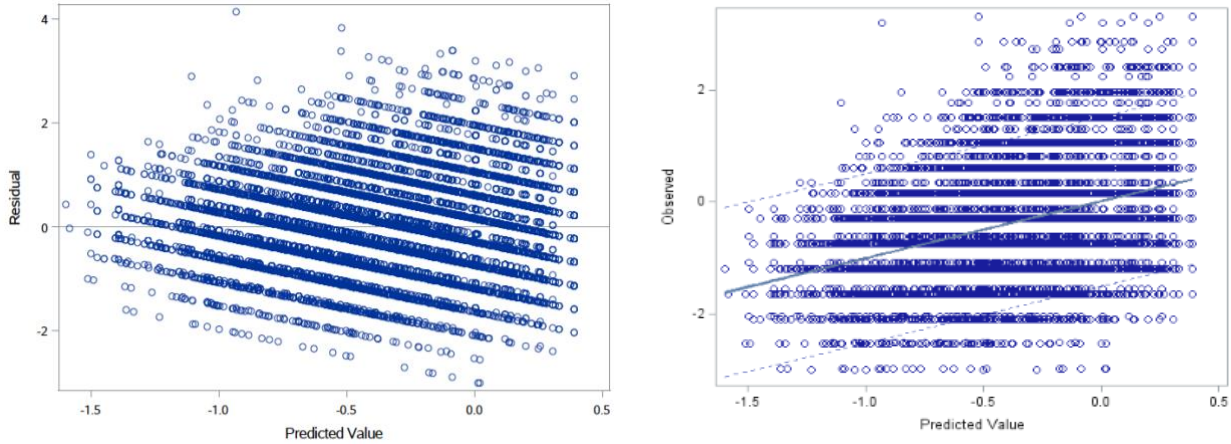

*Note*: The source of the diagram structure used in Appendix F is Rutter, E.[44]

## Appendix F. Model Diagnostic Plots for the Association between Social Isolation and RAVLT I

### Figure F1: Model Diagnostic Plots of Model 1 for the Association between Social Isolation and RAVLT I




### Figure F2: Model Diagnostic Plots of Model 2 for the Association between Social Isolation and RAVLT I




### Figure F3: Model Diagnostic Plots of Model 3 for the Association between Social Isolation and RAVLT I

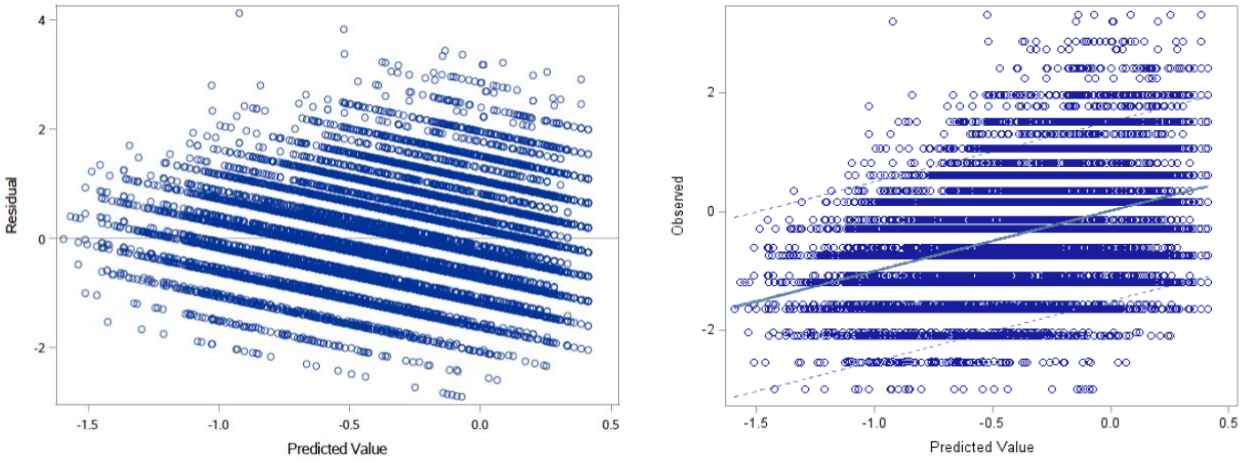


**Figure F4: Model Diagnostic Plots of Model 4 for the Association between Social Isolation and RAVLT I**

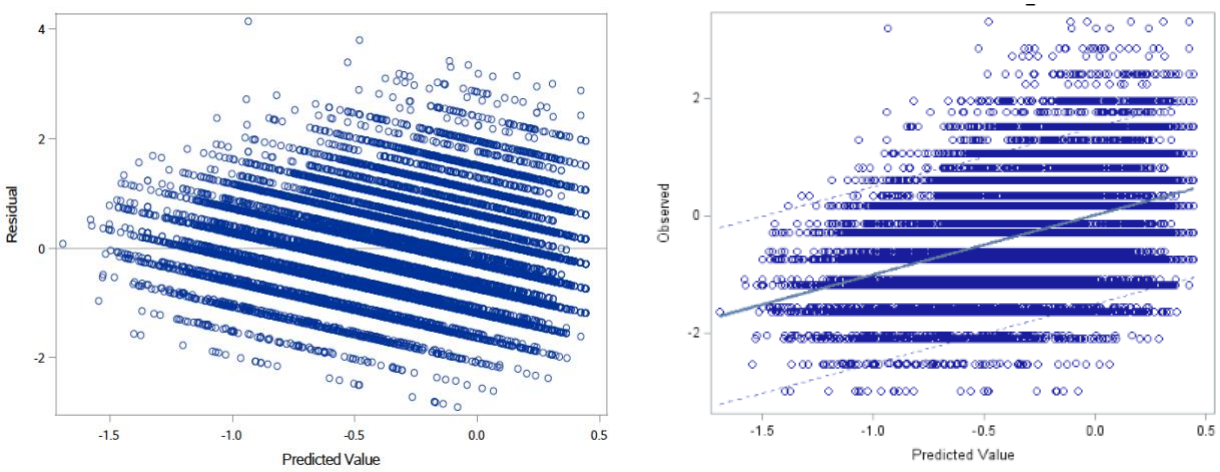
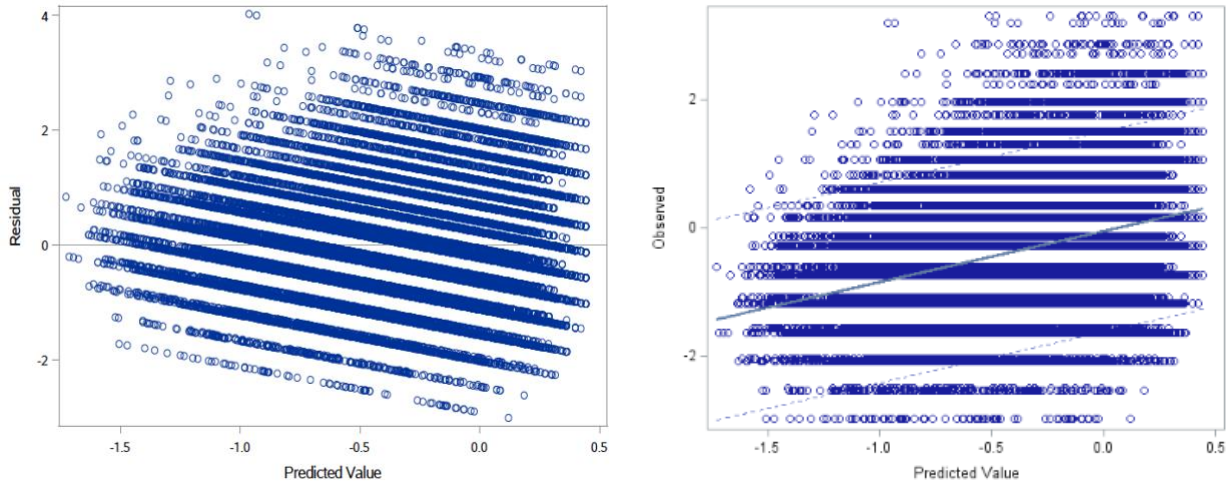
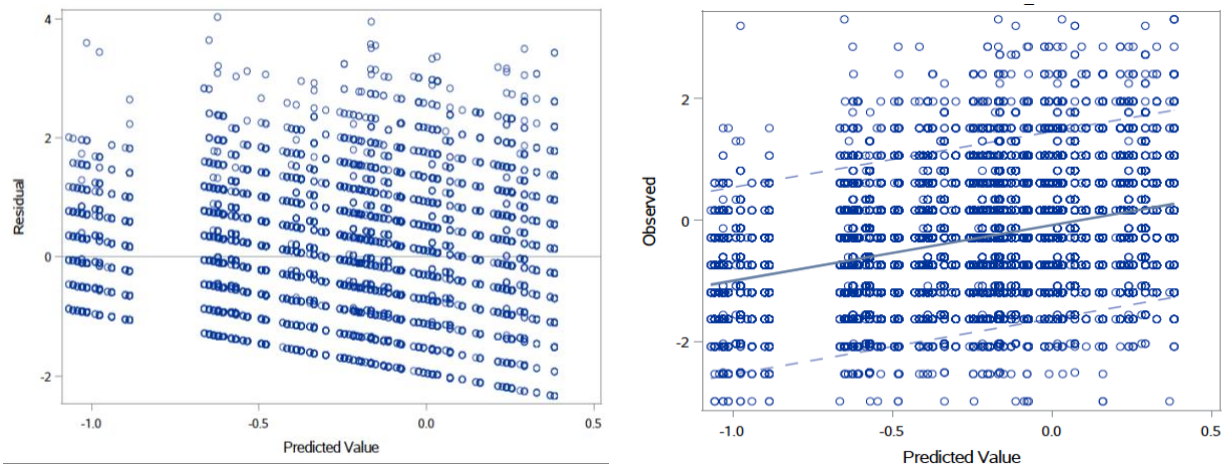



**Figure F5: Model Diagnostic Plots of Model 5 for the Association between Social Isolation and RAVLT I**

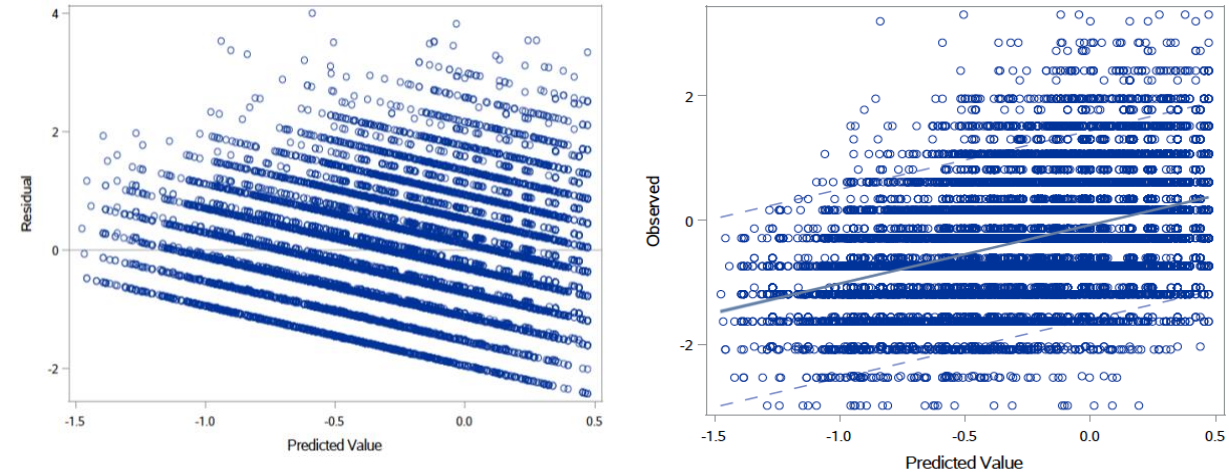


## Appendix G. Model Diagnostic Plots for the Association between Social Isolation and RAVLT II

### Figure G1: Model Diagnostic Plots of Model 1 for the Association between Social Isolation and RAVLT II




### Figure G2: Model Diagnostic Plots of Model 2 for the Association between Social Isolation and RAVLT II




### Figure G3: Model Diagnostic Plots of Model 3 for the Association between Social Isolation and RAVLT II

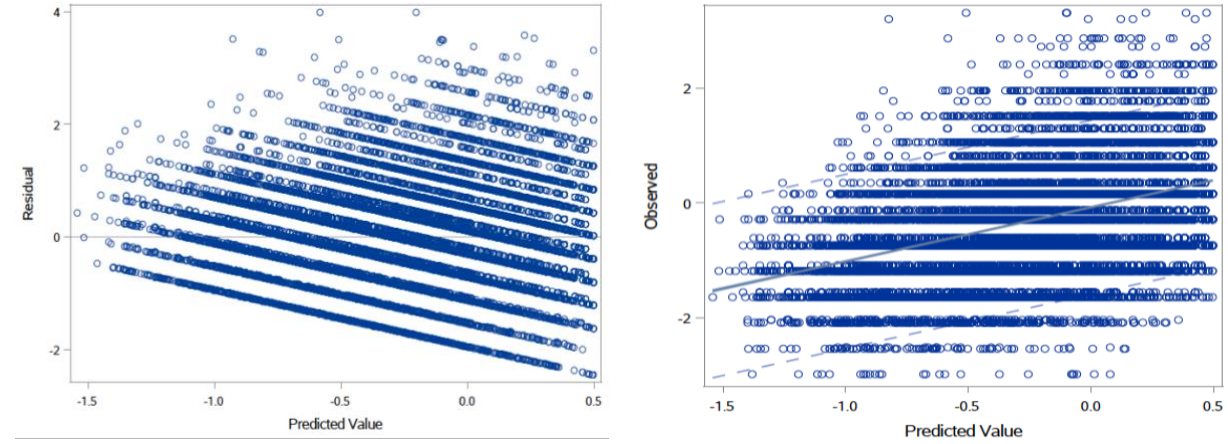


**Figure G4: Model Diagnostic Plots of Model 4 for the Association between Social Isolation and RAVLT II**

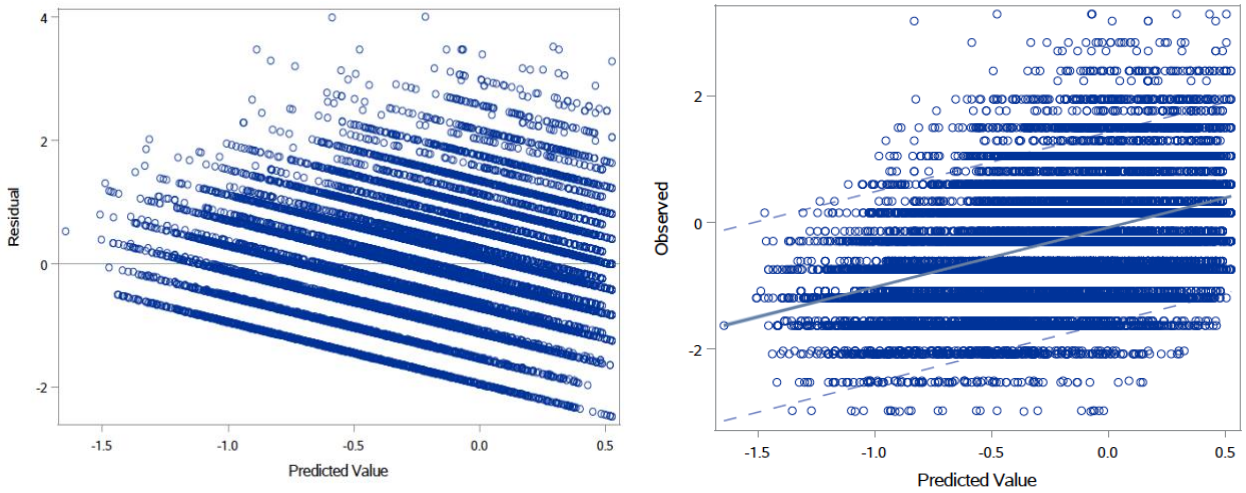



**Figure G5: Model Diagnostic Plots of Model 5 for the Association between Social Isolation and RAVLT II**