The Association between Social Isolation, Functional Social Support, and Memory: A Moderated Mediation Analysis 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

Social support is a widely investigated, modifiable factor thought to promote memory function and successful aging. However, the intertwined effects of the two components of social support – objective social isolation and subjective functional social support – on memory are less understood. Therefore, we explored whether social isolation was associated with memory function in middle-aged and older adults, and whether this association was mediated by functional social support. We also examined moderated mediation by age group and sex.

We analyzed data from the baseline and first follow-up waves of the Tracking Cohort of the Canadian Longitudinal Study on Aging. These data included a derived variable for social isolation, a standardized instrument for self-reported functional social support, and a combined immediate and delayed recall memory score from a modified version of the Rey Auditory Visual Learning Test. Using multiple linear regression and an analytical sample of 12,834, we regressed memory scores at follow-up onto baseline social isolation status, controlling for baseline sociodemographic, health, and lifestyle covariates, baseline memory, and baseline and follow-up functional social support. We further assessed whether functional social support at follow-up mediated the association between baseline social isolation and follow-up memory. To assess moderated mediation, each path of the mediation analysis was stratified by age group and sex

The independent and direct effect of social isolation on memory controlling for covariates showed a non-statistically significant, inverse association ($\hat{\beta}$ = -0.13; 95% confidence interval [CI]: -0.68, 0.45). Social isolation predicted lower levels of functional social support ($\hat{\beta}$ = -0.06; 95% CI: -0.08, -0.04), whereas high functional social support was associated with higher memory scores ($\hat{\beta}$ = 0.59; 95% CI: 0.09, 1.10). Memory scores decreased on average by 0.03 points (95% CI: -0.06, -0.01) in socially isolated participants versus non-isolated participants, when mediated by functional social support. Lastly, some evidence of effect modification was found by the oldest age group (≥ 75 years) on the "a" path of the mediation analysis.

This thesis provides novel findings on the mediating effect of functional social support on the relationship between social isolation and memory. Our findings suggest the association between social isolation and memory operates through, not independently of, functional social support. Health professionals working with socially isolated individuals at risk of, or experiencing, memory problems should pay particular attention to these individuals' levels of functional social support.

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List of Abbreviations

AD	Alzheimer's Disease
ADL	Activities of Daily Living
AIC	Akaike Information Criterion
CCHAS	Charlotte County Healthy Aging Study
CCHS-HA	Canadian Community Health Survey-Healthy Aging
CES-D10	Center for Epidemiologic Studies Short Depression Scale
CHARLS	China Health and Retirement Longitudinal Study
CHMS	Canadian Health Measures Survey
CI	Confidence Interval
CLSA	Canadian Longitudinal Study on Aging
CTUMS	Canadian Tobacco Use Monitoring Survey
DCS	Data Collection Site
FSS	Functional Social Support
HR	Hazard Ratio
HRS	Health and Retirement Study
IADL	Instrumental Activities of Daily Living
IQR	Interquartile Ranges
LSNS-6	Lubben Social Network Scale-6
MDD	Major Depressive Disorder
MI	Multiple Imputation
MIDUS	Midlife in the U.S.
MMSE	Mini-Mental Status Examination
MOS-SSS	Medical Outcomes Study – Social Support Survey
OARS	Older Americans Resources and Services
PM	Proportion Mediated
PMM	Predictive Mean Matching
RAVLT	Rey Auditory Verbal Learning Test
RS	Rotterdam Study
SD	Standard Deviation
SI	Social Isolation
SNAC-K	Swedish National Study on Aging Care in Kungsholmen
T_0	Baseline
T_1	Follow-up
TICS	Telephone Interview for Cognitive Status
WHO	World Health Organization

1. Introduction

Aging is characterized by changes in biological, psychological, behavioural, and social processes[1,2]. As people age, the brain undergoes cortical reorganization and remodelling, leading to changes in cognitive ability[3,4]. These changes occur in one or more of the six different domains comprising overall cognitive function: complex attention, executive function, learning and memory, language, perceptual–motor function, and social cognition[5]. For older adults, maintaining cognitive function can enhance health-related quality of life[6] and prolong independent living[7–9]. Conversely, cognitive impairment is associated with institutionalization[10], lower life expectancy[11,12], depression[13,14], and major neurocognitive disorders such as Alzheimer's disease (AD)[15]. For individuals who suffer from cognitive disorders, memory loss can create interpersonal challenges leading to high levels of distress and social withdrawal, as well as difficulties performing activities of daily living[16,17]. Although many studies have focused on risk factors for memory decline, research also seeks to identify factors that promote memory function[18].

Social support is a modifiable factor shown to promote memory and broader cognitive function[19–21]. Two domains of social support can be defined based on the structure and function of social networks and social engagement[22–27]. Structural social support is the objective size of an individual's social network (e.g., the number of persons in the network and the frequency of contact with these persons) and the frequency of participating in a range of social activities[28]. The objective absence, or low numbers, of social networks and the lack, or low levels, of participation in social activities reflects social isolation (SI)[29]. Functional social support (FSS) refers to an individual's perception of the degree to which they can rely on members of their social networks for support in times of need[30].

Although SI and FSS are distinct concepts, they are also interrelated. Some researchers believe individuals with low SI and abundant social networks have access to a multiplicity of persons to obtain FSS[31]. While larger social networks have been associated with higher levels of FSS, levels of FSS can vary regardless of network size[32,33]. For example, an individual may be objectively isolated yet the few network members they do have may provide strong FSS. On the other hand, one might have an objectively large social network, but low FSS because they do not believe their network members will help in times of need. Studies frequently report that higher levels of FSS are associated with better cognitive function and protect against cognitive decline[34–36], whereas higher SI produces the opposite effect[37–40]. Furthermore, when multiple aspects of the structure and function of social support are included within the same model, the perception of support, rather than the size of social networks, is typically linked to improved cognitive function[34,36,41–45]. For instance, DiNapoli et al.[45] found that perceived support (another term for FSS) among older adults accounted for nearly double the variance in cognitive function when compared to objective levels of SI.

This thesis explores the association between SI, FSS, and the memory domain of cognitive function. Given the intertwined nature of SI and FSS, along with the fact some degree of social network existence is a precondition for FSS[31,46], this thesis investigates whether FSS mediates the relationship between SI and memory. We also examine moderated mediation by age group and sex.

2. Literature Review

2.1. Social Isolation

Research suggests SI increases with age[47–49]. A recent estimate from the Government of Canada reported approximately 30% of Canadian older adults were at risk of becoming socially isolated[50] and the World Health Organization (WHO) identified SI as a key policy issue for aging adults[51]. SI is known to increase neurophysiological inflammatory processes[37] and has been associated with a wide range of negative health outcomes, including high blood pressure[21], cardiovascular disease[27], stroke[27], and Type II diabetes[21]. Studies suggest the risk of mortality related to SI is comparable to smoking[22,25]. SI has also been linked to psychological disorders such as anxiety and depression[24,52,53], cognitive impairment[54–58], and major neurocognitive disorder[59,60].

SI should not be confused with loneliness. Although these concepts appear similar[61–64], SI is the objective absence of social connections and social participation, whereas loneliness is an individual's subjective perception of having inadequate social connections or engagement[24,65,66]. Therefore, one may not be socially isolated, but they may report feeling lonely, or vice versa[24]. In the thesis, SI was the operationalization of structural social support, which aligns with previous literature that distinguishes between SI, loneliness, and FSS [22,23,25–27].

2.1.1. Primary Factors Influencing Social Isolation

2.1.1.1. Age

Social network size tends to decrease as age increases[32]. Advanced age (75 years or older) in particular has been associated with an increased risk of SI because older adults often experience decreased social engagement and participation due to factors such as disability, disease, mobility issues, and life transitions like retirement or the death of social network

members[28,67,68]. Most importantly, spousal loss becomes more common in older adults. Widowhood is a strong driving factor of SI and has been consistently linked to negative effects of SI on health[53,69–71].

2.1.1.2. Sex

Although both males and females experience higher levels of SI with increasing age[72], the structure of such isolation differs. Females often possess larger, more multidimensional and diverse social networks compared to males, regardless of age[73–77], and generally report lower SI than males[78,79]. Indeed, males often show less desire than females to maintain large social networks because they perceive such maintenance as stressful[32,77,80]. Marital status is also a key source of social integration for both males and females[81]. However, studies suggest that being unmarried or widowed may impact the social network size of males more profoundly since older males tend to maintain fewer social connections compared to females[72,82,83].

2.1.1.3. Chronic Disease

A prominent clinical feature of chronic and age-related diseases such as AD or major depressive disorder (MDD) is social dysfunction[84]. Areas of the brain involved in processing social stimuli are particularly vulnerable to pathogenic insult and deficits in social functioning are often noted among individuals who suffer from neuropsychiatric disorders[85–88]. Individuals with AD may express inappropriate social behaviour or lack the cognitive skills and affect to effectively participate in social interactions[89]. Symptoms associated with MDD may result in the inability to form or maintain social relationships and lead to disengagement from social activities[87,88]. The social challenges associated with these disorders place individuals at an increased risk for experiencing SI[84].

2.1.2. Measures of Social Isolation

In the literature, SI is typically identified by low frequencies of contact with friends and family, and low frequencies of engagement in activities outside the home. These activities include travelling or outings with family/friends, participation in volunteerism or religious activities, membership in community groups or associations, and attending social functions[38]. Many studies also include living arrangements (e.g., lives alone versus living with one or more people), marital status, and number of social ties in assessments of SI[23,24,63,65].

Researchers generally measure SI using instruments asking about social network size or the types of activities listed in the previous paragraph. The Lubben Social Network Scale-6 (LSNS-6)[90] is an example of a standardized and often-used scale measuring SI based on the number of and frequency of contact with members in the respondent's social network (e.g., "How many relatives/friends do you see or hear from at least once a month?")[45]. However, the LSNS-6 only includes one aspect of SI (social networks) and researchers have begun to employ the use of indices that incorporate the multiple components of SI described above[23,24,63,65]. One such index was created by Menec, Newall, and colleagues[24]; it contains questions about the size of an individual's social network, their frequency of contact with network members, participation in social activities, living arrangement, marital status, and retirement status. This index was used to measure SI in the thesis, and it is described in more detail in Section 3.2.1 below.

2.2. Functional Social Support

FSS is divided into different subtypes of support, including emotional, informational, tangible, affectionate, and positive social interaction. Emotional support includes providing empathy, caring, and understanding (e.g., the sharing of feelings); informational support involves the provision of feedback, advice, or guidance to resolve a challenge in one's life; instrumental

or tangible support includes physical aid with completing tasks or chores; affectionate support involves showing feelings of love, such as a hug; positive support is the generation of feelings of ease or relaxation as a result of social contact[30,91]. Research has shown that experiencing high levels of FSS can reduce stress[92,93], promote cognitive function[18,94–97], and protect against cardiovascular disease[98–100]. Individuals integrated into social networks providing high levels of FSS are generally healthier[25], live longer[101], and have a decreased risk of developing major neurocognitive disorder[41]. Many risk factors for low FSS are the same as for high SI.

2.2.1. Primary Factors Influencing Functional Social Support

2.2.1.1. Age

Although social network size may decrease with increasing age[68,102], older adults frequently report higher satisfaction with relationships and more positive emotions when interacting with remaining social network members[103,104]. This is likely due to continuing investment in social relationships that yield value-added benefits and removing those relationships that produce stress. The perceived level of overall support may also increase with age as older adults draw upon greater support from their social ties[105,106]. Different subtypes of support may also play varying roles of importance throughout the aging process. According to a recent study, the positive effects of emotional support on cognitive function were stronger among adults over the age of 65 years compared to their younger counterparts[107]. However, no difference in effect was found for instrumental support on cognitive function between the younger and older age groups[107].

2.2.1.2. Sex

The literature shows that females tend to derive FSS from a broader, more multifaceted pool of social ties such as friends and children, which explains why females often possess larger,

more diverse social networks compared to males[32,77,80]. In contrast, males tend to derive FSS from their spouses[32,77,80]. Subtypes of FSS also differ by sex. Multiple studies have shown that females report higher average levels of emotional support compared to males[74,108,109]. The literature appears silent on whether the effects of sex vary across age groups (see Section 2.5 below).

2.2.1.3. Chronic Conditions and Functional Social Support

As previously discussed in Section 2.1.1.3 above, chronic conditions such as dementia or MDD may lead to social dysfunction, including difficulty processing social stimuli and social withdrawal[84,89]. Interestingly, persons with mild dementia tend to report lower levels of FSS compared to those with more advanced dementia[110,111]. Individuals with mild dementia may have better awareness of the psychosocial effects of their condition and thereby report lower levels of FSS, while those with advanced dementia may lack an awareness for their social deficits and report higher perceived levels of support[110,111].

2.2.2. Measures of Functional Social Support

No gold standard exists to assess FSS, and inconsistencies often arise in how it is measured. Some studies measure specific dimensions of FSS, such as emotional or tangible support[34,107,112], and other studies assess FSS through marital quality or satisfaction with social support received[101,113]. However, since FSS is composed of multiple components, suitable instruments should measure multiple subtypes of FSS to generate subtype specific and overall FSS scores. An example of such an instrument is the Medical Outcomes Study-Social Support Survey (MOS-SSS)[30], which is a self-administered questionnaire generating scores for perceived availability of overall FSS and four subtypes of FSS[74,91,114–117]. The composition of the MOS-SSS is described in Section 3.2.2 below and it was used to measure FSS in the thesis.

2.3. Memory

Memory is a complex neural process in which the brain encodes, consolidates, and retrieves information[118]. The four systems most clinically relevant to memory function among older adults are episodic memory, semantic memory, implicit memory, and working memory[119]. Episodic memory is the ability to remember personal experiences and events. Recalling whether you took your medication this morning would be an example of episodic memory[120]. Semantic memory refers to the reservoir of general knowledge stored in the brain, such as recognizing colour names. Implicit memory or automatic memory is involved in the performance of habits, skills, and other daily activities[121]. For example, knowing how to ride a bike does not require intentional recall of how a person was taught to ride a bike. Lastly, working memory is a component of executive function relating to the temporary storage of information, such as the ability to remember several numbers and sum the total[121].

Aging does not impact all forms of memory equally[122,123]. Semantic memory is often maintained in middle-aged and older adults[122], whereas episodic memory can be profoundly impacted by advancing age to the point where it displays the largest degree of age-related decline[122,124–126]. Episodic memory decline follows a pattern known as Ribot's law[127], where memories of recent events are most likely to fade and memories of distant events are usually spared until the later stages of decline. Poor episodic memory function is an early symptom of major neurocognitive disorder[128].

2.3.1. Measures of Memory

Evaluating memory function is done through psychometric testing, which involves the administration of well-validated tools such as the Rey Auditory Verbal Learning Test (RAVLT)[129] or the Wechsler Memory Scale–IV[130], among others. These tools are based on the

notion that memory retrieval can occur in response to both external (cued recall) and internal (free recall) prompts[131]. For example, providing an individual with a word list and prompting the recall of items by category would be an example of an external cue, while asking an individual to recall as many words as possible from a list would require the use of internal cues. Internally cued memory is more likely to be recalled episodically than externally cued memory[131]; therefore, most of the literature surrounding episodic memory uses free recall tasks[31,94,96,97,132]. In this thesis, episodic memory was the outcome of interest, and it was measured using the RAVLT, which is built around internal cues.

2.4. Theoretical Frameworks

Several theoretical frameworks can be used to explain the intertwined nature of SI and FSS, as well as the impact of SI and FSS on cognition. These frameworks include the convoy theory, the cognitive-enrichment hypothesis, the cognitive reserve hypothesis, and the stress hypothesis.

2.4.1. The Convoy Theory

The convoy theory[133,134] was developed to explain the multidimensional nature of social relationships. According to the convoy theory, across the lifespan, including late life, individuals maintain social relationships that vary in closeness and receive differing levels of one or more types of FSS from these relationships[26,133,134]. The convoy theory distinguishes between social support based on structure and function. While early work in social epidemiology focused on how the objective quantity of social support (SI) impacted health outcomes [101,135], later work posited that levels of FSS received from one's social network structure were the true influences on health[38,136,137]. This theory is substantiated by literature showing that higher structural support (or lower SI) predicts higher levels of FSS[138–142].

2.4.2. The Cognitive-Enrichment Hypothesis

Engaging in positive behaviours (e.g., taking care of one's health, staying connected with others through social activities, managing stress, etc.) is key for the maintenance of cognitive functioning throughout the aging process[143]. A key component of the cognitive-enrichment hypothesis is the 'use-it-or-lose-it' hypothesis[143], which suggests exercising cognitive faculties by performing cognitively demanding activities (e.g., social engagement, exercise, etc.) stimulates the brain and preserves cognitive function[143].

Interacting socially requires the use of specific cognitive abilities such as attention, language, and memory[46]. Increased interaction with social ties can facilitate exposure to novel social stimuli including a diversity of ideas, information, activities, verbal and nonverbal social cues, faces, and speech patterns[144,145]. Further, a higher level of perceived support when engaging socially may increase positive affect and cognitive stimulation[143]. Therefore, more meaningful connections and FSS can reinforce and expand the cognitive benefits of social engagement[143].

2.4.3. The Cognitive Reserve Hypothesis

The cognitive reserve hypothesis posits that individuals differ with respect to their levels of resiliency against neuropathological damage[146]. Individuals with a higher level of reserve can have reduced susceptibility to pathological brain damage such as hippocampal atrophy[147] and to the accumulation of amyloid plaque associated with AD[148]. Neuroprotective mechanisms are acquired by individuals differently throughout the lifespan, depending on accumulated levels of cognitive stimulation, which occur through factors such as receiving higher education or having a complex occupation, engaging in regular physical activity, or participating in social activities[149,150]. Neurologically, cognitive reserve translates into the preservation of cognitive

function through the formation of more efficient or extensive neural networks that compensate for age-related changes in pathology[151]. Aspects of both SI and FSS may contribute to these compensatory processes. Studies have shown that individuals with larger and more diverse social networks, and who engage in frequent social activities, have higher cognitive resiliency to neurodegeneration[152,153]. Similarly, individuals with stronger social ties and higher levels of FSS have been shown to display greater cognitive reserve[59,152,154].

2.4.4. The Stress Hypothesis

The stress hypothesis suggests increased social participation and engagement can reduce psychological stress. Managing stress levels is beneficial for overall cognitive function, memory, and executive performance[155,156]. Animal models have shown SI is associated with prolonged neuroendocrine stress responses leading to neuronal changes (e.g., loss of dendritic spines and neuronal cell death) and the impairment of cognitive function[157]. In humans, SI and lack of perceived support are closely related to the stress-inducing effects of objective SI in animal models. Supportive interpersonal relationships in humans may offer coping resources to manage stressful events[158–160], whereas the objective presence of others (without FSS) may not be sufficient to provide socio-emotional support and produce stress-reducing benefits[35,161].

2.5. Structural and Functional Social Support and Cognitive Function

The above frameworks provide the biological and social contexts for the thesis research. These frameworks suggest the quantity of social ties and activity may not be sufficient to affect memory without additional consideration of the quality of social relationships (FSS).

To explore published research on the topic area, the thesis candidate conducted a literature review, including articles from January 2000 to May 2024 (described in Appendix A, Figure A-1). The candidate developed the literature search strategy following consultation with a

health sciences librarian to identify articles that investigated (1) the effects of SI on cognitive function, (2) the effects of FSS on cognitive function, and (3) the effects of SI and FSS on cognitive and memory function. The search terms used in the review can be found in Appendix A, Table A-1.

2.5.1. Social Isolation and Cognitive Function

The following section describes findings from articles that investigated the relationship between SI or structural social support and cognitive function. A summary of the articles is shown in Appendix A, Table A-2.

2.5.1.1. Cross-sectional Studies

The literature search identified seven cross-sectional studies that assessed the impact of SI or structural social support on cognitive function. Sample sizes ranged from 189[56] to 5,059[55] participants, including both middle-aged and older adults[54–56,162–165]. Articles investigated populations from Europe[164], India[164], the United States[54,162,165], Ireland[163], South Africa[55], and Switzerland[56]. Data were drawn from large panel studies of community dwelling middle-aged and older adults from multiple countries[164], a single country[54–56], or a single region[162,165]. One study included participants from multiple cohort studies in Dublin, Ireland[163].

Two studies assessed SI through an index including frequency of contact with social network members and frequency of participation in social activities[162,164]. The remaining studies assessed participation in social activities[54], number of network members[54–56], frequency of contact[55,165], and social engagement[163] (measured by the Wenger Social Support Network Type Assessment[166]).

Five studies assessed cognitive impairment through the Clinical Dementia Rating Scale [162,167], the Mini-Mental Status Examination (MMSE)[56,163,168], the Montreal Cognitive

Assessment[54,169], and a composite measure of orientation in time, immediate and delayed recall, and the ability to follow counting patterns[55]. One article assessed global cognition through a composite measure of verbal fluency, learning, and delayed recall[164]. The remaining study assessed memory function through the Wechsler Memory Scale[165,170].

SI was associated with decreased cognitive function[164] and an increased odds of cognitive impairment[162]. Further, less participation in social activities[54] and smaller social networks[54–56] were associated with increased risk of cognitive impairment, and higher social engagement was associated with less risk of cognitive impairment[163]. However, in the single study assessing memory function, no association was found between contact frequency with social network members and memory[165]. Due to the potential for reverse causality bias, the results of cross-sectional studies must be interpreted with caution.

2.5.1.2. Longitudinal Studies

The search identified 19 longitudinal studies that assessed the relationship between SI or structural social support and cognitive function. The sample sizes varied between 804[171] and 19,832[172] participants with up to 12 years[173] of follow-up. The locations of recruitment included Korea [173–176], the United States[19,177–181], Europe[172], China[58,182,183], Taiwan[184], Spain[185,186], England[187], and Sweden[171]. Minimum recruitment ages ranged from 40 years or older at baseline[171] to 65 years or older at baseline[177,180,186]. Data were drawn from large panel studies of community dwelling adults across multiple countries[172], a single country[19,58,171,173–176,180,182–185,187], or a single region[177–179,181,186].

In five studies, SI was operationalized through (1) the lack of social contact and participation in social activities[178], (2) living arrangements, visits with family, frequency of interaction with friends, and frequency of participation in social activities[182], or (3) marital status,

living arrangements, frequency of contact with children, family, and friends, and participation in social activities[183,185,187]. The reverse of SI–structural social support–was assessed using a multiplicity of variables, including social networks (marital status, number of ties, and frequency of contact)[171,184], social integration (marital status, volunteer activities, and frequency of contact)[19], and social engagement (frequency of contact and participation in social activities)[58,180]. Other studies explored individual aspects of SI, with participation in social activities (i.e., leisure, cultural, religious, and community engagements) being the most common measure of an single aspect of structural social support[172–177,179,184], followed by the frequency of contact with social network members[175–177].

Cognitive function was assessed through validated neuropsychological tests such as the MMSE[168,173–177,181,182], the Telephone Interview for Cognitive Status (TICS)[180,183,188], the Short Portable Mental Status Questionnaire[184,189], and the Leganés Cognitive Test[186,190]. Two studies used a composite measure of multiple cognitive domains to assess cognitive function[179,185], while one study used a similar composite measure to characterize cognitive impairment[58]. Three studies assessed executive function through tests of verbal fluency[172,187] or visuospatial ability[171]. Six studies measured memory function using immediate and delayed recall tasks[19,171,172,178,183,187], as well as semantic memory via tests of synonym identification[171].

Having high levels of SI was associated with greater cognitive decline[182,183,185] and worse episodic memory over time[178,183,187]. Increased participation in social activities[172,173,175–177,179,184,186], more frequent social contact[175,181], and more social engagement[180] were associated with slower cognitive decline. Son and Sung[176] identified that social participation was more important for cognitive function than the frequency of contact with social network members. Béland et al.[186] found that low frequency of participation in social activities was significantly

associated with cognitive decline, but the number of social ties and the frequency of social contact was not related to cognitive function. Further, higher levels of social engagement were associated with a lower risk of cognitive impairment[58]. Larger social networks were associated with preservation of semantic and episodic memory function over time[171], and higher levels of social integration predicted slower memory decline[19].

Piolatto et al.'s[57] meta-analysis from 2022 included 17 articles examining structural aspects of social support and cognitive function. Measures of structural social support included social activity (i.e., participation to social clubs, community/religious organisations, voluntary work), network size (i.e., number of contacts and frequency of contact), and social engagement (i.e., indices of social activity and network size). Cognitive function was assessed through validated neuropsychological tests of global cognition or specific cognitive domains. Participants in the included articles averaged 67.7 years of age, the average follow-up was 11 years, and the average sample size was 5,672 (range: 529 to 19,832). The pooled, random effects odds ratio (OR) for all the measures of structural social support and cognition across the 17 studies was 1.11 (95% Confidence Interval [CI]:1.08, 1.14), confirming previous reports that low structural social support is associated with cognitive decline[57]. In meta-analyses researchers employ an I^2 statistic to determine the extent to which differences in effect sizes across studies is due to inconsistencies in study designs. An $I^2 \geq 0.50$ represents high heterogeneity. The meta-analysis by Piolatto et al.[57] highlighted the vast amount of heterogeneity in measures of structural social support and cognitive function in the literature, which was demonstrated quantitatively with an $I^2 = 0.82$ and $p < 0.01$ on the Q-test. However, the authors did not conduct a meta-regression to explore sources of heterogeneity.

2.5.1.3. Summary

Generally, studies found an inverse association between SI and cognitive function, and positive associations between increased structural social support and cognitive function. The most commonly used scale to assess cognitive function was the MMSE[168]. However, only seven of the twenty-six studies included a comprehensive measure of SI and, of these, three different types of SI indices were featured in the research. Further, structural social support was assessed through various approaches, including single components of structural support such as social participation, composite measures including multiple aspects of structural social support, and validated scales. These findings emphasize the need for consistency in how SI is measured in the literature.

2.5.2. Functional Social Support and Cognitive Function

A recent review article published in 2023 by Mogic et al.[18] examined the association between FSS and cognitive function/impairment. The review included 85 articles of participants aged 40 years or older from any residential setting. Of the 85 articles, 44 were cross-sectional and 41 were cohort studies. Sample sizes ranged from 20 to 30,029 participants. The included articles measured overall FSS or subtypes such as emotional/informational support, tangible support, affectionate support, and positive social interactions. Outcomes of interest included cognitive function or incidence or prevalence of a neurological condition. Cognitive function was assessed globally (38 articles) and/or by domain (e.g., memory, executive function [20 articles]) using multiple different instruments (see Table 1 [pp. 4 to 14] in the published review for a list of instruments). Nineteen articles examined dementia including AD. Most of the included articles found a positive association between overall and subtype-specific FSS and cognitive function. Further, higher levels of affectionate support and positive social interactions

were associated with decreased risk for neurocognitive outcomes such as dementia[18]. The review article assessed the literature published prior to 2022. An additional 8 studies[94–97,191–194] exploring the impact of FSS on cognitive function and neurocognitive disorders have been published since the Mogic et al. review. A summary of these 8 studies is shown in Appendix A, Table A-3.

Of the eight additional studies, two assessed FSS on cognitive function[95,191], four assessed FSS on memory function[94,96,97,194], one assessed FSS on neurocognitive disorders[193], and one assessed FSS on cognitive function and neurocognitive disorders[192]. Further, three of the studies assessed both overall FSS as well as subtypes[96,97,193]. The sample sizes varied between 1,319[191] and 24,719[97] participants. The locations of recruitment included the United States[191], Canada[96,97], China[94,95,194], Korea[193], the Netherlands[192], and Sweden[192]. Data were drawn from large national panel studies[94–97,191–194] or a single region[192] comprising community-dwelling adults.

Using longitudinal data over 10 years of follow-up across four measurement occasions from the China Health and Retirement Longitudinal Study (CHARLS)[195] of participants aged 65 years or older, Ma et al.[95] found that FSS was associated with reduced risk of incident cognitive impairment (Hazard Ratio [HR]: 0.96; 95% CI: 0.93, 0.98). However, in a study of participants also aged 65 years or older from the Health and Retirement Study (HRS)[196], Du et al.[191] did not find significant associations between perceived levels of support and changes in cognitive function over eight years of follow-up across three measurement occasions. However, because an additional area of interest for Du et al.[191] was to assess support by relationship type, their analytical sample was limited to only those participants who were married or partnered and had children.

Among the four of the eight studies that specifically assessed memory, high levels of overall FSS or subtypes of FSS were consistently associated with better memory function. A cross-sectional study using CLSA data found overall and subtypes of FSS (affectionate, emotional/informational, positive, and tangible support) were positively, and significantly, associated with immediate and delayed recall memory in participants aged 45 to 85 years, with the exception of positive social interactions and delayed recall memory ($\hat{\beta}$ = 0.02; 95% CI: 0.00, 0.04)[97]. A similar study from the CLSA found that although positive associations existed between overall and subtypes of FSS and memory, only tangible support was significantly associated with higher memory function over three years ($\hat{\beta}$ = 0.07; 95% CI: 0.01, 0.14)[96]. Using three waves of data collected over five years from the CHARLS[195] of participants aged 45 years or older, Peng et al.[94] found that perceived availability of support was associated with higher memory function at baseline ($\hat{\beta}$ = 0.25; $p<0.05$) and slower memory decline over time ($\hat{\beta}$ = 0.32; $p<0.01$). However, in disagreement with these findings, a second study from the CHARLS[195], which enrolled participants aged 60 years or older from four waves of data collected over seven years, found that perceived availability of support was associated with higher memory function at baseline ($\hat{\beta}$ = 0.442; 95% CI: 0.207, 0.678), but increased memory decline over time ($\hat{\beta}$ = -0.068; 95% CI: -0.123, -0.013)[194]. The authors of the second CHARLS article reasoned that FSS was measured using a single item about perceived availability of support in the future, which may not be detailed enough to capture the true extent of FSS[194].

A single study looked at the impact of two subtypes of FSS (emotional and tangible) on the incidence of neurocognitive disorders[193]. Using data from the Korean Longitudinal Study on Cognitive Aging and Dementia[197], which enrolled participants aged 60 years or older for follow-ups every two years over eight years total, Oh et al.[193] found that low emotional support was

associated with an increased hazard of all-cause dementia (HR:1.42; 95% CI: 1.04, 1.93) and AD (HR: 1.45; 95% CI: 1.00, 2.11)[193]. In contrast, Freak-Poli et al.[192] did not find an association between FSS and neurocognitive disorders or cognitive decline among participants aged 55 years or older from the Rotterdam Study (RS)[198] and the Swedish National Study on Aging Care in Kungsholmen (SNAC-K)[199]. Although both cohort studies had long follow-up periods (10 and 14 years, respectively), the authors reasoned their null results may have been due to a healthy volunteer bias, as evidenced by the large proportion of participants who showed optimal levels of FSS[192].

2.5.3. Social Isolation, Functional Social Support, and Cognitive Function

In general, some literature found both structural and functional aspects of social support to be associated with cognitive function when measured separately. However, as described in Section 1 – Introduction above, both types of social support are interrelated with one another, thereby necessitating a review of findings from articles that included both SI and FSS as explanatory variables of global or subdomains of cognitive function. A summary of this literature is shown in Appendix A, Table A-4 and described below. An overview of the literature from articles that included SI and FSS as explanatory variables of memory function follows in Section 2.5.4 below.

Ten articles analyzed SI and FSS as explanatory variables of cognitive function in the same regression models. A cross-sectional study by DiNapoli et al.[45], containing community-dwelling adults aged 70 years or older in West Virginia, investigated the effects of SI and FSS on cognitive function by parsing out the structural and functional aspects of the LSNS-6[90]. When both aspects of structural and functional support were included in the same model, FSS accounted for 10.2% of the variance in cognitive functioning, while SI accounted for 5.7%.

A second cross-sectional study of adults aged 50 years or older from the Survey of Health, Ageing and Retirement in Europe[200] found that higher objective levels of participation in social activities (social engagement) and subjective emotional closeness (social connectedness) were associated with higher overall cognitive function ($\hat{\beta} = 0.83$; $p<0.001$ and $\hat{\beta} = 0.23$; $p<0.001$, respectively)[201]. The authors also found a significant interaction between social engagement and connectedness such that individuals with high levels of social engagement and social connectedness had the highest cognitive function, whereas individuals with low social engagement and social connectedness had the lowest levels of cognition. Individuals with low social engagement, but high levels of social connectedness, had similar cognitive function to those with low social connectedness and high levels of social engagement[201].

Three additional cross-sectional studies found significant effects between functional and structural support, and cognitive function. Studying adults aged 65 years or older from the Rush Memory and Aging Project in Chicago[202], Krueger et al.[132] found that when social network, social activity, and FSS were included in the same model, social activity and FSS were significantly associated with global cognitive function ($\hat{\beta} = 0.16$; $p<0.001$ and $\hat{\beta} = 0.069$; $p = 0.003$, respectively). From the Population Study of Chinese Elderly[203] in the US, which contained adults aged 60 years or older, Li and Dong[204] found that general cognitive function was significantly associated with network size ($\hat{\beta} = 0.049$; $p<0.001$) and emotional closeness ($\hat{\beta} = 0.076$; $p<0.01$). Further, Yeh and Liu[33] found that being married/partnered ($\hat{\beta} = 0.13$; $p<0.005$) and having a higher perception of social support ($\hat{\beta} = 0.11$; $p<0.001$) were associated with higher scores on the Short Portable Mental Status Questionnaire[189].

Three studies found that aspects of FSS, but not SI, were associated with cognitive function. Chen and Chang's[44] investigation of participants aged 65 years or older from the

Taiwan Longitudinal Study on Aging[205] reported emotional support, but not participation in social activities, reduced the odds of cognitive decline among individuals who previously had low cognitive function (OR = 0.77; 95% CI: 0.60 to 0.99). In middle-aged and older adults between the ages of 35-85 years, enrolled in the Midlife in the U.S. (MIDUS)[206] study, Seeman et al.[34] found that baseline emotional support, but not structural social support (including marital status, frequency of contact, living arrangements, and social network size) was associated with higher scores on the Brief Test of Adult Cognition by Telephone[207] at follow-up after seven and a half years. Lastly, Hughes et al.[36] observed a high level of satisfaction with support, but not social network size or frequency of contact, was associated with baseline cognitive function ($\hat{\beta}$=0.45; p=0.02). However, this association did not remain significant after five years of follow-up[36].

A longitudinal study by Fan et al.[112] found that high social activity levels and larger social networks, but not FSS, protected against cognitive decline after three years of follow-up among participants between the ages of 65-110 years, who were enrolled in the Chinese Longitudinal Healthy Longevity Survey[208]. In a multivariable regression model containing social activity, social networks, and FSS, only social activity (OR = 0.80; 95% CI: 0.65-0.98) and social networks (OR = 0.70; 95% CI: 0.56-0.87) were inversely and significantly associated with incident cognitive decline. These results ran contrary to most other articles, where structural support was non-significant and functional support was significant. It is possible that the participants who had poor cognitive health may have received more functional support during the study period therefore, the association between FSS and cognitive function may have been attenuated[112].

Lastly, one cross-sectional study of persons aged 70 years, recruited into the Lothian Birth Cohort of 1936,[209] found that neither structural (contact with friends/family, marital status and living arrangement) nor functional support (support received and level of satisfaction with support) yielded significant results with cognitive ability[210].

2.5.3.1. Summary

Five studies found significant effects between SI or aspects of structural social support and FSS on cognitive function[33,45,132,201,204]. Three studies only found significant, positive effects between FSS and cognitive function[34,36,44], whereas a single study only found significant, positive effects between structural social support and cognitive function[112]. Lastly, one study did not find significant effects between any aspect of social support and cognitive function[210]. The inconsistent results found among both cross-sectional and longitudinal studies assessing the association between aspects of SI and FSS, and cognitive function could be due to differences in study samples (i.e., sample size and sampling frames), differing measures used to assess SI, FSS, and cognitive function, or differing sets of covariates.

2.5.4. Social Isolation, Functional Social Support, and Memory

Since this thesis focuses specifically on the memory domain of cognitive function, the following section contains a summary of findings from articles that assessed aspects of SI and FSS together in multivariable regression models with memory as the outcome. A summary of the included studies can be found in Appendix A, Table A-5.

The literature search identified 11 pertinent articles. Of the eleven articles, five articles[36,45,132,204,210] were previously identified in the literature search described in Section 2.5.3 above. The overlap consisted of studies that assessed SI, FSS, and cognitive function, while also conducting subgroup analyses on one or more domains of cognitive function, including memory.

Two studies measured SI and FSS, and memory function, by parsing the structural and functional aspects of the LSNS-6[90]. One was a cross-sectional study by DiNapoli et al.[45], of community-dwelling adults aged 70 years or older in West Virginia, that reported both lower SI and higher perceived support were associated with better memory function in the same regression model. The other was a longitudinal study by Hughes et al.[36], containing adults aged 65 years or older from Charlotte County, Florida, that found satisfaction with support, but not SI, was associated with memory decline over five years of follow-up.

Five studies found statistically significant effects between both structural and functional aspects of support and memory function. A cross-sectional study by Krueger et al.[132], drawing participants aged 65 years or older from the Rush Memory and Aging Project[202] in Chicago, found that having increased social activity and higher FSS was associated with better working memory function; however, neither social contact frequency nor social network size was found to have significant effects on memory function[132]. Similarly, a longitudinal study by Peng et al.[94], using data from participants aged 45 years or older in the CHARLS[195], found that individuals who lived alone experienced more memory decline than those who did not. Peng et al.[94] also found that greater perceived availability of support was associated with slower memory decline.

Zahodne et al.'s[46] longitudinal study of American adults aged 50 years or older from the HRS[196] found a higher frequency of social contacts, and being married/partnered, were associated with higher baseline memory ($\hat{\beta}$ = 0.10; 95% CI: 0.08, 0.12 and $\hat{\beta}$ = 0.02; 95% CI: 0.00, 0.04, respectively), and slower memory decline ($\hat{\beta}$ = 0.09; 95% CI: 0.04, 0.15 and $\hat{\beta}$ = 0.08; 95% CI: 0.02, 0.13, respectively). A lower quality of support was negatively associated with memory at baseline ($\hat{\beta}$ = -0.30; 95% CI:-0.05,-0.01), but not over time ($\hat{\beta}$ = -0.30; 95% CI:-0.09, 0.02)[46]. Seeman et al.'s[211] study of adults between the ages of 35-85 years, recruited into the

MIDUS[206] study, found that greater frequency of social contacts and higher FSS were associated with better episodic memory function ($\hat{\beta}$ = 0.049; p<0.01 and $\hat{\beta}$ = 0.051; p<0.01, respectively).

An additional study from the HRS,[196] by Meister and Zahodne[212], found that social contact frequency was associated with improved episodic memory function over time among participants aged 50 years or older. However, in contrast to their initial hypothesis, these authors found that a combined measure of emotional and informational social support was negatively associated with episodic memory after three and a half years of follow-up. Counterintuitive results may have occurred because cognitive measures were only taken at the follow-up visit; therefore, participants with poor memory function at baseline, whose memories were more likely to decline over time, began the study with higher levels of emotional and informational support than persons with better memory function[212].

Three articles found statistically significant associations between measures of structural (not functional) social support and memory function, while one article found no significant associations between measures of structural or functional support and memory function. Using HRS[196] data from participants aged 50 years or older, Hülür et al.[31] found that being married/partnered ($\hat{\beta}$ = 0.04; p< 0.01) and having more social contacts ($\hat{\beta}$ = 0.02; p< 0.01) were associated with less episodic memory decline. Although their analysis showed that high levels of emotional support prevented memory decline, the association was no longer significant after inclusion of age, sex, education, number of functional health limitations, and depressive symptoms[31]. Li and Dong[204] observed that a larger social network size was positively associated with episodic memory among participants aged 60 years or older from the American-based Population Study of Chinese Elderly[203] ($\hat{\beta}$ = 0.059; p<0.001); however, they did not find a significant association between emotional closeness and episodic memory. The studies by

Hülür[31] and Li and Dong[204] only assessed emotional support with a 3-item measure and a single item measure, respectively. Therefore, these studies were unlikely to capture the full essence of emotional support or the wider construct of FSS.

A cross-sectional analysis utilizing the Wisconsin Registry for Alzheimer's Prevention[213], which contained participants between the ages of 40 to 65 years at baseline, found high levels of verbal interactions (suggestive of low SI) were significantly associated with higher verbal learning and memory scores ($\hat{\beta}$ = 0.16; 95% CI: 0.02, 0.30), while a positive though nonsignificant association was found between high perceived support and memory[214]. The absence of an association between FSS and memory may be because of the overly healthy sample of participants that was recruited from a single data collection site[214]. Lastly, the associations between structural and functional support, and memory function, produced null effects among participants aged 70 years from the Lothian Birth Cohort of 1936[209,210]. The null results between structural and functional social support, and memory may have been due to survival bias among the birth cohort thereby creating a sample of overly healthy individuals.

2.5.4.1. Summary

In summary, some studies found statistically significant effects between SI, structural social support, and FSS on memory[45,46,94,132,211]; however, other results were not significant and the point estimates did not uniformly indicate the same direction of effect. Three studies found significant, positive effects between structural social support and memory[31,115,204]; a single study only found significant, positive effects between FSS and memory[36]. In contrast, one study found an inverse association between FSS and memory[212]. Lastly, one study did not find statistically significant effects between social support and memory[210]. The inconsistent results could be due the lack of consistent measures used to assess SI, FSS, and memory, the differences in study

populations (i.e., sampling frames), or the differing sets of covariates including in the analyses. Covariates commonly included in multivariable models from the 11 articles described above were sociodemographic variables (age[31,36,45,46,94,132,204,211,214,215], sex[31,36,45,46,94,132,204,210–212,214,215], education[31,34,36,45,46,94,132,204,211,212,214,215], income[45,94,204,212]), health status (chronic conditions[45,46,132,204,211], depressive symptoms[31,45,46,132,210,211,215], functional impairment[31,94,132,211]), and lifestyle behaviours (smoking[211,214] and alcohol consumption[211,214]). Other covariates included social class[210] , personality[36,132], BMI[215], physical activity[132], race[212], self-rated health[46], and apolipoprotein E-ε4 carrier status[214].

2.5.5. Factors that Moderate the Association Between Social Support and Cognitive Function

Studies examining age and sex as effect modifiers have yielded inconclusive results. Seeman et al.[211] found no difference between the positive effects of increased social contact frequency on episodic memory function between younger (< 65 years) and older (≥ 65 years) adults; however, the relationship between FSS and episodic memory was weaker in the older age group. These results are contradicted by Meister and Zahodne[212], who found that FSS was more strongly associated with memory function in older (≥75 years) compared to younger adults (<75 years), but contact frequency was more strongly associated with episodic memory in the younger age group compared to the older age group.

Hughes et al.[36] found that only one element of structural social support, i.e., having higher contact frequency with friends, was negatively associated with general cognitive ability in adults aged 74 years or older, but positively associated with general cognitive ability in adults aged less than 74 years. Further, LaFleur and Salthouse[165] found that between the age groups 18-39 years, 40-59 years, and 60-96 years, age did not modify any of the associations between

structural or functional aspects of social support and memory function. Varying results regarding age as an effect modifier may be due to the inconsistent cut-off points used to define age groups.

In a study by Joyce et al.,[215] among participants between the ages of 70-94 years, SI and low FSS were consistently associated with lower cognitive function in females, but not males. However, Hsiao et al.[216] found that among participants aged and 50 over, being married was associated with lower risks of cognitive impairment in males, but not females, over four years. Li and Dong[204] found structural aspects of support, including network size and frequency of contact, had larger positive effects on global cognitive function and episodic memory in males aged 60 years or older compared to females aged 60 years or older. However, the positive effect sizes associated with emotional closeness and cognitive function were larger for females than males[204]. On the other hand, Read et al.[217] and LaFleur and Salthouse[165] found no meaningful difference between SI or FSS in males and females.

2.6. The Effect of Social Isolation on Memory – Mediation by Functional Social Support

The literature search described above did not identify any previously published study that assessed FSS as a mediator of the relationship between SI and memory. However, one study reported that the relationship between structural social support and cognitive function was mediated by loneliness[218]. Using a single wave of data from the CHARLS[195], including persons aged 60 years or older, Yang et al.[218] found loneliness to be a partial mediator of the relationship between SI and cognitive function. SI was measured on a 4-point scale based on level of social activity engagement, weekly contacts with adult children, provision of caregiving for grandchildren, and living arrangements. Loneliness was measured using the 'loneliness question' from the Center for Epidemiologic Studies Short Depression Scale (CES-D10)[219], which asks 'How often you have felt lonely during the past week'. A score for overall cognitive function

was computed by combining assessments of orientation and attention measured by the TICS[188], episodic memory measured by immediate and delayed word recall, and visuospatial functioning measured by figure drawing.

The authors found a significant indirect (mediated) effect of SI on cognitive function through loneliness ($\hat{\beta}$ = -0.15; 95% CI: -0.07, -0.23). Further, the direct effect of SI on cognitive function, controlling for loneliness, was significant ($\hat{\beta}$ = -0.83; 95% CI: -1.18, -0.48), as was the total effect of SI on cognitive function ($\hat{\beta}$ = -0.98; 95% CI: -1.35, -0.61)[218].

Although loneliness and FSS are distinct concepts, both are subjective interpretations of one's state of being, with loneliness occurring when an individual believes their social network interactions or social participation levels fall below a desired threshold. In comparison, FSS is a person's perception of whether members of their social network (however large or small) can be relied upon to help in times of need.

The thesis candidate believes objective counts of acquaintances (friends, family, etc.) and social activities do not function completely independently of subjective or perceptual factors such as FSS. The negative impact of SI on memory may be ameliorated by strong perceived FSS in cases where individuals believe they can rely on even one person to satiate unmet needs. On the other hand, the possible protective effects of low SI on memory may not be realized in situations where one thinks their large social network will be unable to help alleviate unmet needs[34,41–43,46]. Therefore, it is plausible that FSS indirectly accounts for at least some of the effect of SI on memory, which highlights the need to explore the as yet unknown mediating role of FSS in the relation between SI and memory. Indeed, one cannot assume they will receive support from others (FSS) in the complete absence of social ties or other forms of objective social engagement. Thus, FSS emerges from structural social support/SI (the "a" path of a

mediation model)[138–142] and it is also a factor that affects memory on its own (the "b" path of a mediation model)[18]. Likewise, evidence shows SI is directly associated with memory (the "c-prime" or direct path of the mediation model)[19,178,182,183,183,185,187,220].

These connections between SI, FSS, and memory are supported by the theoretical frameworks discussed in Section 2.4. The convoy theory believes FSS is derived from a person's social network and an inverse association between SI and FSS is expected on the "a" path of the mediation model. The stress buffering hypothesis posits that FSS may buffer the deleterious effects of stress on cognitive function by either attenuating or preventing stress responses at the outset of potentially stressful experiences[161]. The effects of the stress buffering hypothesis may be seen on the "b" path of the mediation model, where higher FSS is likely to be positively associated with memory function. Further, on the "c-prime" path, low SI may preserve memory through diverse interactions with social contacts and participation in cognitively stimulating activities (i.e., the cognitive enrichment hypothesis), which build cognitive reserve.

2.7. Conclusion

The literature review showed that some positive associations generally existed between FSS and memory, whereas some inverse associations existed between SI and memory. We did not find any discernable differences in results between cross-sectional and longitudinal studies. Article-specific differences in the strength and direction of regression coefficients, and width of CIs, as shown in Appendix A, Tables A-4 and A-5, resulted from numerous factors that differed across studies, e.g., measures of FSS or SI, sample characteristics, sample size, length of follow-up, type of memory or cognition construct and how they were measured, and covariates included in the regression models. Importantly, many articles assessed SI using social network size rather

than multi-faceted measures incorporating elements such as social participation, living arrangements, etc.

Despite a total of 10 articles exploring associations between SI, FSS, and cognitive function, and a total of 11 articles exploring associations between SI, FSS, and memory (of which 5 overlapped), none investigated whether FSS mediated the association between SI and memory. Therefore, the research questions listed below constitute a novel line of research inquiry.

Aim 1: Is social isolation associated with memory across two timepoints of data from the Tracking Cohort of the Canadian Longitudinal Study on Aging (CLSA)?

Aim 2: Does the association in Aim 1 above change after adjusting for relevant sociodemographic, health, and lifestyle covariates?

Aim 3: Does functional social support mediate the association between social isolation and memory?

Aim 4: Does age group or sex moderate the effect of (i) SI on FSS, (ii) FSS on memory, (iii) SI on memory indirectly through FSS, and (iv) SI on memory (direct and total effects)?

3. Methods

3.1. Data source

3.1.1. The Canadian Longitudinal Study on Aging

The CLSA is a population-based, panel study collecting biological, physical, psychological, social, health, and environmental data from a sample of middle-aged and older adults[221]. The CLSA's key aim is to understand the determinants of health that contribute to successful aging, with the resulting information being used to guide public health practices and policies[221].

During initial recruitment between 2011 and 2015, the CLSA enrolled 51,338 participants aged 45-85 years at baseline (t_0)[222]. Participants are followed up every three years and the first set of longitudinal data collection was complete in 2018 (t_1)[222]. Participants provide a common set of core data, including demographic, social, psychological, economic, and health service utilization information relevant to health and aging.

The CLSA is composed of two separate cohorts–Tracking and Comprehensive–distinguished by the sample frames and data collection methodologies. The Tracking Cohort comprised 21,241 of the 51,338 t_0 participants. These individuals were recruited from all 10 provinces and data are being collected through computer-assisted telephone interviews by trained CLSA staff. The Comprehensive Cohort comprised 30,097 of the 51,338 t_0 participants. These persons were recruited within 25-50 kilometers of 11 data collection sites (DCSs) located in 7 provinces (except Saskatchewan, New Brunswick, and Prince Edward Island). Comprehensive Cohort data are collected through in-home interviews and in-person visits to the DCSs[222]. Besides the core data described above, individuals in the Comprehensive Cohort undergo

physical performance and clinical testing at their local DCS and may also choose to provide optional blood and urine samples[222].

The differences in sampling frames and modes of data collection raise questions about the validity of combining both cohorts in analyses. This is especially the case when investigating cognitive outcomes because the mode of administration of neuropsychological tests – in this case, telephone versus in person – can affect participants' test performance[223]. Therefore, this thesis utilized data from the Tracking Cohort only[224]. The Tracking Cohort was also chosen because its sample frame is less restrictive than the Comprehensive Cohort, i.e., recruitment across all geographical areas in the 10 provinces versus recruitment within 25-50 kilometers of 11 DCSs in 7 provinces.

3.1.2. Analytical Sample

Participants in the Tracking Cohort were recruited from three sources: a subset of participants enrolled in Statistics Canada's Canadian Community Health Survey-Healthy Aging 4.2 (CCHS-HA 4.2)[225], the registries of provincial healthcare systems (e.g., Ontario Hospital Insurance Plan rolls), and random digit dialing of landline telephones[222]. Participants were excluded from the study if they could not complete the study measures in either English or French; showed overt signs of cognitive impairment at the time of recruitment; resided in a Canadian territory; were a full-time member of the Canadian Armed Forces; were institutionalized (i.e., resided in a long-term care home); or resided on a First Nations settlement[222]. The CLSA recruited participants into pre-defined age and sex strata established for each province and later expanded their stratified sampling to enrol more persons with less than high school education[226]. Further information about the CLSA's sampling procedure is available elsewhere[226].

This thesis drew upon two timepoints of data for analyses (t_0 and t_1). Complete case analysis was used to handle missing data on all three main variables of interest, namely SI, FSS, and memory. Participants were removed from the analytical sample if they: (1) had missing data on SI at t_0; and/or (2) had missing data on FSS or memory at t_0 or t_1. Participants with missing covariate data were retained in the analytical sample by creating 'missing' response categories for all instances of missing covariate data. All descriptive, regression, and mediation analyses were undertaken using the analytical sample described in this paragraph.

3.2. Measures

3.2.1. Social Isolation

The main exposure variable was SI at t_0. SI was measured using an index developed by Menec et al.[24], which itself was based on Steptoe et al.'s work with the English Longitudinal Study on Ageing[63]. The index converts questions from the CLSA's Social Support, Social Network, Social Participation, Retirement Status, and Socio-Demographic Characteristics modules into a 5-point scale ranging from 0 to 5, with higher scores representing greater SI. Points are allocated based on an individual's marital/cohabiting status; retirement status; number and frequency of participation in social activities; and number/frequency of contact with friends, neighbours, relatives, siblings, or children within the past six months. Based on Menec et al.[24]'s recommendation, scores were dichotomized at a cut point of 2, with persons scoring 2-5 classified as socially isolated and those scoring 0-1 classified as not socially isolated. Complete details about the composition and computation of the SI index are provided in Appendix B.

3.2.2. Functional Social Support

The mediator variable was FSS at t_1. FSS scores were derived from the 19-item MOS-SSS[30] (Appendix C). Eighteen questions on the scale pertain to different subtypes of FSS,

including emotional/informational (8 questions), tangible (4 questions), affectionate (3 questions), and positive social interactions (3 questions). The 19th question - "someone to do things with to help you get your mind off things" - is not included in any of the subscales yet is used to compute the overall FSS score. The CLSA used the RAND scoring formula[227] to transform all question responses into an overall FSS score ranging from 0-100.

Due to the novelty of the thesis research and in line with previous research[116,132,214], only overall FSS was used as the mediator in the analysis. Since participants in the CLSA generally report high levels of FSS, descriptive analyses showed that FSS scores at both t_0 and t_1 were highly left skewed (see Section 4.2.2 below). To account for left skewness, FSS scores were dichotomized at the median (88.2 at t_0 and 89.5 at t_1) to create a "high" FSS group and a "low" FSS group.

To determine whether FSS at t_0 or t_1 was a better fit for mediation, a model containing a base set of covariates (Section 3.4.2 below provides a description of these covariates) and FSS at t_0 was compared to a model containing the same covariates and FSS at t_1. The two models were compared using the Akaike Information Criterion (AIC); a lower AIC value was computed for the model with FSS at t_1, suggesting this model was a better fit to the data. Using FSS at t_1 as the mediator variable was further substantiated by literature suggesting the need for a latency period to observe the effects of exposures on mediator and outcome variables[228].

3.2.3. Memory

The main outcome was memory function at t_1. A modified version of the RAVLT was used to measure participants' immediate (RAVLT I) and delayed (RAVLT II) recall memory. While the original RAVLT is a comprehensive test to evaluate short-term memory, working memory, and long-term memory[229], CLSA investigators modified the RAVLT to fit within the

time constraints of the participant interviews. The CLSA's modified RAVLT eliminates an interference list recall and reduces the number of recall administrations from five to two[224]. Therefore, the CLSA's modified RAVLT only measures working and episodic memory[230].

During the telephone interview, participants hear a recorded list of 15 words and are asked to immediately recall as many words as possible within 90 seconds (RAVLT I); five minutes later, participants are again asked to recall as many of the words as possible in 60 seconds, without hearing the recording again (RAVLT II). One point is assigned to each correctly recalled word or variant word. Variant words are those that sound similar to the 15 original words. The same variant word must be recalled at both administrations to receive points. Participants' responses to RAVLT I and II were recorded and later scored by trained CLSA staff.

CLSA created a derived variable for memory ($\mu = 100$, $\sigma = 15$) that combined scores from RAVLT I and RAVLT II when the raw scores for both test administrations were available[231]. This derived variable was used to quantify memory function at t_0 and t_1.

3.3. Covariates

Based on the literature about SI, FSS, and memory[31,35,36,45,46,94,132,204,210–212,214], the following variables were included as covariates in the analyses for Aims 2-4 above: (1) Sociodemographic variables: age group, sex, province, education, income; (2) Health status: depressive symptoms, number of chronic conditions, functional impairment; and (3) Lifestyle behaviours: smoking and alcohol consumption. Covariate levels reported at t_0 were included in the analysis. See Appendix D for a complete description of the covariates.

3.3.1. Sociodemographic

The CLSA dataset includes a four-level variable for age group: 45-54 years, 55-64 years, 65-74 years, and 75 years or older. Categories for sex were male and female. Education was

categorized into four groups representing one's highest level of educational attainment: less than high school, high school diploma, some post-secondary education, and post-secondary degree/diploma. Province of residence was listed as one of the ten Canadian provinces. Total annual household income was categorized into five levels: 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 more.

3.3.2. Health Status

The presence of severe depressive symptoms was measured using the CES-D10[219]. The CES-D10[219] is a well-validated depression screening tool that scores depressive symptomology on a scale from 0 to 30. Reports have shown the CES-D10 to have high internal consistency, test–retest reliability, and measurement invariance regarding factors such as language of administration, age group, and level of educational attainment[219,232]. Further, performance on the CES-D10 is correlated with other self-report measures and clinical ratings of depression[219]. A cut-off score of 10 or more is used to indicate the presence of severe depressive symptoms versus mild or no depressive symptoms[219]. This cut-off was utilized to control for depressive symptoms in the thesis.

Chronic conditions are assessed by self-report of doctor diagnosis of 11 chronic conditions that are associated with cognitive function. The conditions include high blood pressure, diabetes, cancer, hypothyroidism, chronic obstructive pulmonary disease, chronic cardiac conditions, stroke-related conditions, peripheral vascular disease, and asthma. The presence of chronic conditions was summed and assessed dichotomously as 'no chronic conditions' versus 'one or more chronic conditions'.

Functional status was assessed using measures of activities of daily living (ADL) and instrumental activities of daily living (IADL) from the Older Americans Resources and Services (OARS) Multidimensional Assessment Questionnaire[233]. ADLs refer to participants' ability to perform seven basic daily tasks such as eating, dressing, grooming, and walking. IADLs refer to the ability to perform seven high-level daily functions such as grocery shopping, money handling, meal preparation, and taking medications. The CLSA transforms participants' responses to the ADL and IADL questions into a derived variable for functional status on a five-level scale ranging from (1) no functional impairment, (2) mild impairment, (3) moderate impairment, and (4) severe impairment to (5) total functional impairment. In the thesis, functional status was dichotomized into 'no functional impairment' versus 'any level of functional impairment'[234].

3.3.3. Lifestyle Behaviours

The CLSA provides a derived variable for alcohol use[235] similar to the one used by Statistics Canada's CCHS-HA 4.2[236]. The variable represents participants' drinking habits within the past year and is coded into three groups. Participants who did not drink in the last 12 months comprised the 'not at all' group; participants who drank on occasion throughout the year, but less than once a month, comprised the 'occasionally' group; and participants who drank at least once a month comprised the 'regularly' group.

Smoking status was measured using a self-report questionnaire derived from the Canadian Health Measures Survey (CHMS)[237] and the Canadian Tobacco Use Monitoring Survey (CTUMS)[238]. Participants were asked about current smoking habits within the last month. Participants who did not smoke in the past 30 days were characterized as 'non-user'; participants who smoked at least one cigarette in the past 30 days, but not every day, were characterized as

'occasional user'; and participants who used at least one cigarette every day for the past 30 days were characterized as 'daily user'.

3.4. Data Analyses

3.4.1. Descriptive Analysis

T_0 descriptive statistics were computed for SI and all 10 covariates; t_0 and t_1 descriptive statistics were computed for overall FSS and dichotomized FSS, and overall memory scores. Categorical variables were summarized as frequencies and percentages. Continuous variables were summarized using medians and interquartile ranges (IQRs) if non-normally distributed or means and standard deviations if normally distributed. Simple linear regression was employed to conduct bivariate analyses by regressing memory scores at t_1 onto: (1) SI at t_0, (2) FSS at t_0 and t_1, (3) memory scores at t_0, and (4) covariates at t_0.

3.4.2. Regression Analysis

Aim 1: To assess if SI was associated with memory, memory scores at t_1 were regressed onto t_0 SI status, controlling for FSS at t_0 and t_1, and memory at t_0. Based on CLSA recommendations to address the complex survey design, the model in Aim 1 (the 'base' model) included age group, sex, and province as covariates. The base regression model equation was:

$$Memory_{t1} = \hat{\beta}_{intercept} + \hat{\beta}_{SI_{t0}} + \hat{\beta}_{AgeGroup_{t0}} + \hat{\beta}_{Sex_{t0}} + \hat{\beta}_{Province_{t0}} + \hat{\beta}_{FSS_{t1}} + \hat{\beta}_{FSS_{t0}} + \hat{\beta}_{Memory_{t0}} + \varepsilon \quad [1]$$

Aim 2: The remaining covariates at t_0 (i.e., sociodemographic, health status, lifestyle behaviours) were added to the base model from Aim 1 to create the 'adjusted' model. The change in the regression coefficient ($\hat{\beta}$) for SI was compared between the base and adjusted models to determine whether the base or adjusted model should be used for the analyses in Aims 3 and 4 below. The 10% rule[239] was applied to assess whether the covariates included in the adjusted model confounded the association between SI and memory, such that if the change in $\hat{\beta}$

for SI in the adjusted model compared to the base model was ± 10% or greater, then the adjusted model would be used. If the change was less than ± 10%, then the base model would be used for Aims 3 and 4.

3.4.3. Aim 3 – Mediation Analysis

3.4.3.1. Methodological background

Mediation analyses are used to explore whether part or all of the association between an exposure (X) and an outcome (Y) is linked through an intermediary variable, known as a mediator (M). A mediation model (such as the one depicted in Figure 1 below) comprises an indirect, a direct, and a total effect. The indirect effect (or the "ab" path) represents the effect of X on Y that passes through M. This effect, also known as the 'mediation effect', is the product of (1) $\hat{\beta}_X$ for the regression of M on X ("a" path) and (2) $\hat{\beta}_M$ for the regression of Y on M controlling for X ("b" path).

The direct effect of X on Y (or the "c-prime" path) represents the association between X and Y, controlling for M. The summation of the "ab" and "c-prime" paths produces the total effect ("c" path) of X on Y. All these pathways may be adjusted for covariates, in which case the interpretation of results changes to include the covariates. For example, "the effect of X on Y, passing through M and adjusted for covariates, is [EFFECT SIZE]." Effect sizes in mediation

analyses are not restricted to continuous units and may take on forms such as log odds ratios or log relative risks, among others.

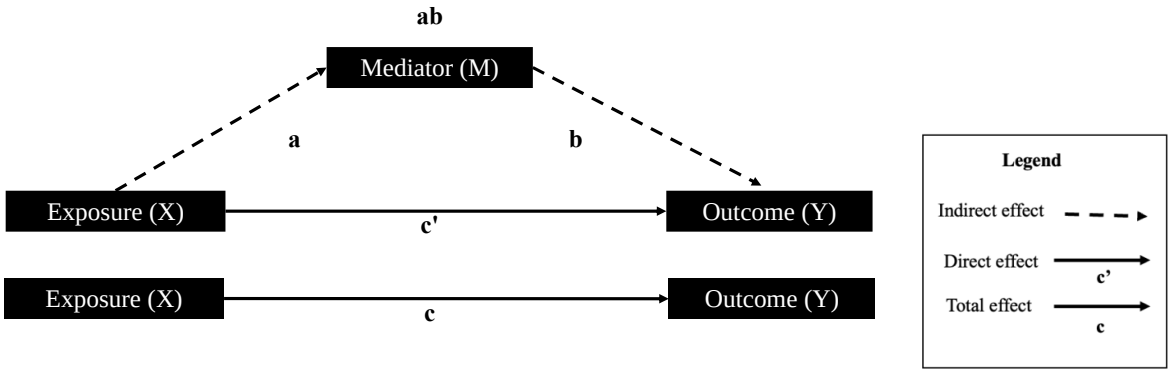

Figure 1. Mediation Model Conceptual Diagram

Notes: The mediator (M) and the outcome (Y) are both dependent variables. M is dependent upon the exposure (X) ("a" path), while Y is dependent upon X and M ("b" and "c-prime" paths).

The joint significance test[240] is an approach to assess the presence of an indirect/mediation effect. Under this test, mediation is present if the $\hat{\beta}s$ for the "a" and "b" paths are both statistically significant. The joint significance test is different from the index approach recommended by Hayes[241] et al. in the conditional process analysis macro. The index approach relies on a single statistical significance test of the "ab" path to conclude whether mediation is present. The joint significance test is preferred over the index approach because Yzerbyt et al. found that checking the significance of the "a" and "b" paths individually reduces the risk of Type I error – concluding the presence of mediation when no mediation exists – compared to checking the "ab" path[240].

3.4.3.2. Analytical approach

Based on the joint significance test[240], mediation was considered to be present if the 95% CIs for $\hat{\beta}_{SI_{t_0}}$ on the "a" path and $\hat{\beta}_{FSS_{t_1}}$ on the "b" path both did not include 0. Following the approach of Imai et al.[242–245] and Yamamoto[246]: (1) FSS_{t1} was regressed on SI_{t0} to obtain $\hat{\beta}_{SI_{t_0}}$ for the "a" path; (2) $memory_{t1}$ was regressed on SI_{t0}, and FSS_{t1} to obtain $\hat{\beta}_{FSS_{t_1}}$ for the "b" path. Table 1 outlines all the variables contained in the models for the "a" path and "b" path. The mediation diagram depicting the effects of SI on memory, channelled through FSS as the mediator, is found in Figure 2.

Table 1. Components of the "a" and "b" Paths

	"a" Path: regress M on X	"b" Path: regress Y on M
Base model	**Exposure (X):** Social Isolation (t_0) **Outcome (M):** Functional Social Support (t_1) **Baseline adjustment:** Functional Social Support (t_0) Memory Function (t_0) **Covariates:** Age group (t_0) Sex (t_0) Province (t_0)	**Exposure (X):** Functional Social Support (t_1) **Outcome (M):** Memory function (t_1) **Baseline adjustment:** Social Isolation (t_0) Functional Social Support (t_0) Memory Function (t_0) **Covariates:** Age group (t_0) Sex (t_0) Province (t_0)
Adjusted Model	Same as base model with adjustment for sociodemographic, health status, and lifestyle behaviour covariates for the "a" and "b" paths • **Sociodemographic:** Education (t_0), Total annual household income (t_0) • **Health:** Functional status (t_0), Chronic conditions (t_0), Depressive symptoms (t_0) • **Lifestyle:** Smoking status (t_0), Alcohol consumption (t_0)	

Notes: t_0=Baseline, t_1=Follow-up

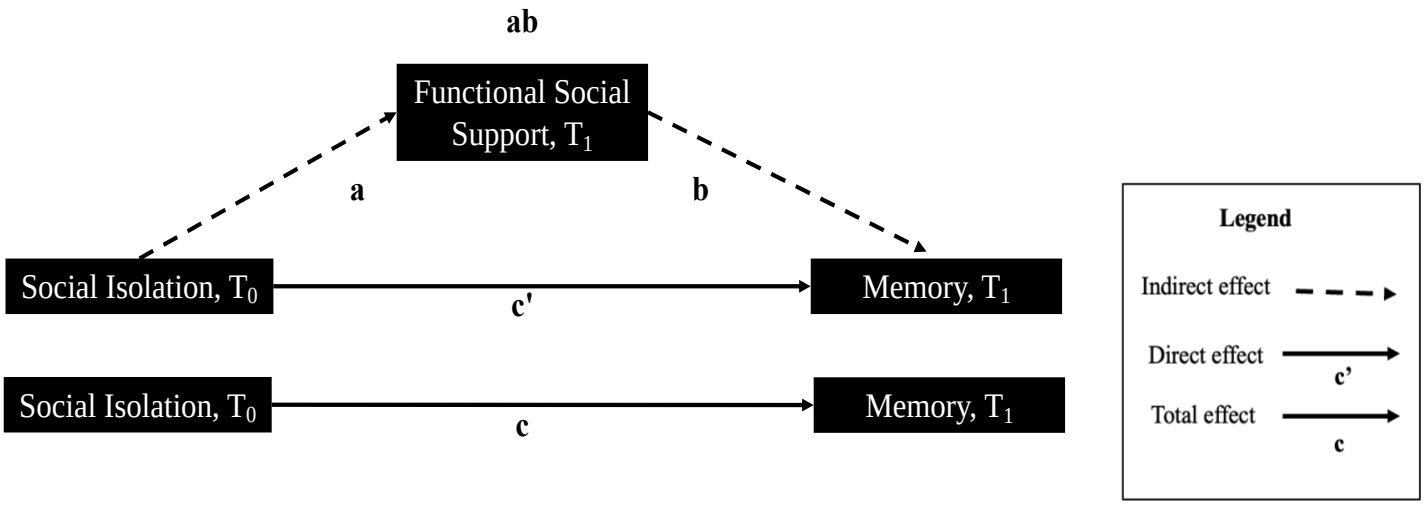

Figure 2. Proposed Mediation Diagram
Notes: T_0 = baseline; T_1 = follow-up

To complete the mediation analysis, the "a" and "b" path models were used to calculate $\hat{\beta}$s for the "ab", "c-prime", and "c" paths. The mathematical calculations to obtain the $\hat{\beta}$s for these three paths are shown in Imai et al.[242–245] and Yamamoto[246]. The calculations were implemented using R v4.3.0 (The R Foundation for Statistical Computing, Vienna, Austria) and the mediation package[247]. This package generated 95% CIs around the $\hat{\beta}$s for the "ab", "c-prime", and "c" paths via the Monte Carlo sampling method, White's heteroskedasticity-consistent estimator for the covariance matrix, and 10,000 simulations[240]. The CLSA's sample weights were not employed in the mediation analysis because Imai et al.[242–245] and Yamamoto's[246] calculations were not designed to handle sample weights.

As noted above, the total effect of a mediation analysis comprises the indirect and direct effects. An additional component of mediation analysis that was estimated in this thesis was the proportion mediated (PM), obtained by dividing (i) the $\hat{\beta}$ for the indirect effect of SI on memory that acts through FSS ("ab" path) by (ii) the $\hat{\beta}$ for the total effect of SI on memory ("c" path):

$$\mathrm{PM} = \frac{\mathrm{ab}}{\mathrm{c}} \qquad [2]$$

The mediation package's output provides a point estimate of the PM and a 95% CI for the point estimate.

The $\hat{\beta}$s for the "a" and "b" paths should ideally be based on the same scale (linear, logistic, etc.) to permit the calculation of the mediation effect ("ab" path). However, the "a" path of the mediation model was computed using logistic regression because the outcome (FSS_{t1}) was a binary variable, whereas $memory_{t1}$ on the "b" path was continuous. To permit the mediation package to compute the "ab" path, the "a" path's $\hat{\beta}_{SI_{t_0}}$ and 95% CI were rescaled from the logistic to the linear scale following Kenny's procedure[248], thereby matching the "b" path, whose $\hat{\beta}$s and CIs were obtained through multiple linear regression. Section 3.4.3.3 below describes additional components of the mediation analysis.

3.4.3.3. Baseline Outcome Adjustment

As informed by Hayes[241], associations in regression models with t_1 variables as outcomes may be inflated by not controlling for t_0 values of these variables. Therefore, the "a" and "b" path regression models were both controlled for FSS_{t0}. Although FSS_{t1} was not the outcome variable in the "b" path model (it was the outcome in the "a" path model), FSS_{t0} was added to both models to ensure a common set of covariates were utilized in the calculation of the "ab", "c-prime", and "c" paths. The inclusion of FSS_{t0} was empirically substantiated because the change in median FSS score between t_0 and t_1 was statistically significant ($p < 0.05$) according to a Wilcoxon signed rank test. Furthermore, the Spearman's correlation between FSS_{t0} and FSS_{t1} was 0.57, which suggested a lack of agreement between FSS at t_0 and t_1.

For memory function, the same logic as with FSS was employed to control for memory at t_0 in the "a" and "b" path models. Descriptively, a scatterplot (Appendix E, Figure E-1) showed a positive relation between t_0 and t_1 memory scores; however, a Bland-Altman plot (Appendix E,

Figure E-2) showed individual-level variation between t_0 and t_1 memory scores because numerous data points fell outside the limits of agreement. Therefore, t_0 memory scores did not neatly predict t_1 memory scores.

3.4.4. Aim 4 – Moderated Mediation

To investigate the possibility of moderated mediation by age group and sex, the analysis described for Aim 3 above was repeated for each of the four levels of age group (45-54, 55-64, 65-74, 75+ years). For all five mediation pathways, Cuzick's forest plot method[249] was used to check for effect modification by comparing the 95% CI of the relevant $\hat{\beta}$ within each stratum of age group to the unstratified $\hat{\beta}$ from Aim 3 above. Moderated mediation on any path was identified if all the stratum-specific 95% CIs excluded the unstratified $\hat{\beta}$. The moderated mediation analysis was repeated by stratifying on female versus male sex. When stratifying on age group or sex, the stratification variable in question was removed as a covariate from the regression models.

3.4.5. Missing data

The thesis candidate assessed the potential impact of missing data by exploring associations between dropping out of the CLSA post-baseline (yes/no) and SI_{t0} status, $memory_{t0}$ scores, and FSS_{t0} scores. A simple logistic regression model was utilized to obtain the odds of dropping out among persons with SI versus no SI at baseline. Mean memory scores and median FSS scores at baseline were compared across dropouts versus non-dropouts using the t-test and the Mann-Whitney U test, respectively.

To further assess the impact of missing data, two sensitivity analyses were conducted by modifying the analytical sample described in Section 3.1.2 above. For the first modification, Aims 2-4 were repeated in an analytical sample that excluded participants with missing data on

any covariate. For the second modification, Aim 3 was repeated using multiple imputation (MI) to replace missing covariate values with imputed values.

For the MI approach, variables with high levels of missingness (> 2%) were identified and imputed using predictive mean matching (PMM)[250] in R's mice package[251]. In PMM, the analytical sample (S) is partitioned into individuals with complete information on all covariates (S_C) and individuals with missing information on one or more covariates (S_M)[250]. For every S_M participant, a set of candidate participants from S_C whose characteristics are similar to those of the S_M participant is formed. Then, a single participant from the set of candidates is selected randomly and that person's data are used to replace the missing values for the S_M participant in question.

Nine imputation cycles (each yielding one imputed dataset) were conducted to impute for missing data. The mediation analysis for Aim 3 in Section 3.4.3 above was repeated on each of the nine imputed datasets. The relevant $\hat{\beta}$s for each of the five pathways across the nine datasets were combined using Rubin's Rules[252,253], whose equations were programmed into an Excel spreadsheet and independently double-verified for accuracy. The resulting single set of combined $\hat{\beta}$s served as the final result of the MI procedure.

The MI procedure emerged from work conducted for a Masters-level research project in the University of Waterloo's Department of Statistics and Actuarial Science[254]. This thesis was the first practical test of the procedure; the imputed results were presented solely as a trial run to inform future use of MI. Therefore, MI was not undertaken to explore moderated mediation in Aim 4.

4. Results

4.1. Derivation of the Analytical Sample

The analytical sample was derived by removing participants who did not provide any t_1 information, who had missing information on the exposure at t_0, or who had missing information on the mediator or outcome variables at t_0 or t_1. Overall, 17,052 of the 21,241 participants at t_0 (80.3%) provided t_1 information. After removing participants who had missing SI information at t_0 and those who had missing FSS and memory information at t_0 or t_1, 12,834 out of 17,052 participants (75.4%) remained in the analytical sample. Figure 3 below depicts the sequential removal of participants from the study.

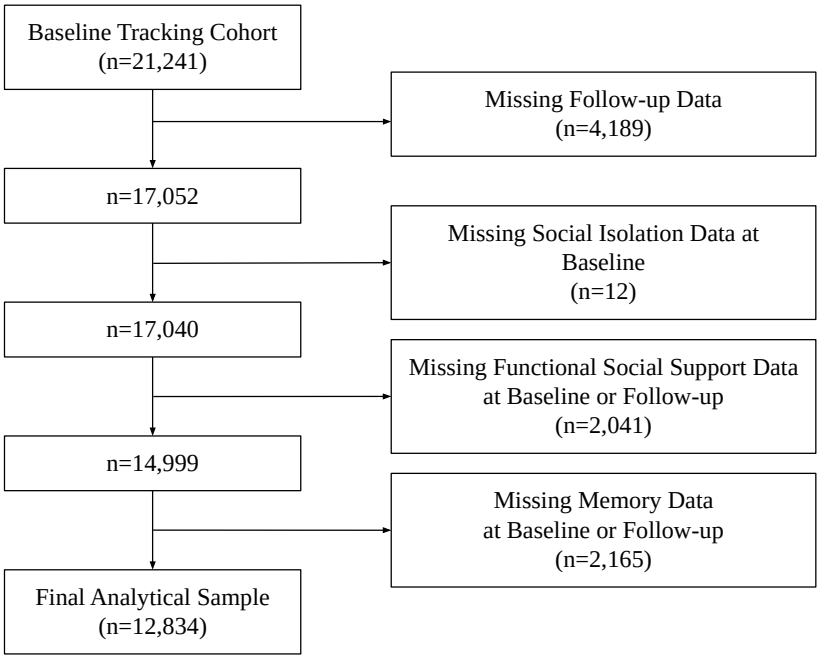

Figure 3. Derivation of Analytical Sample

4.2. Descriptive Analyses

4.2.1. Social Isolation

The distribution of SI at t_0 is shown in Figure 4. Approximately 20.5% of participants in the analytical sample were socially isolated (n = 2,632). Descriptive results for t_0 SI status are summarized in Table 2 below.

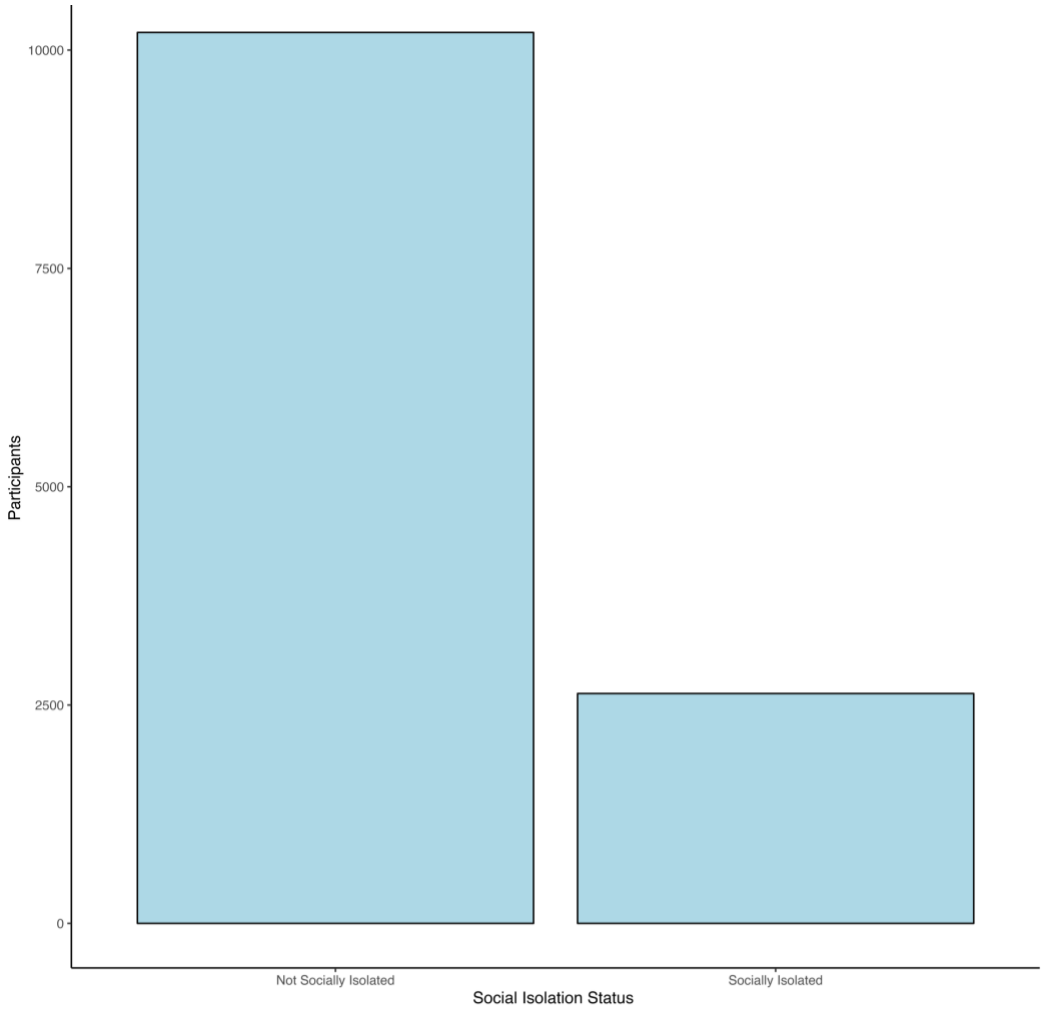

Figure 4. Distribution of Baseline Social Isolation Index (Dichotomized)

Table 2. Analytical Sample Characteristics: Overall and by Social Isolation Status at Baseline

Characteristic	Total (n = 12,834)	Not Socially Isolated (n = 10,202)	Socially Isolated (n = 2,632)
	n (%)	n (%)	n (%)
Sex (t_0)			
Male	6,182 (48.2)	4,923 (48.3)	1,259 (47.8)
Female	6,652 (51.8)	5,279 (51.7)	1,373 (52.2)
Age (t_0)			
45-54 years	3,973 (30.1)	3,326 (32.6)	647 (24.6)
55-64 years	4,287 (33.4)	3,370 (33.0)	917 (34.8)
65-74 years	2,721 (21.2)	2,118 (20.8)	603 (22.9)
75 years or older	1,853 (14.4)	1,388 (13.6)	465 (17.7)
Education (t_0)			
Less than high school	875 (6.8)	660 (6.5)	215 (8.2)
High school diploma	1,680 (13.1)	1,355 (13.3)	325 (12.3)
Some post-secondary education	930 (7.3)	719 (7.0)	211 (8.0)
Post-secondary degree/diploma	9,349 (72.9)	7,468 (73.2)	1,881 (71.5)
Province of residence (t_0)			
Alberta	1,235 (9.6)	1,015 (9.9)	220 (8.4)
British Columbia	1,437 (11.2)	1,085 (10.6)	352 (13.4)
Manitoba	896 (7.0)	724 (7.1)	172 (6.5)
New Brunswick	826 (6.4)	638 (6.3)	188 (7.1)
Newfoundland and Labrador	711 (5.5)	586 (5.7)	125 (4.7)
Nova Scotia	964 (7.5)	781 (7.7)	183 (7.0)
Ontario	3,007 (23.4)	2,452 (24.0)	555 (21.1)
Prince Edward Island	679 (5.3)	542 (5.3)	137 (5.2)
Québec	2,239 (17.5)	1,702 (16.7)	537 (20.4)
Saskatchewan	840 (6.5)	677 (6.6)	163 (6.2)
Total annual household outcome (t_0)			
< $20,000	573 (4.5)	**283 (2.8)**	**290 (11.0)**
$20,000 to < $50,000	3,132 (24.4)	**2,254 (22.1)**	**878 (33.4)**
$50,000 to < $100,000	4,569 (35.6)	**3,760 (36.9)**	**809 (30.7)**
$100,000 to < $150,000	2,271 (17.7)	**2,005 (19.7)**	**266 (10.1)**
≥ $150,000	1,622 (12.6)	**1,450 (14.2)**	**172 (6.5)**
Missing	667 (5.2)	**450 (4.4)**	**217 (8.2)**
Functional status (t_0)			
No assistance required	11,626 (90.6)	**9,355 (91.7)**	**2,271 (86.3)**
Assistance required ≥ 1 activity	1,152 (9.0)	**812 (8.0)**	**340 (12.9)**
Missing	56 (0.4)	**35 (0.3)**	**21 (0.8)**
Chronic conditions (t_0)			
No chronic conditions	1,255 (9.8)	**1,081 (10.6)**	**174 (6.6)**
≥ 1 chronic conditions	11,549 (90.0)	**9,095 (89.1)**	**2,454 (93.2)**
Missing	30 (0.2)	**26 (0.3)**	**4 (0.2)**

Depressive symptoms (t_0)			
Not severe	10,907 (85.0)	**8,853 (86.8)**	**2,054 (78.0)**
Severe	1,093 (14.8)	**1,328 (13.0)**	**575 (21.8)**
Missing	24 (0.2)	**21 (0.2)**	**3 (0.1)**
Current smoking status (t_0)			
Non-smoker	7,700 (60.0)	**6,164 (60.4)**	**1,536 (58.4)**
Occasional smoker	214 (1.7)	**155 (1.5)**	**59 (2.2)**
Daily smoker	953 (7.4)	**679 (6.7)**	**274 (10.4)**
Missing	3,967 (30.9)	**3,204 (31.4)**	**763 (29.0)**
Alcohol consumption (t_0)			
Non-drinker	1,369 (10.7)	**998 (9.8)**	**371 (14.1)**
Occasional drinker	1,924 (15.0)	**1,466 (14.4)**	**458 (17.4)**
Regular drinker	9,152 (71.3)	**7,428 (72.8)**	**1,724 (65.5)**
Missing	389 (3.0)	**310 (3.0)**	**79 (3.0)**
Functional Social Support (t_0)			
Low	6636 (51.7)	**4905 (48.1)**	**1731 (65.8)**
High	6198 (48.3)	**5297 (51.9)**	**901 (34.2)**
Functional Social Support (t_1)			
Low	6653 (51.8)	**4960 (48.6)**	**1693 (64.3)**
High	6181 (48.2)	**5242 (51.4)**	**939 (35.7)**

Notes: Chi-square p-value< 0.05 in bolded font; frequencies shown are column %; t_0 = baseline; t_1 = follow-up; Not severe depressive symptoms $<$ 10; Severe depressive symptoms $\geq$ 10.

4.2.1.1. Distribution of Covariates by Social Isolation Status

Table 2 shows the distribution of participants' sociodemographic, health, and lifestyle covariates at t_0, both overall and stratified by t_0 SI status. Of the entire sample, just over half the participants were female (51.8%), a third were between the ages of 55-64 years (33.4%), and almost three-quarters had a post-secondary degree or diploma (72.9%). Most participants lived in Ontario (23.4%), Québec (17.5%), or British Columbia (11.2%). Just over one-third of participants (35.6%) reported annual household incomes from $50,000 to under $100,000 and approximately one-third of participants (30.3%) reported annual household incomes over $100,000.

After stratifying on SI status, the distributions of males and females and across all age groups in the socially isolated and not socially isolated groups were roughly the same (Table 2). The proportionate distribution of educational levels was relatively even across both SI groups, as was the proportionate distribution of province of residence. Compared to the proportion of persons who were not socially isolated, a greater proportion of socially isolated participants had an annual household income from $20,000 to under $50,000, whereas a lower proportion of socially isolated participants had an annual household income over $100,000.

Regarding the distribution of the health status covariates in the overall sample, most participants reported not requiring assistance for any daily activity (90.6%), although most participants had at least one chronic condition (90.0%). Most participants also reported not having severe depressive symptoms (85.0%). A greater proportion of persons who were socially isolated, compared to the proportion of persons who were not socially isolated, reported requiring assistance with at least one daily activity, had one or more chronic condition(s), and had severe depressive symptomology.

Turning to the lifestyle variables, most participants in the total sample were non-smokers and regular drinkers (60.0% and 71.3%, respectively). Furthermore, greater proportion of persons who were not socially isolated, compared to the proportion of persons who were socially isolated were non-smokers and regular drinkers

Lastly, at t_0 and t_1, a greater proportion of socially isolated participants had low compared to high FSS.

4.2.2. Functional Social Support

The distribution of FSS scores at both t_0 and t_1 were left skewed (Figure 5a and Figure 5b). Scores ranged from 0-100, with 75% of participants scoring above 75 at both time points. The median scores for overall FSS were 88.2 (IQR: 22.4) at t_0 and 89.5 (IQR: 23.7) at t_1. To account for the left skewedness of FSS, the scores for each timepoint were dichotomized at the median to create "high" and "low" FSS groups. Roughly even proportions of participants – based on the median – were spread across the high and low groups (Figure 5c and Figure 5d).

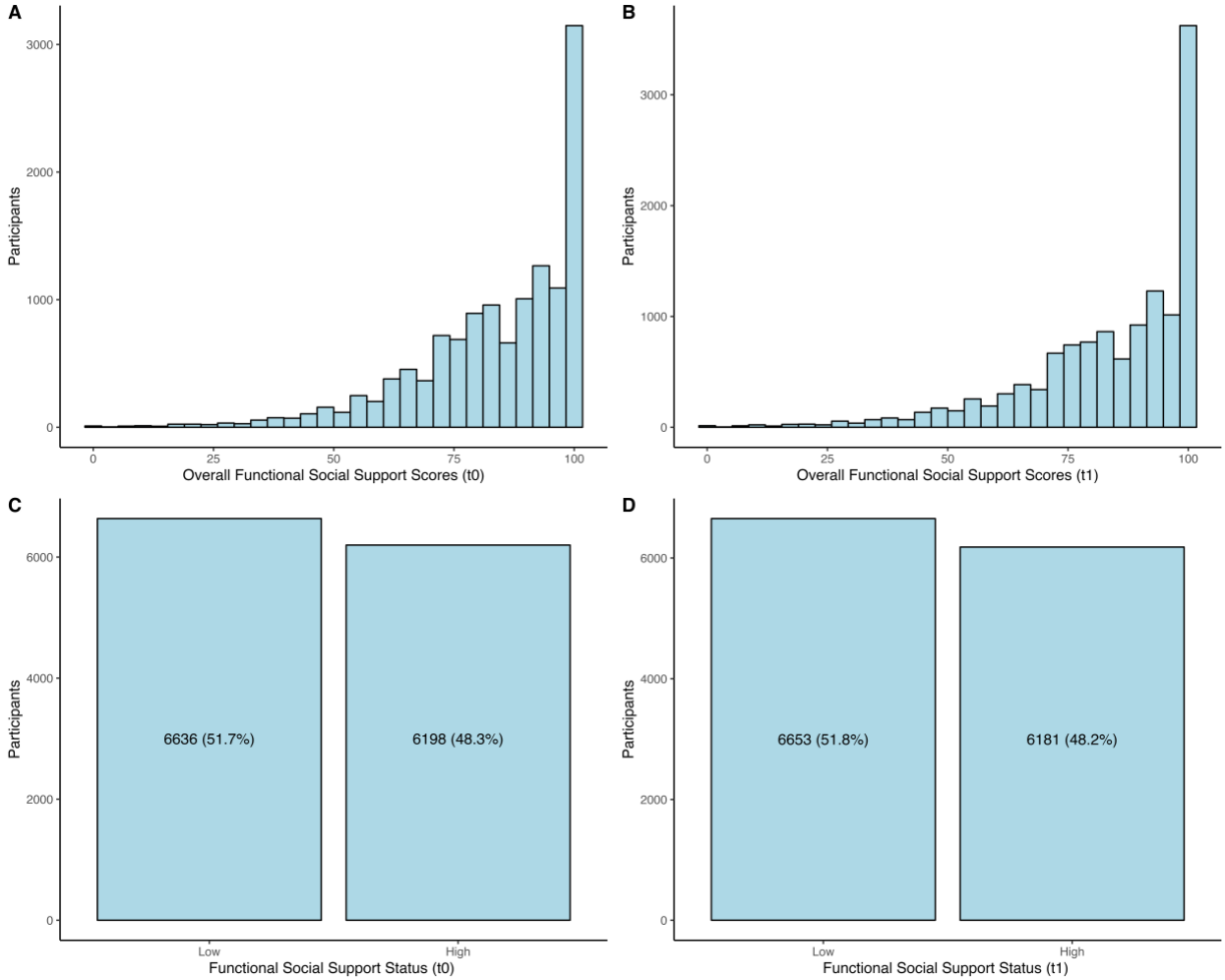

Figure 5. Distribution of Functional Social Support

Figure 5 (A): Distribution of Baseline (t_0) Functional Social Support - Continuous
Figure 5 (B): Distribution of Follow-up (t_1) Functional Social Support - Continuous
Figure 5 (C): Distribution of Baseline (t_0) Functional Social Support - Dichotomized
Figure 5 (D): Distribution of Follow-up (t_1) Functional Social Support – Dichotomized

The distribution of covariates remained relatively stable in the low and high FSS groups between both timepoints (Table 3). The proportionate distributions of sociodemographic, health status, and lifestyle behaviour covariates in the low and high FSS groups did not change between t_0 and t_1. However, at t_0 and t_1, a greater proportion of participants in the low FSS group were socially isolated compared to in the high FSS group ($p<0.0001$).

Table 3. Analytical Sample Characteristics by Dichotomous Functional Social Support Scores at Baseline and Follow-up

Characteristic	Baseline FSS		Follow-up FSS	
	Low (n = 6636)	**High** (n = 6198)	**Low** (n = 6653)	**High** (n = 6181)
	n (%)	**n (%)**	**n (%)**	**n (%)**
Sex (t_0)				
Male	3095 (46.6)	3087 (49.8)	3022 (45.4)	3160 (51.1)
Female	3541 (53.4)	3111 (50.2)	3631 (54.6)	3021 (48.9)
Age Group (t_0)				
45-54 years	2069 (31.2)	1904 (30.7)	2037 (30.6)	1936 (31.3)
55-64 years	2228 (33.6)	2059 (33.2)	2175 (32.7)	2112 (34.2)
65-74 years	1355 (20.4)	1366 (22.0)	1401 (21.1)	1320 (21.4)
75 years or older	984 (14.8)	869 (14.0)	1040 (15.6)	813 (13.2)
Province (t_0)				
Ontario	1515 (22.8)	1492 (24.1)	1518 (22.8)	1489 (24.1)
Alberta	669 (10.1)	566 (9.1)	700 (10.5)	535 (8.7)
British Columbia	772 (11.6)	665 (10.7)	771 (11.6)	666 (10.8)
Manitoba	491 (7.4)	405 (6.5)	457 (6.9)	439 (7.1)
New Brunswick	424 (6.4)	402 (6.5)	416 (6.3)	410 (6.6)
Newfoundland and Labrador	354 (5.3)	357 (5.8)	360 (5.4)	351 (5.7)
Nova Scotia	459 (6.9)	505 (8.1)	486 (7.3)	478 (7.7)
Prince Edward Island	339 (5.1)	340 (5.5)	345 (5.2)	334 (5.4)
Québec	1157 (17.4)	1082 (17.5)	1176 (17.7)	1063 (17.2)
Saskatchewan	456 (6.9)	384 (6.2)	424 (6.4)	416 (6.7)
Education (t_0)				
Less than secondary	490 (7.4)	385 (6.2)	465 (7.0)	410 (6.6)
Completed secondary	886 (13.4)	794 (12.8)	856 (12.9)	824 (13.3)
Some post-secondary	490 (7.4)	440 (7.1)	489 (7.4)	441 (7.1)
Post-secondary degree or diploma	4770 (71.9)	4579 (73.9)	4843 (72.8)	4506 (72.9)

Total annual household outcome (t_0)				
< $20,000	418 (6.3)	155 (2.5)	424 (6.4)	149 (2.4)
$20,000 to < $50,000	1808 (27.2)	1324 (21.4)	1865 (28.0)	1267 (20.5)
$50,000 to < $100,000	2244 (33.8)	2325 (37.5)	2278 (34.2)	2291 (37.1)
$100,000 to < $150,000	1071 (16.1)	1200 (19.4)	1012 (15.2)	1259 (20.4)
≥ $150,000	696 (10.5)	926 (14.9)	669 (10.1)	953 (15.4)
Missing	399 (6.0)	268 (4.3)	405 (6.1)	262 (4.2)
Functional Status (t_0)				
No assistance required	5894 (88.8)	5732 (92.5)	5901 (88.7)	5725 (92.6)
Assistance required ≥ 1 activity	712 (10.7)	440 (7.1)	718 (10.8)	434 (7.0)
Missing	30 (0.5)	26 (0.4)	34 (0.5)	22 (0.4)
Chronic Conditions (t_0)				
No chronic conditions	590 (8.9)	665 (10.7)	557 (8.4)	698 (11.3)
≥ 1 chronic conditions	6031 (90.9)	5518 (89.0)	6082 (91.4)	5467 (88.4)
Missing	15 (0.2)	15 (0.2)	14 (0.2)	16 (0.3)
Depressive Symptoms (t_0)				
Not severe	5217 (78.6)	5690 (91.8)	5291 (79.5)	5616 (90.9)
Severe	1407 (21.2)	496 (8.0)	1346 (20.2)	557 (9.0)
Missing	12 (0.2)	12 (0.2)	16 (0.2)	8 (0.1)
Smoking Status (t_0)				
Non-smoker	3922 (59.1)	3778 (61.0)	3948 (59.3)	3752 (60.7)
Daily smoker	559 (8.4)	394 (6.4)	555 (8.3)	398 (6.4)
Occasional smoker	124 (1.9)	90 (1.5)	124 (1.9)	90 (1.5)
Missing	2031 (30.6)	1936 (31.2)	2026 (30.5)	1941 (31.4)
Alcohol Consumption (t_0)				
Non-drinker	785 (11.8)	584 (9.4)	787 (11.8)	582 (9.4)
Regular drinker	4556 (68.7)	4596 (74.2)	4571 (68.7)	4581 (74.1)
Occasional drinker	1101 (16.6)	823 (13.3)	1091 (16.4)	833 (13.5)
Missing	194 (2.9)	195 (3.1)	204 (3.1)	185 (3.0)
Social Isolation Status (t_0)				
Not Socially Isolated	4905 (73.9)	5297 (85.5)	4960 (74.6)	5242 (84.8)
Socially Isolated	1731 (26.1)	901 (14.5)	1693 (25.4)	939 (15.2)

Notes: t_0 = baseline; t_1 = follow-up; FSS= functional social support; Not severe depressive symptoms < 10; Severe depressive symptoms ≥ 10.

4.2.3. Memory

Memory scores at both time points were roughly normally distributed with some right skewness (Figure 6a and Figure 6b) and means of 100.3 and 102.0 at t_0 and t_1, respectively (Table 4). The distribution of memory among the male and female groups was also normal at t_0 and t_1, with similar sets of mean values at both timepoints (Table 5). Across the age groups, t_0 memory scores were also normally distributed with comparable mean values (Table 5).

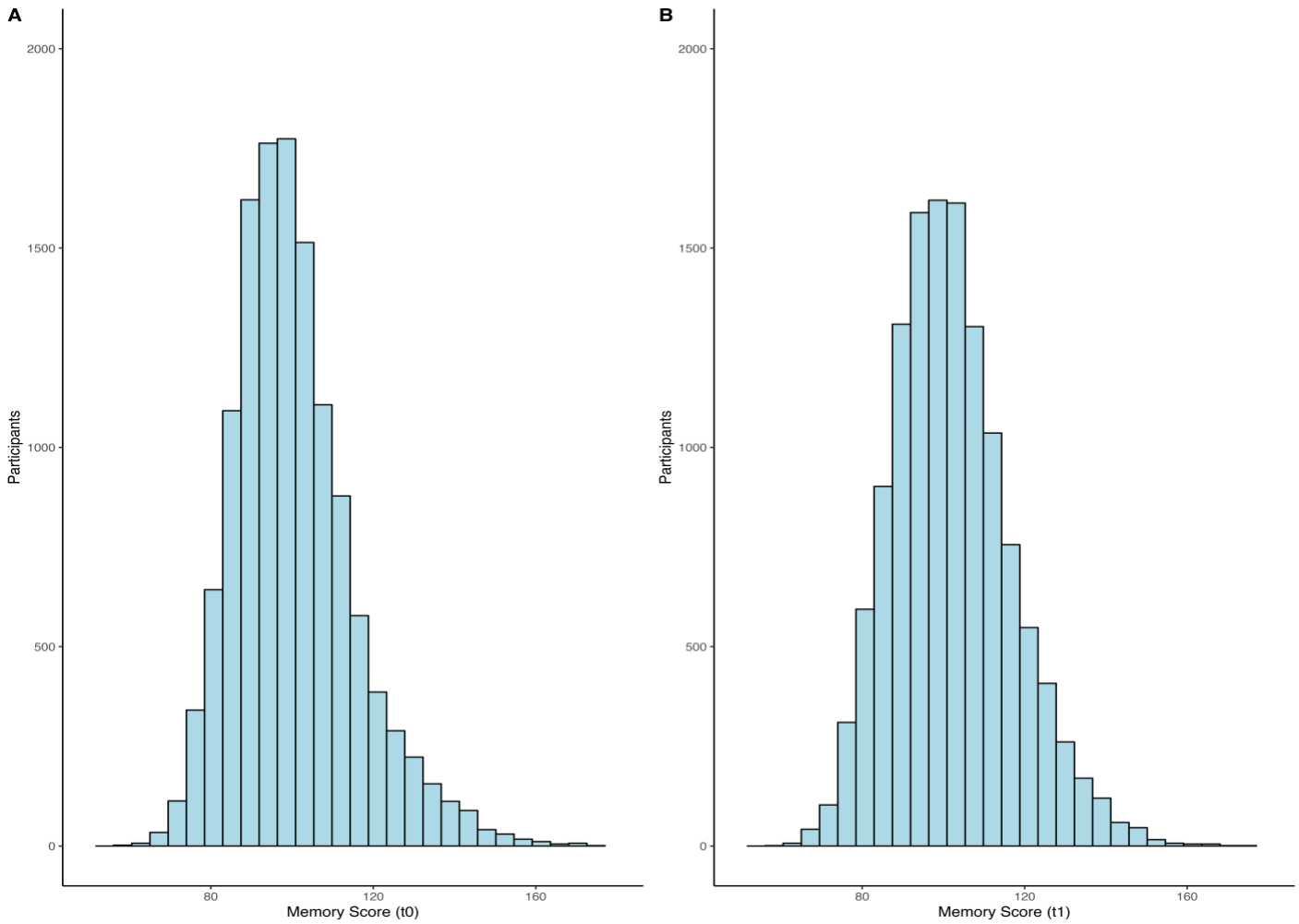

Figure 6. Distribution of Memory Scores
Figure 6 (A): Distribution of Baseline Memory Scores
Figure 6 (B): Distribution of Follow-up Memory Scores

Table 4. Continuous Memory Scores at Baseline and Follow-up

Memory score	Mean (SD) (95% CI)	Median (IQR)	Minimum	Maximum
Baseline	100.3 (14.8) (100.1,100.7)	98.4 (18.1)	59.2	174.6
Follow-up	102.0 (14.7) (101.7,102.2)	100.7 (19.0)	57.8	180.4

Notes: SD = standard deviation; CI = confidence interval; IQR = interquartile range.

Table 5. Baseline and Follow-up Memory Scores: Stratified by Sex and Age Group

Memory score		Mean (SD)	Median (IQR)	Minimum	Maximum
Baseline	Male	100.5 (14.9)	98.4 (17.7)	61.0	174.6
	Female	100.2 (14.7)	98.4 (18.3)	59.2	162.7
Follow-up	Male	101.9 (14.6)	100.5 (18.5)	63.7	180.4
	Female	102.0 (14.8)	100.9 (19.6)	57.8	161.3
Baseline	45-54 years	99.4 (14.1)	98.1 (17.7)	59.2	170.4
	55-64 years	100.8 (14.8)	99.0 (18.0)	59.8	162.7
	65-74 years	101.9 (15.6)	99.5 (18.6)	64.3	174.6
	75+ years	99.1(14.8)	96.8 (17.4)	68.0	171.6
Follow-up	45-54 years	102.4 (13.8)	101.3 (18.2)	57.8	156.5
	55-64 years	102.7 (14.5)	101.8 (18.5)	62.6	173.5
	65-74 years	102.7 (15.7)	101.2 (19.5)	65.9	178.7
	75+ years	98.3 (15.0)	96.1 (18.9)	65.1	180.4

Notes: SD = standard deviation; IQR = interquartile range.

4.2.3.1. Bivariate Associations – Covariates and Memory

The associations between t_1 memory regressed on t_0 SI status, t_0 sociodemographic, health status, and lifestyle behaviour covariates, and t_0 and t_1 FSS are shown in Table 6. Being socially isolated at t_0 was significantly associated with lower t_1 memory scores, suggesting that SI adversely impacts memory over three years of follow-up ($\hat{\beta}$ = -1.43; 95% CI: -2.06, -0.80).

Memory scores at t_1 were not statistically significantly different for females compared to males ($\hat{\beta}$ = 0.12; 95% CI: -0.39, 0.63. Compared to persons aged 45-54 years, participants aged 55-64 years and 65-74 years had slightly better memory scores ($\hat{\beta}$ = 0.34; 95% CI: 0.29, 0.97; $\hat{\beta}$ = 0.30; 95% CI: 0.42, 1.01, respectively), whereas participants aged 75 years or older had worse memory scores ($\hat{\beta}$ = -4.14; 95% CI: -4.94, -3.33). Across the 10 provinces, only individuals from New Brunswick had significantly lower memory scores compared to individuals from Ontario ($\hat{\beta}$ = -1.42; 95% CI: -2.55, -0.28).

None of the associations between educational attainment and memory were significant; however, income was significantly positively associated with memory in a dose-response manner, except for the missing category, which had a regression coefficient like that of the "less than $20,000" group.

Among the health status variables, requiring assistance for at least one daily activity and having missing information on functional status were both significantly associated with lower memory scores, compared to not needing any assistance for any activity ($\hat{\beta}$ = -4.54; 95% CI: -5.43, -3.65; $\hat{\beta}$ = -4.42; 95% CI: -8.27, -0.57, respectively). Having one or more chronic condition(s) was also significantly negatively associated with memory score ($\hat{\beta}$ = -1.86; 95% CI: -2.72, -1.00), compared to having no chronic conditions. Similarly, memory scores were

significantly lower among those with severe depressive symptomology compared to those without ($\hat{\beta}$ = -2.57; 95% CI: -3.29, -1.86).

Regarding lifestyle behaviours, smoking occasionally was positively associated with memory compared to not smoking at all and smoking daily was negatively associated with memory compared to not smoking at all; however, none of these effects were significant. Having missing information on smoking status was associated with better memory scores compared to not smoking at all ($\hat{\beta}$ =1.40; 95% CI: 0.84, 1.96). Furthermore, regularly consuming alcohol was significantly associated with higher memory scores compared to not consuming alcohol at all ($\hat{\beta}$ = 2.26; 95% CI: 1.43, 3.10).

Regarding lifestyle behaviours, Missing information on smoking status was associated with better memory scores compared to not smoking at all ($\hat{\beta}$ =1.40; 95% CI: 0.84, 1.96) and regularly consuming alcohol or occasionally consuming alcohol were significantly associated with higher memory scores compared to not consuming alcohol at all ($\hat{\beta}$ =2.26 95% CI:1.43, 3.10 and $\hat{\beta}$ =1.53; 95% CI: 0.51, 2.55 respectively).

High compared to low FSS at both t_0 and t_1 were significantly associated with higher memory scores ($\hat{\beta}$ =1.49; 95% CI: 0.98, 2.00 and $\hat{\beta}$ = 1.91; 95% CI: 1.40, 2.42, respectively), suggesting that FSS positively impacts memory cross-sectionally and over three years of follow-up. Similarly, higher baseline memory scores were associated with higher t_1 memory scores ($\hat{\beta}$ = 0.44; 95% CI: 0.43, 0.46).

Table 6. Bivariate Associations Between Analytical Sample Characteristics and Follow-up Memory Score

Characteristic	**Memory (t_1)** $\hat{\beta}$ (95% CI)
Exposure	
Social Isolation Status (t_0)	
(Ref: Not socially isolated)	
Socially isolated	**-1.43 (-2.06, -0.80)**
Sociodemographic	
Sex (t_0)	
(Ref: Male)	
Female	0.12 (-0.39, 0.63)
Age Group (t_0)	
(Ref: 45-54 years)	
55-64 years	**0.34 (0.29, 0.97)**
65-74 years	**0.30 (0.42, 1.01)**
75 years +	**-4.14 (-4.94, -3.33)**
Province (t_0)	
(Ref: Ontario)	
Alberta	-0.01 (-1.01, 0.88)
British Columbia	0.23 (-0.70, 1.15)
Manitoba	-1.07 (-2.17, 0.03)
New Brunswick	**-1.42 (-2.55, -0.28)**
Newfoundland and Labrador	-0.96 (-2.17, 0.03)
Nova Scotia	0.56 (-1.63, 0.51)
Prince Edward Island	-0.90 (-2.13, 0.32)
Quebec	0.37 (-0.44, 1.17)
Saskatchewan	-0.74 (-1.87, 0.39)
Education (t_0)	
(Ref: Less than secondary)	
Completed secondary	0.03 (-0.96, 1.02)
Some post-secondary	0.33 (-0.43, 1.10)
Post-secondary degree or diploma	0.52 (-0.50, 1.54)
Income (t_0)	
(Ref: < $20,000)	
< $20,000	**2.40 (1.10, 3.70)**
$20,000 to < $50,000	**4.78 (3.51, 6.05)**
$50,000 to < $100,000	**5.49 (4.15, 6.83)**
$100,000 to < $150,000	**6.45 (5.06, 7.85)**
Missing	**2.72 (1.09, 4.36)**

Health Status	
Functional Status (t_0)	
(Ref: No assistance required)	
Assistance required for ≥ 1 activity	**-4.54 (-5.43, -3.65)**
Missing	**-4.42 (-8.27, -0.57)**
Chronic Conditions (t_0)	
(Ref: No chronic conditions)	
≥ 1 chronic condition(s)	**-1.86 (-2.72, -1.00)**
Missing	-0.06 (-5.39, 5.26)
Depressive Symptoms (t_0)	
(Ref: Not Severe)	
Severe	**-2.57 (-3.29, -1.86)**
Missing	-5.07 (-10.95, 0.82)
Lifestyle Behaviours	
Smoking (t_0)	
(Ref: Not at all)	
Daily	-0.32 (-1.31, 0.67)
Occasionally	0.35 (-1.65, 2.34)
Missing	**1.40 (0.84, 1.96)**
Alcohol Consumption (t_0)	
(Ref: Not at all)	
Regularly	**2.26 (1.43, 3.10)**
Occasionally	**1.53 (0.51, 2.55)**
Missing	1.55 (-0.11, 3.20)
Functional social support (t_0)	
(Ref: Low)	
High	**1.49 (0.98, 2.00)**
Functional social support (t_1)	
(Ref: Low)	
High	**1.91 (1.40, 2.42)**
Memory score (t_0)	**0.44 (0.43, 0.46)**

Notes: $p < 0.05$ in bolded font; $\hat{\beta}$=regression coefficient; CI=confidence interval; Ref=reference category; t_0=baseline, t_1=follow-up; Not severe depressive symptoms < 10; Severe depressive symptoms ≥ 10.

4.3. Aim 1 and 2 - Multivariable Linear Regression Analyses

In the base model, SI status at t_0 had a small and statistically significant, inverse association with memory at t_1, thereby indicating the average memory score among socially isolated persons was lower than the average score among non-socially isolated participants ($\hat{\beta}$ = -0.75; 95% CI: -1.32, -0.18). However, after adjusting for all the t_0 sociodemographic, health, and lifestyle covariates, the effect of SI remained negative, but was no longer significant ($\hat{\beta}$ = -0.13; 95% CI: -0.68, 0.45). The extent of change between the $\hat{\beta}$ for SI in the base model compared to the adjusted model exceeded the threshold amount of 10%, thereby indicating confounding[255]. Therefore, the adjusted model was employed to undertake the moderated mediation analysis (Aims 3-4). The full regression output is shown in Appendix F.

4.4. Aim 3 - Mediation Analysis

Figure 7 depicts the results of the mediation analysis. On the "a" path, t_0 SI significantly and negatively impacted FSS at t_1, after adjusting for all covariates, such that the odds of having high compared to low FSS decreased by 36% in the socially isolated versus not socially isolated group (OR = 0.64; 95% CI: 0.58, 0.70). After following guidance from Kenny[248] and converting the odds ratio from the "a" path to the linear scale, the $\hat{\beta}$ was -0.06 (95% CI: -0.08, -0.04). On the "b" path, t_1 FSS was significantly and positively associated with t_1 memory after adjusting for all covariates ($\hat{\beta}$ = 0.59; 95% CI: 0.09, 1.10). Since the $\hat{\beta}$s from the "a" and "b" paths were both statistically significant, the effect of SI on memory was mediated by FSS, according to the joint significance test[240].

In line with the hypothesis, SI at t_0 impacted memory scores at t_1 indirectly through FSS at t_1 ("ab" path). On the "ab" path, memory scores decreased on average by 0.03 points (95% CI: -0.06, -0.01) in socially isolated participants versus non-isolated participants, as mediated by FSS

and adjusted for all baseline covariates. The direct effect of SI on memory ("c-prime" path) was not significant – though still inverse – after adjustment for all covariates (with FSS treated as a covariate in this pathway [$\hat{\beta}$ = -0.13; 95% CI: -0.68, 0.45]). No evidence existed to suggest the total effect of SI on memory ("c" path [$\hat{\beta}$ = -0.16; 95% CI: -0.72, 0.41]) or the PM (PM = 0.07; 95% CI: -1.46, 1.41) were different from 0.

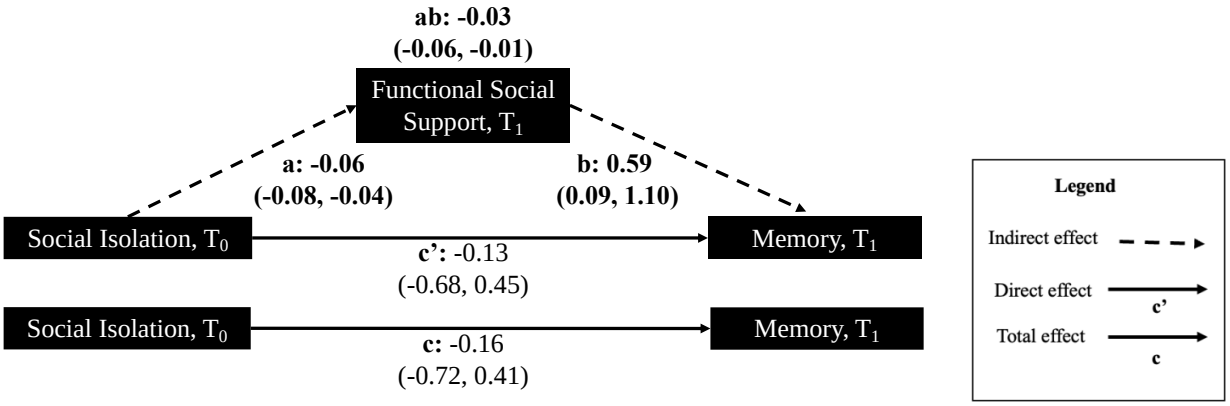

Figure 7. Mediation Model: Social Isolation, Functional Social Support, and Memory

Notes: $p < 0.05$ in bolded font; Adjusted for baseline functional social support, baseline memory, baseline sociodemographic factors, health status, and lifestyle behaviours. T_0 = baseline; T_1 = follow-up.
Full regression output for the "a" and "b" paths can be found in Table G-1 (Appendix G).
Output from the Mediation Package in "R" can be found in Figure G-1 (Appendix G).

4.5. Aim 4 - Moderated Mediation Analysis

Table 7 shows the $\hat{\beta}$s and 95% CIs for each path in the mediation analysis stratified by sex and age group. Graphical depictions of the moderated mediation analysis are shown in Figure 8a and Figure 8b. No evidence of moderated mediation was found by sex on any of the paths. However, evidence existed for some effect modification in the oldest age group (≥ 75 years) on the "a" path of the mediation model, as per Cuzick's test, since the 95% CI did not include the unstratified $\hat{\beta}$. However, the 95% CI for the ≥ 75 years age group partially overlapped with the 95% CIs for the 45-54-year and 65-74-year age groups, indicating the effects in the ≥ 75 years age group only differed from the 55-64-year age group. The stratified $\hat{\beta}$ for the ≥75 years age group suggested a weaker inverse association between SI and FSS compared to the 55-64-year age group.

Table 7. Moderated Mediation Analysis: Social Isolation and Memory – Stratified by Sex and Age Group

	a	b	ab	c-prime	c
	$\hat{\beta}$ (95% CI)	$\hat{\beta}$ (95% CI)	$\hat{\beta}$ (95% CI)	$\hat{\beta}$ (95% CI)	$\hat{\beta}$ (95% CI)
Sex					
Male	**-0.05 (-0.08, -0.02)**	0.44 (-0.28, 1.17)	-0.05 (-0.13, 0.03)	0.15 (-0.70, 0.98)	0.10 (-0.75, 0.93)
Female	**-0.06 (-0.09, -0.03)**	**0.76 (0.06, 1.47)**	-0.08 (-0.16, 0.00)	-0.35 (-1.19, 0.46)	-0.43 (-1.27, 0.39)
Age Group					
45.54	**-0.05 (-0.09, -0.01)**	0.36 (-0.53, 1.22)	-0.04 (-0.13, 0.05)	1.03 (-0.27, 2.12)	0.99 (-0.20, 2.08)
55-64	**-0.10 (-0.14, -0.06)**	0.45 (-0.40, 1.30)	-0.06 (-0.19, 0.05)	-0.46 (-1.46, 0.52)	-0.52 (-1.51, 0.45)
65-74	**-0.06 (-0.11, -0.02)**	0.80 (-0.39, 2.00)	-0.09 (-0.24, 0.04)	-0.38 (-1.71, 0.92)	-0.47 (-1.80, 0.84)
75+	-0.01 (-0.04, 0.03)	1.30 (-0.10, 2.71)	-0.01 (-0.11, 0.06)	-1.01 (-2.46, 0.42)	-1.03 (-2.49, 0.41)

Notes: $p < 0.05$ in bolded font; Adjusted for baseline functional social support, baseline memory score, baseline sociodemographic factors, health status, and lifestyle behaviours. $\hat{\beta}$ = regression coefficient; CI = confidence interval.

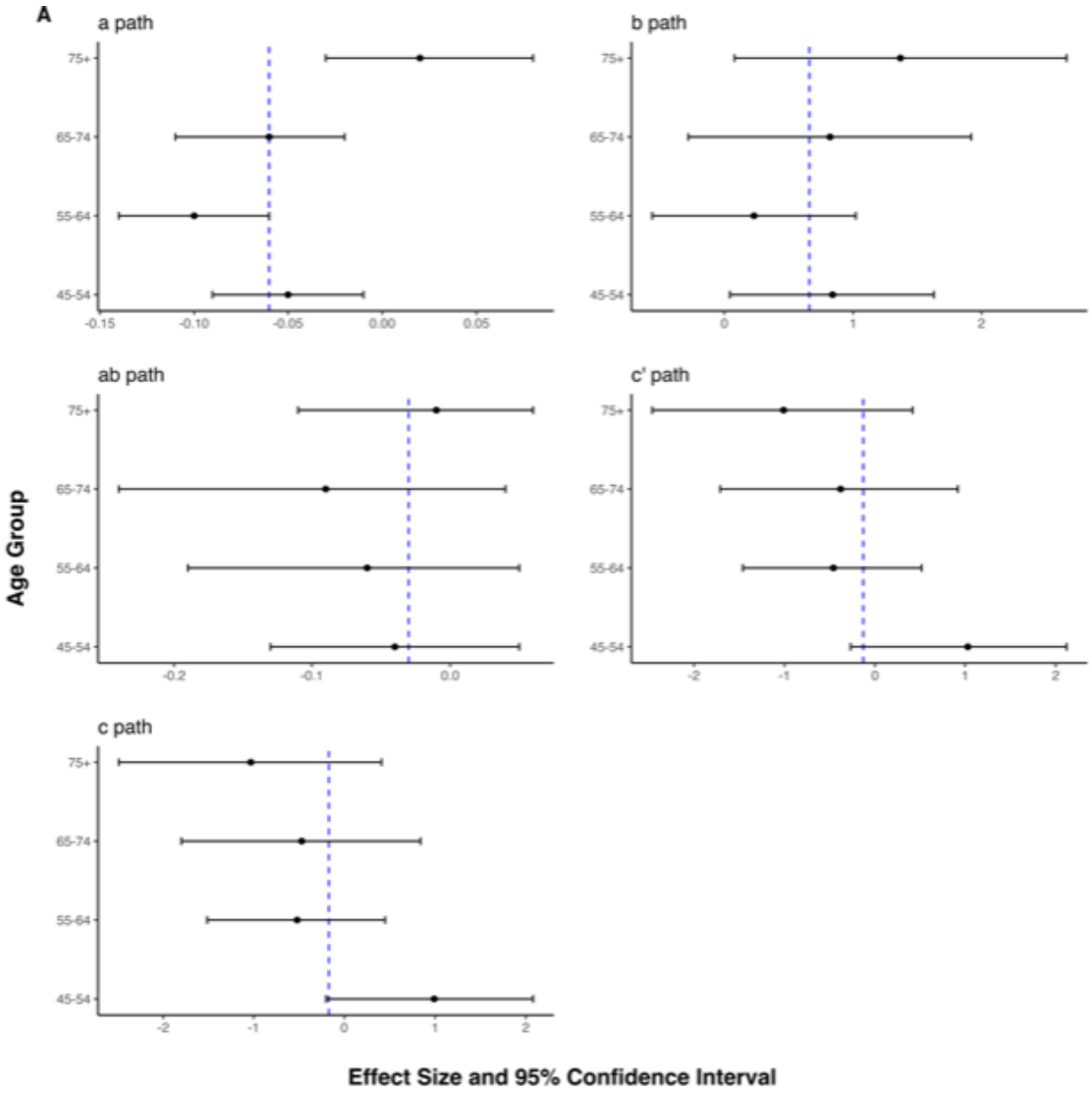

Figure 8. Forest Plots: Moderated Mediation Analysis by Effect Modifiers Age Group and Sex

Figure 8. (A): Forest Plots: Moderated Mediation Analysis by Age Group

Notes: Adjusted for baseline functional social support, baseline memory score, baseline sociodemographic factors, health status, and lifestyle behaviours.; vertical line represents the unstratified regression coefficient.

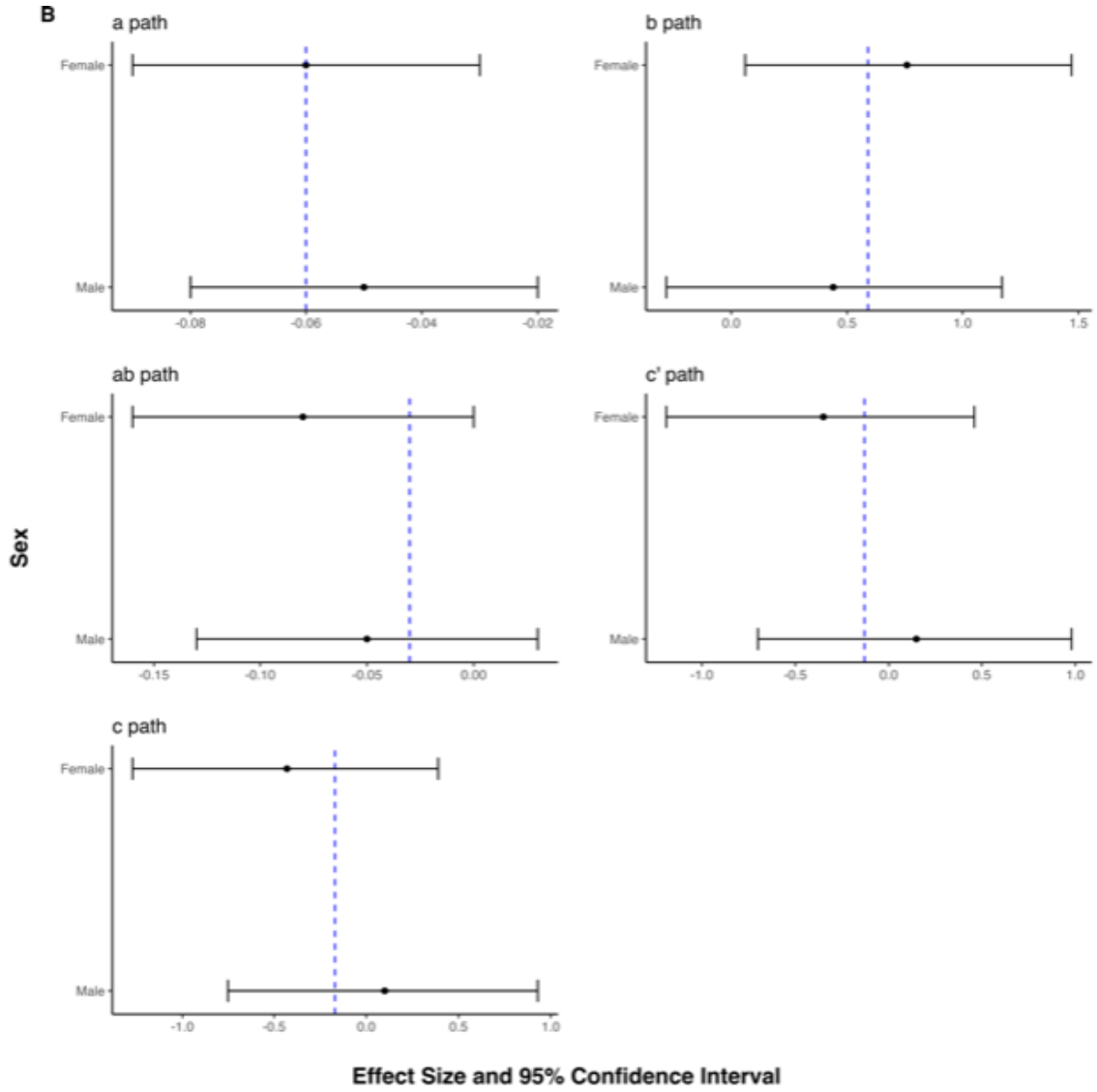

Figure 8. (B): Forest Plots: Moderated Mediation Analysis by Sex
Notes: Adjusted for baseline functional social support, baseline memory score, baseline sociodemographic factors, health status, and lifestyle behaviours.; vertical line represents the unstratified regression coefficient.

4.6. Differential Dropouts Over Follow-up

On average, participants who were socially isolated at t_0 had 42% higher odds of dropping out of the CLSA before the first follow-up period, compared to those who were not isolated at t_0 (OR = 1.42; 95% CI: 1.31 to 1.53). Similarly, those who dropped out had slightly lower average t_0 memory scores than those who did not drop out. As shown by the independent group t-test, evidence suggests the difference in means between the dropouts and the non-dropouts was significant ($p<0.001$ [Table 8]). While median FSS scores were roughly the same between dropouts and non-dropouts, the Mann-Whitney U test suggested a significant difference in median FSS score between dropouts and non-dropouts ($p<0.001$ [Table 9]).

Table 8. Mean Baseline Memory Scores: Dropouts versus Non-dropouts

	Mean (SD)	Minimum	Maximum
Baseline Score: Dropouts	97.6 (15.6)	63.4	166.5
Baseline Score: Non-dropouts	100.0 (14.9)	59.0	174.6

Notes: SD = standard deviation; $p<0.001$

Table 9. Mean Baseline Functional Social Support Scores: Dropouts versus Non-dropouts

	Median (IQR)	Minimum	Maximum
Baseline Score: Dropouts	85.5 (19.6)	0	100
Baseline Score: Non-dropouts	86.8 (17.3)	0	100

Notes: IQR = interquartile range; $p<0.001$

4.7. Sensitivity Analysis

In the results presented above, participants with missing data on a covariate were assigned to a category called 'missing' for that covariate. This permitted persons with missing covariate data to be retained in the analysis. For the sensitivity analysis, 3,967 participants with missing values on any covariate were removed from the analytical sample, leaving 8,867 participants in the complete case analysis. Table H-1 compares the point estimates and 95% CIs for the base and the adjusted models across both analyses (Appendix H). The point estimates generally moved closer to the null after removing participants with missing covariate information, although the directions of effect did not change (Table H-1). Further, the $\hat{\beta}$ for SI was no longer statistically significant in the base model following the removal of participants with missing covariate data.

4.7.1. Sensitivity Analysis – Mediation

The point estimates in the "a", "b", and "ab" paths remained relatively unchanged; however, the "b" and "ab" paths were no longer significant after removing participants with missing covariate data, as shown in Table H-2. The point estimates in the "c-prime" and "c" paths became positive after removing participants with missing covariate data but remained statistically non-significant (Table H-2).

For the multiple imputation analysis, the point estimate for the "ab" path remained unchanged compared to the missing covariate category analysis; however, it was no longer significant. The point estimates in the "c-prime" and "c" paths remained negative and statistically non-significant.

A forest plot depicting the effect sizes and confidence intervals for the original analysis, the complete case analysis, and the multiple imputation analysis on the "ab", "c-prime", and "c" paths is found in Figure 9.

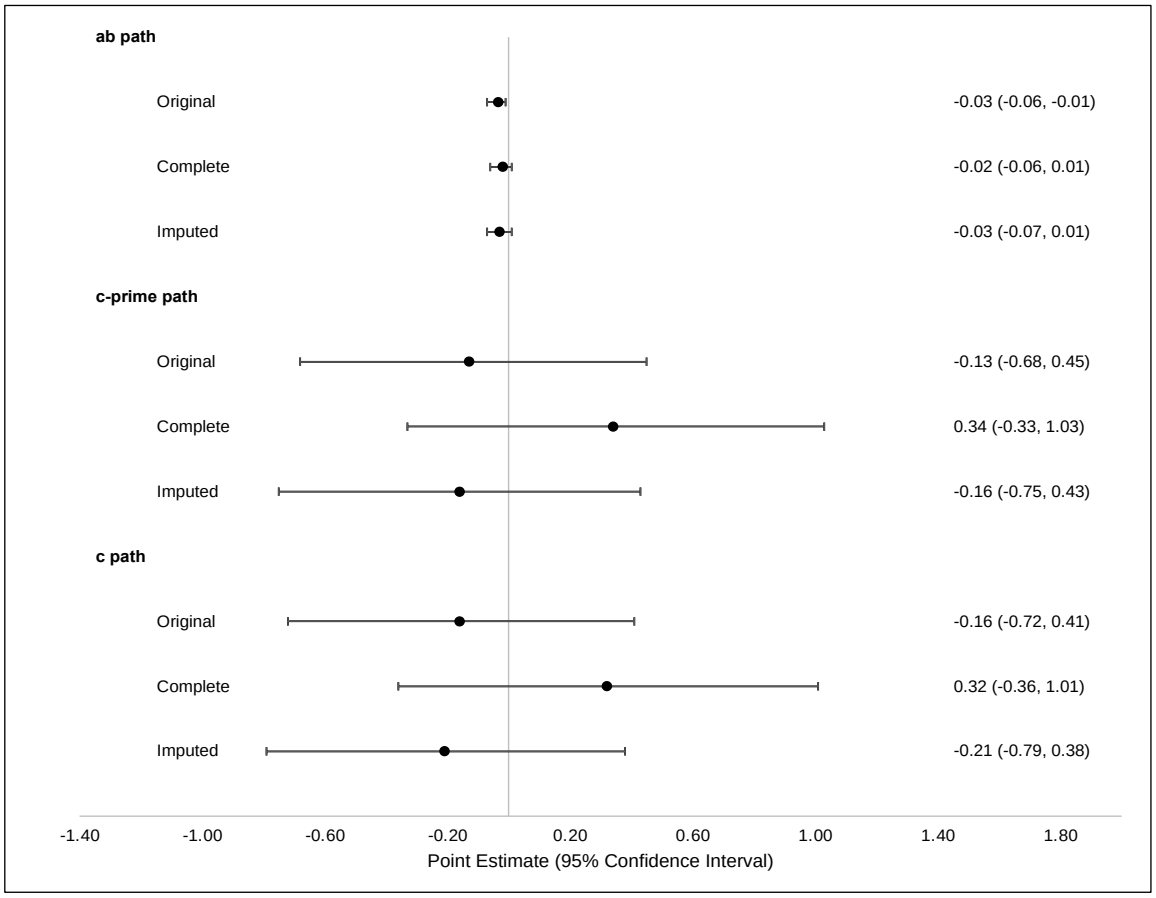

Figure 9. Forest Plot Depicting the Sensitivity Mediation Analysis

Notes: Original = analysis with participants with missing covariates retained in the model; Complete = analysis with participants with missing covariates removed from the model; Imputed = analysis with imputed values for participants with missing covariates
Adjusted for functional social support, baseline memory score, baseline sociodemographic factors, health status, and lifestyle behaviours.

4.7.2. Sensitivity Analysis – Moderated Mediation

The point estimates for the "a", "b", "ab", "c-prime", and "c" paths in each sex and age group stratum remained relatively stable after removing participants with missing covariate data, as shown in Table H-3. However, in general, the 95% CI widened after removal of participants.

4.8. Model Diagnostics

For the primary analysis utilizing 'missing' covariate categories, the assumptions of logistic regression were not violated for the "a" path model in the mediation triangle (Appendix I). There were no influential outliers in our analysis because all the data points fell within the Cook's distance threshold of 1 (Figure I-1). Multicollinearity was not a problem because the Variance Inflation Factors (VIF) for our explanatory variables were all less than 10.

The assumptions of linear regression were not violated for our model of the "b" path in the mediation triangle (Appendix I). No discernible pattern existed among the residuals, which were spread randomly along the horizontal line marked in red in Figure I-2, thereby suggesting the model satisfied the homoskedasticity assumption. The normality assumption was also met because the residuals in Figure I-3 followed a straight dashed line. Further, outliers and multicollinearity were not problematic because Cook's distance and VIF values did not exceed the thresholds mentioned above.

5. Discussion

5.1. Summary of Study Findings

Aim 1: Is SI associated with memory across two timepoints of data from the Tracking Cohort of the Canadian Longitudinal Study on Aging?

The regression analysis produced a significant, negative result ($\hat{\beta}$ = -0.75; 95% CI: -1.32, -0.18), indicating that on average, the memory score was 0.75 points lower in persons who were socially isolated compared to those who were not socially isolated at baseline.

Aim 2: Does the association between SI and memory change after adjusting for relevant covariates, i.e., sociodemographic factors, health status, and lifestyle behaviours?

Although the effect of SI on memory was still negative, the inclusion of covariates rendered the relationship between baseline SI and follow-up memory non-significant ($\hat{\beta}$ = -0.13; 95% CI: -0.68, 0.45). Therefore, we do not have evidence to suggest that changes in SI lead to changes in memory, after controlling for covariates.

Aim 3: Does FSS mediate the association between SI and memory?

We found significance on the "a" path ($\hat{\beta}$ = -0.06; 95% CI: -0.08, -0.04) and the "b" path ($\hat{\beta}$ = 0.59; 95% CI: 0.09, 1.10) of the mediation triangle, after adjusting for all covariates. Therefore, according to the joint significance test[240], FSS acted as a mediator of the relationship between SI and memory. The indirect effect ("ab" path) was also significant ($\hat{\beta}$ = -0.03; 95% CI: -0.06, -0.01) in the adjusted model, indicating that memory scores decreased on average by 0.03 points (95% CI: -0.06, -0.01) in socially isolated participants versus non-isolated participants, when mediated by FSS. The direct effect ("c-prime" path) was not significant in the mediation analysis ($\hat{\beta}$ = -0.13; 95% CI: -0.68, 0.45). Similarly, the total effect ("c" path) and the PM were

also not significant ($\hat{\beta}$ = -0.16; 95% CI: -0.72, 0.41; PM = 0.07; 95% CI: -1.45, 1.41, respectively).

Aim 4: Does age group or sex moderate the (i) effect of SI on FSS, (ii) effect of FSS on memory, (iii) indirect effect of SI on memory through FSS, and the (iv) direct and total effects of SI on memory?

Evidence of some effect modification by age group was found on the "a" path of the mediation model. More specifically, the regression coefficient between SI and FSS in the oldest age group (≥75) shifted toward the null and was weaker than in the 55-64-year age group. However, effect modification on age group was not identified on the "b" path, indirect effect ("ab" path), nor on the direct ("c-prime" path) or total ("c" path) effects. Similarly, no effect modification by sex was present on any of the paths in the mediation triangle.

5.2. The Indirect Effect

The finding of an indirect effect (mediation) points to the role of FSS in the relationship between SI and memory. Since the $\hat{\beta}$ for SI is closer to 0 (smaller magnitude of effect) in the indirect path than in the direct path (-0.03 compared to -0.13, respectively), FSS appears to mitigate the adverse effect of SI on memory. Individuals who were socially isolated seemed to perform better on the RAVLT if they reported high levels of support (high FSS) compared to individuals who were socially isolated with low levels of FSS.

After the systematic literature search described in Section 2.5 above, only two published studies out of the 4,361 screened citations were found to bear any relation to the thesis topic. First, Yang et al.[218] conducted a cross-sectional analysis of the CHARLS[195], which included 7,410 participants aged 60 years or older. These authors investigated whether SI affected cognitive function directly or indirectly through loneliness. The study found that loneliness acted

as a partial mediator of the association between objective SI and cognitive function, accounting for some of the negative effects of SI on cognition. While Yang et al.'s work offers useful insights, its results do not directly apply to the thesis because loneliness was the mediating variable of interest, not FSS. However, Yang et al.'s study does have some relevance because loneliness and FSS are both subjective assessments of participants' state of being that are linked to SI.

The second article from the literature search described a longitudinal cohort study by Santini et al.[256], containing 3,005 older adults aged 57 to 85 years from the National Social Life, Health, and Aging Project[257]. The authors argued that perceived social support is a better indicator for mental health outcomes among older adults compared to structural social support. The researchers quantified levels of social disconnectedness (a measure of SI) and investigated the association with depression and anxiety. They also investigated whether perceived isolation (a measure of FSS) mediated this relationship. Although the direct relationship between social disconnectedness and the two outcomes was not significant, perceived isolation mediated the relationship such that social disconnectedness predicted higher amounts of perceived isolation, which in turn predicted greater symptoms of depression and anxiety. While Santini et al.[256] highlight a key mediating role for a form of FSS, the results are distally applicable to the thesis because of the differing outcomes and operationalizations of SI and FSS. However, just as in the thesis, Santini et al. found a mediating effect in the absence of a direct or total effect. The lack of studies directly investigating the mediating effect of FSS on the association between SI and memory emphasizes the novelty of the thesis research.

A negative association between SI and FSS and a positive association between FSS and memory are consistent with Santini et al.[256] and other findings in the

literature[23,36,91,94,117,214,256,258–263]. Being socially isolated may lead to the perception of low support. Further, adults who perceive a high level of support from their social network may have better memory function. Although FSS can vary regardless of network size, SI is consistently linked to reports of low FSS[256,258–260]. Conversely, research suggests individuals with more diverse and integrated social networks (low SI) report higher levels of FSS compared to individuals with more restricted and less integrated networks[23,261,262]. As a case in point, Cloutier-Fisher and Kobayashi[264] showed that socially isolated older adults are more likely to report less FSS than non-isolated adults. They believed participating in social activities could facilitate a sense of belonging and create opportunities to engage socially with other individuals, thereby generating perceptions of strong FSS through reciprocal communication and feelings of being valued by others[264].

Positive associations between FSS and memory have been reported in the literature. Many studies suggest greater levels of FSS, after controlling for structural aspects of support, are associated with better memory function[91,115,117,214] and are protective against memory decline[36,94]. The stress buffering hypothesis, briefly described in Section 2.4.4 above, is often used to explain these findings. In essence, high FSS may offer the socio-emotional support necessary to cope with stress during hard times. This coping effect mitigates the neurotoxic effects of stress and prevents deterioration in brain regions with high densities of glucocorticoid receptors, such as the hippocampus (an area of the brain that is important for memory encoding and consolidation)[156,265,266]. The stress-buffering hypothesis has been substantiated by neuroimaging studies showing that individuals who maintain high levels of perceived support as they age tend to have larger volumes of gray matter in brain regions associated with memory[267,268].

Altogether, the impact of SI on memory could be mitigated in persons with high levels of FSS. Although SI was shown to indirectly impact memory function through FSS, the effect sizes for the indirect effect are small and, without evidence of a statistically significant direct effect, the thesis is unable to draw firm conclusions about whether FSS is a partial or full mediator of the relationship between SI and memory [241].

5.3. The Direct Effect

The direct effect of SI on memory was inverse after adjustment for FSS and other covariates, but it was also small and statistically non-significant. In contrast, the existing literature has generally reported strong and statistically significant associations between SI and memory [31,45,46,94,132,204,211,214]. Five reasons may help explain the discrepant findings between the thesis and the published literature. First, while the thesis analysis adjusted for the same general set of covariates as the aforementioned studies (i.e., sociodemographic, health, and lifestyle), these studies adjusted for fewer numbers of covariates than the thesis, meaning the published results could have been affected by residual confounding that exaggerated true effects.

Second, the missing data analysis in Section 4.6 above suggested the presence of attrition bias between baseline and follow-up. Participants who were socially isolated at baseline had higher odds of dropping out of the CLSA and were therefore not included in the analytical sample. The participants who dropped out of the study after baseline also had lower FSS and memory scores on average compared to the individuals in our analytical sample. Consequently, attrition on all three main variables of interest could have biased the results of this thesis to the null, thereby producing very small $\hat{\beta}$s for SI.

Third, CLSA staff excluded potential participants during the recruitment interview who appeared to be cognitively impaired. Due to this recruitment bias, the analytical sample

contained an overrepresentation of cognitively healthy participants, which may have further shifted the inverse association between SI and memory toward the null. Previous studies have noted that overly healthy samples may hamper the examination of memory change. For example, using data from the Charlotte County Healthy Aging Study (CCHAS)[269] Hughes et al.[36] reported that both social network size and frequency of contact with network members (components of SI) were not associated with episodic memory. However, their sample showed stable cognitive function over the 5-year follow-up period. The researchers believed the CCHAS's screening protocol for cognitive impairment at baseline, using the MMSE[270], led to the enrolment of a cognitively healthy sample, thereby reducing the ability to detect an association between SI and memory. Likewise, Gow et al.[210] found small and non-significant effects between components of SI (marital status, living arrangements, and social contact) and overall memory function in a sample drawn from the Lothian Birth Cohort of 1936[209]. The authors believed the voluntary nature of recruitment into the birth cohort, and the possibility that only the healthiest subset of the initial sample remained alive at the time of study in 2013, biased the effect sizes to the null.

Fourth, data from the CLSA included participants aged 45 years or older. As discussed in Section 2.3 above, episodic memory is the most age sensitive, long-term aspect of memory. Longitudinal studies have found that age 60 years is the average mark where one may begin observing the onset of episodic memory decline[271]. While including a middle-aged sample could have dampened the findings in the thesis, stratification by age group did not uncover notable differences in memory between the older and younger age groups.

Fifth, the direct ("c-prime") effects in the unstratified and stratified mediation models are likely underpowered[272]. A post-hoc power analysis using the POWER procedure in SAS Studio v9.4 (The SAS Institute, Cary, NC) estimated that approximately 61,522 participants would be

required to detect a minimum $\hat{\beta}$ of 0.13 at 80% power and alpha = 0.05 on the direct path. Due to the power issue, one cannot draw firm conclusions from the thesis about the presence or absence of a direct effect on the "c-prime" path[273–276]. However, absence of evidence does not automatically equate to absence of effect. Future research in this area will need to devote careful attention to statistical power as a means of generating strong inferential data.

5.4. The Total Effect

The total effect of SI on memory is the sum of the indirect and direct effects. In the thesis, the total effect is not significant, despite the significance of the indirect effect, because of what Kenny and Judd[272] refer to as a 'power anomaly'. When the effect sizes on the indirect and total paths are close in magnitude, which is seen in this thesis, achieving 80% power on each of the indirect and total effects would require a sample size that is approximately 8 times larger on the total path compared to the indirect path[33]. This is because the indirect path is the product of two effects ("a" path and "b" path); the multiplicative nature of the indirect path enhances statistical power over the single effect on the total path[272,275].

5.5. Moderated Mediation

The results of this thesis found evidence for some effect modification by oldest age group (≥ 75 years) on the "a" path of the mediation triangle. The strength of the association between SI and FSS was weaker in the ≥ 75-year age group compared to the 55-64-year group. Studies have shown that social networks narrow in aging adults; however, levels of FSS remain more stable[48]. According to the literature[277], aging leads to changes in motivation for seeking social contact, as older adults focus on fostering finite numbers of close social relationships rather than maintaining many diverse relationships. Therefore, peripheral relationships are thought to be "pruned," and closer, more emotionally satisfying relationships remain[277,278]. This trend could

explain the stratified results on the "a" path for the oldest age group because SI may not have a large influence on FSS compared to the younger 55-64-year age group, who may rely on FSS from wider social networks.

Beyond the "a" path, age group did not moderate any other path of the mediation triangle. This could be due to the length of follow-up, which may not have been long enough to explore age trends over time. The literature notes inconsistencies regarding age as an effect modifier in the relationship between SI and memory. When stratifying by age (< 65 years/≥ 65 years), Seeman et al.[211] found no evidence of effect modification on the relationship between social contact frequency and episodic memory function. These results also echo the work of LaFleur and Salthouse[165], who found no significant interaction between age group and measures of structural and functional support, and memory function.

Further, sex was not identified as an effect modifier on any path of the mediation triangle. In terms of the direct and total effect, previous research has also produced inconclusive results when stratifying the association between SI and memory by sex. For example, a cross-sectional analysis of 24,531 participants from the Comprehensive Cohort of the CLSA did not find any difference in effects of SI on memory across males and females[230]. Li and Dong's[204] cross-sectional investigation of 3,157 Chinese Americans aged 60 years or older found that both social network size and frequency of social contacts were positively associated with memory among both males and females; however, they reported insufficient evidence for effect modification by sex.

The absence of effect modification in the moderated mediation analysis for the moderated mediation analysis may also be due to the lack of power described in Section 5.3 above. Since effect modification was assessed by stratifying each path of the mediation analysis, the

moderated mediation analyses were even further underpowered compared to the unstratified analyses.

5.6. Strengths

This thesis has multiple strengths. First, many previous studies exclusively examined older adults; however, our analysis included both middle-aged and older adults, allowing us to capture the experiences of mid-life, which is known to influence health outcomes later in life[222]. Second, the sampling frame of the Tracking Cohort included adults from all 10 provinces, allowing the results of this thesis to apply to a broader target population compared to previous studies that have been limited to narrow geographic areas such as single cities or counties[36,45,132].

Third, we utilized the measure of SI that Menec et al.[24] created specifically for CLSA. This measure was based on research emerging from other panel studies[23,63]. Further, unlike many previously published studies[31,36,45,46,94,165,204,210–212,214], the SI index employed in this thesis contained a larger number of items to more broadly measure SI. Therefore, compared to earlier literature, the results of this thesis may provide a more valid assessment of the relationship between SI and memory.

Fourth, this study adjusted for a larger group of covariates than previous research[31,36,45,46,94,165,204,210–212,214], thereby minimizing confounding. Further, adjusting for baseline memory accounted for the differences between baseline and follow-up memory scores, as well as potential residual confounding that may manifest in memory function.

Fifth, the associations that we saw between the covariates and memory shown in the regression output in Appendix F yielded expected values. For example, the covariates education and income are positively associated with memory in a dose-response fashion. Additionally, requiring assistance for at least one activity compared to not requiring assistance at all, is

significantly inversely associated with memory function. A similar pattern is seen between memory function and severe compared to not severe depressive symptoms. These results align with previous literature[230,279,280] and indicate the underlying validity of the data and analytical approach, lending credence to the results of the mediation analysis.

Sixth, we conducted two types of sensitivity analysis to look at the impact of different ways of handling missing data. The effects sizes obtained from sensitivity analyses yielded similar values to our main analyses further validating our data and the soundness of our analytical approach.

Lastly, and most importantly, while many studies have assessed the effects of SI or FSS on memory, the thesis candidate is unaware of any published studies that explored the mediation effects of FSS on the relationship between SI and memory. As such, this thesis adds novel information to the current literature about the effects of SI on memory.

5.7. Limitations

This study is not without limitations. Participants in the CLSA were generally healthier than average[222]. Previous CLSA-based studies found these individuals reported higher levels of education, income, and health compared to the average Canadian between the ages of 45 and 85 years[230,279]. In the analytical sample for the thesis, after the completion of baseline data collection, approximately one-third of participants had an average household income over $100,000 in the same year (2015) that the median household income in Canada was $56,000[281]. Further, the 2016 census[282] estimated that 53.0% of the 45-54-year age group and 44.3% of the 55-64-year age group in Canada had post-secondary education, while the corresponding age groups in our analytical sample reported post-secondary education levels of 78.7% and 72.7%, respectively. Therefore, the thesis results optimally apply to the subset of the study population

with similar characteristics as the analytical sample. Caution must be exercised when applying the results to other subgroups of the target population.

To handle missing covariate data, categories on variables such as functional status, chronic conditions, and depressive symptoms were collapsed into binary categories. For example, the categories for functional status were 0 or ≥ 1 functional limitation(s) however, by collapsing categories, participants who had few limitations were group in with those who had multiple limitations. This prevented the study from assessing confounding by severity, which may have led to residual confounding.

Although the PM has an intuitive interpretation, caution must be exercised when drawing upon it to describe the results of a mediation analysis. Of note: (1) a large sample size ($n \geq 500$) is required to rely on the PM as a description of the magnitude of the indirect effect when the outcome is a continuous variable[283]; (2) the estimate of the PM may be uninformative when the $\hat{\beta}$'s for the direct and indirect effects have opposite signs (i.e., one is positive, one is negative), which is known as 'inconsistent mediation'[284,285]; and (3) the PM may also not have a meaningful interpretation when the contributing effect estimates (the indirect and direct effects) are small and clinically irrelevant[286].

The thesis produced what is called inconsistent mediation, where the "a" path and "b" path components of the indirect effect ("ab" path) showed opposite signs ($\hat{\beta}$ = -0.06; and $\hat{\beta}$ = 0.59, respectively). Further, the coefficients for the direct and total effects were not significant, meaning a lack of evidence exists to suggest the true direction of these estimates. Since the PM is calculated by dividing the indirect effect by the total effect, the presence of inconsistent mediation suggests the PM could be an inaccurate representation of the true degree of mediation

in the SI-FSS-memory triangle shown in Figure 7 above [284–286]. As such, the PM obtained in this thesis should not be used to help explain the results of the mediation analysis.

According to our missing data analysis, attrition bias was likely present in the CLSA. Participants in the analytical sample who were socially isolated at baseline had higher odds of dropout. Participants without follow-up data also had lower median or mean baseline FSS and memory scores. Recruitment bias may have also influenced the thesis results because the CLSA excluded participants with overt signs of cognitive impairment during study recruitment. Taken together, attrition and recruitment biases may have biased the results of the thesis toward the null and led to small effect sizes. Therefore, it is unclear whether the small effect sizes reported above indicate the true absence of clinically important effects or partially reflect the impact of concerns such as bias.

For the bulk of this thesis project, the CLSA had only two timepoints of data available for analysis (baseline, follow-up 1). Additionally, in May 2024, the combined memory variable described in Section 3.2.3 above was only available for these two timepoints. However, some literature proposes that three timepoints is optimal to test for mediation and allow time to elapse between each exposure and effect [287]. Moreover, the CLSA collected follow-up data three years after baseline, which may not be long enough to observe clinically relevant changes in memory scores in a cognitively healthy baseline sample.

5.8. Implications and Future Directions

From a public health standpoint, this thesis may have important implications for the prevention of memory loss in middle-aged and older adults. The findings show that SI is associated with memory indirectly through FSS, although the effect size is small and unlikely to be clinically important. Given the biases discussed above – which likely biased the thesis results

to the null – the true effect size of the mediation effect could be much larger, especially in less healthy target populations. Therefore, public health authorities should consider the possibility of evaluating the extent to which social relationships meet the support needs of older adults during regular gerontological care appointments. This approach is captured by the notion of social prescribing[288]. Social prescribing is a holistic approach to health in which healthcare providers connect patients with local or community services that target social health, with the goal of improving their mental and physical wellbeing[288]. Since the thesis found that FSS mediated the association between SI and memory, policies designed to identify and connect socially isolated adults to health and social services should pay particular attention to these individuals' perceived levels of FSS.

Additional research with more follow-up periods is warranted to further assess the relationship between SI and memory. As time passes, ever increasing numbers of CLSA participants will experience memory decline and the emergence of neurocognitive disorders. This will allow us to better understand the characteristics of those who are lost to follow-up. For example, do participants who dropout after multiple follow-up timepoints have a larger cognitive decline trajectory compared to those who remain in the study. More timepoints will also allow for mediation effects to be tested with exposure, mediator, and outcome in sequence: exposure at baseline, mediator at intermediate follow-up, and outcome at the last available timepoint.

To expand upon the current study, future studies may investigate one or more of the different subtypes of FSS as mediators in the relationship between SI and memory. Exploring FSS subtypes will provide insight regarding how policies tailored to one subgroup may be more effective than policies tailored toward other subgroups. These deeper analyses may further contribute to the development of targeted interventions for maintaining memory function.

6. Conclusion

Few studies have considered how different types of social support are interrelated through mediating pathways that impact cognitive health. This thesis was the first to examine the mediating effect of FSS on the relation between SI and memory. Though FSS indirectly accounted for some of the association between SI and memory, the effect was quite small. Furthermore, no evidence of a direct effect of SI on memory (controlling for FSS) was detected. Therefore, a conclusion regarding partial or full mediation cannot be made. Despite the limitations, this thesis offers valuable insights into the relationship between SI, FSS, and memory in middle-aged and older adults. The results serve as a base upon which future studies may build.

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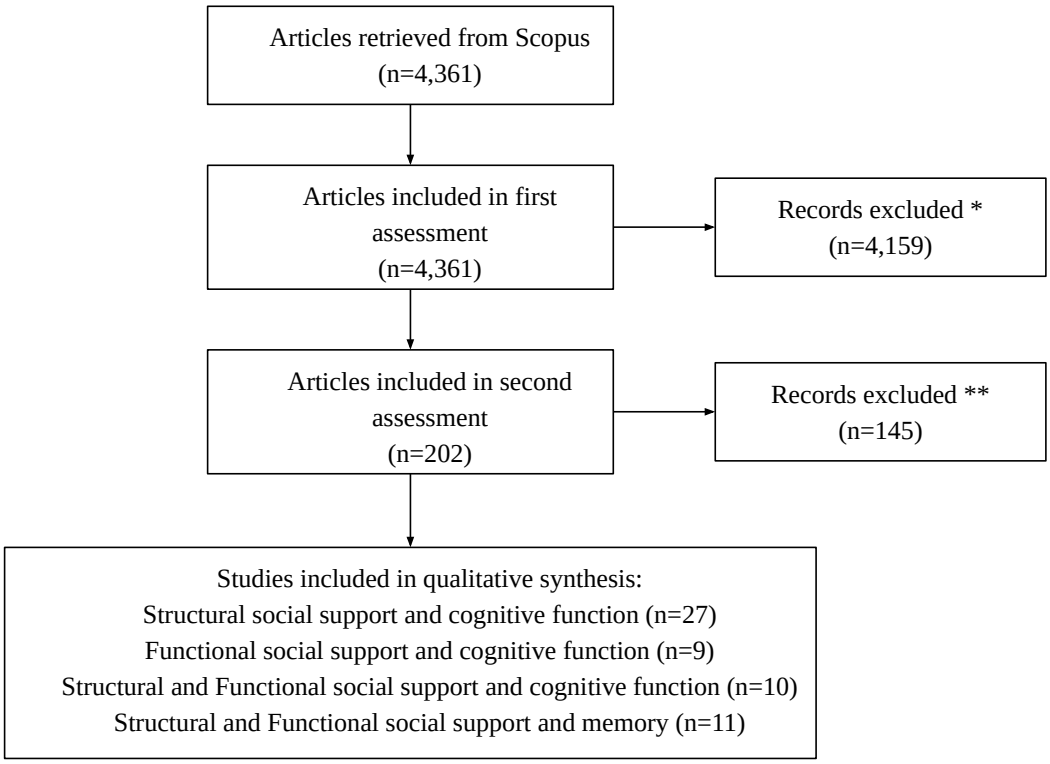
Appendices

Appendix A. Literature Review of the Evidence for the Association Between Social Isolation, Functional Social Support, and Memory



*Exclusion criteria:

1. Study conducted on caregivers.
2. Predictor variable is neither social support nor cognitive function.
3. Outcome variable is neither social support nor cognitive function.
4. Study population has been diagnosed with dementia.
5. Study population is non-community-dwelling adults.

**Exclusion criteria:

1. Study assessed structural social support and functional social support as a combined measure.
2. Outcome variable is incident dementia or Alzheimer's disease.

Figure A-1. Literature Search Process

Table A-1 Literature Search Strategy

Scopus
(TITLE (*"Social Support*"* OR *"social isolation"* OR *"social network*"* OR *"social resources"* OR *"social engagement"* OR *"social connectedness"* OR *"social relationships"* OR *"Social environment"* OR *"social cohesion"* OR *"community networks"*) AND ABS (*memory* OR *"Cognitive function"* OR *dementia** OR *"Cognitive Decline"* OR *"Cogni*"*)
Retrieved 4,361 retrieved as of May 2nd 2024

Table A-2. Summary of the Literature on the Association between Social Isolation and Cognitive Function

Author(s)	Title	Study Design	Study Population	Predictor Measures	Outcome Measures	Covariates	Conclusions and Findings
Bae[173], 2021	Autoregressive cross-lagged modelling of the relationship between social activity, depressive symptoms, and cognitive function in Korean elderly	Longitudinal	5549 participants aged 60 and older from the Korean Longitudinal Study of Aging (KLoSA) across 4 waves of data over 12 years.	Social activity including social gatherings, participation in leisure, culture, or sports, and involvement in community engagements on a 11-point scale (0=no activity to 10=almost every day)	Cognitive function assessed through the Korean version of the Mini-Mental State Examination (K-MMSE) on a scale from 0-30, with higher scores indicating higher cognitive function	Sociodemographic: Age and education	Social activity was found to have a significant positive relationship with cognitive function (β=0.1040; $p<0.001$)
Barnes et al.[177], 2004	Social Resources and Cognitive Decline in a Population of Older African Americans and Whites	Longitudinal	3,899 participants from the Chicago Health and Aging Project aged 65 and older across two follow-up timepoints over 6 years	Social networks: frequency of contact with network members Social engagement: participation in social and productive activities	Cognition function Episodic memory: East Boston Story immediate and delayed recall test Perceptual speed: Symbol Digit Modalities Test Global cognition: Mini-Mental State Examination (MMSE)	Sociodemographic: Age, sex, race, education, marital status, income Lifestyle: Cognitive and physical activity Health status: Depressive symptoms, chronic conditions	Greater social networks and engagement were significantly associated with better cognitive function β=0.003; $p<0.001$ and β=0.060; $p<0.001$ respectively) For every point decrease on the social engagement scale an average decrease of 0.009 was observed in cognitive function overtime

Béland et al.[186], 2005	Trajectories of Cognitive Decline and Social Relations	Longitudinal	1,571 participants aged 65 and older from the Aging in Leganés study including 4 waves of data collection across 7 years	Social networks: number of social ties and frequency of social engagement Social integration: frequency of participation in four social activities/community events	Overall cognitive function assessed by the Leganés Cognitive Test	Sociodemographic: Age, gender, education Health status: Chronic conditions (stroke hypertension, heart disease, and diabetes), depressive symptoms, and functional limitations	Low social integration was associated with accelerated cognitive decline overtime
Belessiotis-Richards et al.[164], 2022	A Cross-Sectional Study of Potentially Modifiable Risk Factors for Dementia and Cognitive Function in India: A Secondary Analysis of 10/66, LASI and SAGE Data	Cross-sectional	2,004 participants aged 65 years or older from the 10/66 survey, 1,638 participants aged 45 and older from the Longitudinal Aging Study in India (LASI), and 2,441 participants aged 65 years or older from the Study of global AGEing (SAGE)	Social isolation including frequency of contact with social and participation in social activities	Cognitive function index across all three studies including verbal fluency, learning, and delayed recall	Sociodemographic: Age, socioeconomic position, locality (Urban/Rural), sex, income, food insecurity	Social isolation was associated with lower cognitive scores in all three datasets. In 10/66 (β=-0.40; 95% CI: -0.54 to -0.25), in LASI (β=-0.31; 95% CI:-0.53 to -0.09), and in SAGE (β=-0.22; 95% CI:-0.36 to -0.08)
Bourassa et al.[172], 2017	Social Participation Predicts Cognitive Functioning in Aging Adults over time: Comparisons with Physical Health, Depression, and Physical Activity	Longitudinal	19,832 participants aged 50 and older from the Survey of Health, Ageing, and Retirement in Europe (SHARE) study across three waves of data over 6 years	Social Participation: frequency of participation in various social activities	Cognitive functioning including Executive function: verbal fluency Memory: immediate and delayed recall	Sociodemographic: Age, gender, and income Health status: Depressive symptoms, self-reported health Lifestyle: Physical activity	At each timepoint (baseline, follow-up one, and follow-up two) increased social participation was positively associated with memory function and executive function

Choi et al.[174], 2016	A Change in Social Activity affect Cognitive Function in Middle-aged and Older Koreans: Analysis of a Korean Longitudinal Study on Aging	Longitudinal	6,076 participants aged 45 and older from the Korean Longitudinal Study of Aging (KLoSA) across 4 waves of data over 6 years	A composite score from 0-6 of frequency of participation in social activities Change in participation overtime was categorized as (1) "consistent participation" (2) "consistent non-participation" (3) "non-participation to participation" and (4) "participation to non-participation"	Cognitive function assessed through the Korean version of the Mini-Mental State Examination (K-MMSE) on a scale from 0-30, with Normal: ≥24 Mild cognitive impairment: 18-23 Severe cognitive impairment: ≤17	Sociodemographic: Sex, age, marital status, education, income, employment status, region Health status: chronic diseases Lifestyle: Exercise	The "no participation to participation" group (β=0.778, p<0.001) and the "consistent participation" group β=0.968, p<0.001 showed reduced cognitive decline compared to the "consistent non-participation" group
Duan et al.[182], 2023	Association of Social Isolation and Cognitive Performance: A Longitudinal Study using a Four-Wave Nationwide Survey	Longitudinal	9,367 participants from the China Health and Retirement Longitudinal Study (CHARLS) over the age of 45 at baseline, followed-up every 2 years over four waves of data	Social Isolation Measured on a scale from 0-5 with higher scores indicating higher levels of social isolation including: Living arrangements, Visits with family (parents, children) Frequency of interaction with friends, Frequency of participation in social activities within the past month	Overall cognition measured by an adapted version of the Mini-Mental State Examination (MMSE) on a scale from 0-21 with higher scores indicating higher cognitive performance	Demographic: Age, Gender, and Education Lifestyle: Smoking and Alcohol use Chronic diseases: Hypertension, Dyslipidemia, Diabetes, Cancer Instrumental activities of daily living and Activities of daily living Depressive symptoms: CES-D10	Social isolation was associated with poor cognitive scores at baseline (β=-1.38; p<0.001). Higher social isolation was also associated with greater cognitive change (decline) over 6 years of follow-up (β=0.17; p<0.001)

Ertel et al.[19], 2008	Effects of Social Integration on Preserving Memory Function in a Nationally Representative US Elderly Population	Longitudinal	16, 638 participants aged 50 and older from the Health and Retirement Study (HRS) over 6 years	Social integration: marital status, volunteer activities, frequency of contact with network members	Memory: Immediate and delayed recall task	Sociodemographic: Age, gender, race, income, education Health status: chronic conditions, functional limitations, activities of daily living, instrumental activities of daily living, depressive symptoms	Increase social integration at baseline predicted slower declines in memory overtime ($p<0.01$) Memory declined at double the rate in the least integrated group compared to the most integrated

Fang et al.[162], 2023	Social Isolation and Loneliness in a Population Study of Cognitive Impairment: The MYHAT Study	Cross-sectional	1,982 participants, 65 years or older (mean age=77.65 years) from the Monongahela-Youghiogheny Healthy Aging Team (MYHAT)	Social Isolation Social activities: Volunteering, Organization meeting, Provision of unpaid help to network members, Interaction with friends or family (not living in the same household)	Cognitive Impairment: The Clinical Dementia Rating Scale (0-5), with 0=cognitively normal and ≥0.5 =cognitively impaired	Demographic: Age, Gender, Education, Race, Marital status, Living arrangement, Working status Lifestyle: Smoking status, Alcohol consumption, Exercise Vascular health: Hypertension, Cardiovascular disease, Cerebrovascular disease, Diabetes, Irregular heartbeat, Obesity Sleep complaints Depressive symptoms (mCES-D) General health: Self-rated health, Number of medications, Instrumental activities of daily living	The odds of cognitive impairment were 54% higher in socially isolated individuals compared to non-socially isolated individuals (OR=1.54; 95% CI: 1.28-1.86). The odds of cognitive impairment in socially isolated compared to non-socially isolated individuals decreased approximately 20% when loneliness was added to the model, but remained significant (OR=1.35; 95% CI: 1.16-1.58)

Fankhauser et al.[56], 2017	Social Network and Cognitive Functioning in Old Age	Cross-sectional	189 participants between the ages of 59-94 years	Structural support: size of social network, frequency of contact	Cognitive function: Mini-Mental State Examination	Sociodemographic: Age, gender, education Health status: Depressive symptoms and activities of daily living	Number of social contacts was associated with lower odds of cognitive impairment (OR=0.96; 95% CI: 0.93-0.99)
Glei et al.[184], 2005	Participating in Social Activities helps Preserve Cognitive Function: An Analysis of a Longitudinal, Population-Based Study of the Elderly	Longitudinal	2,387 participants aged 60 or older from the Study of Health and Living Status of the Elderly in Taiwan across 4 follow-up timepoints over 11 years	Social network: marital status, number of ties and frequency of contact Participation in social activities: 'no activities', 'one or two activities', 'three or more activities'	Cognitive impairment: 5 items from the Short Portable Mental Status Questionnaire	Sociodemographic: Sex, age, occupational status, economic satisfaction Health status: functional status, depressive symptoms	Participants who participated in 'one or two' social activities failed on average 13% less cognitive tests compared to those who participated in no social activities. Those who participated in 'three or more' social activities failed on average 33% less cognitive tests compared to those who participated in no social activities
Goldberg et al.[178], 2021	Effects of Restriction of Activities and Social Isolation on Risk of Dementia in the Community	Longitudinal	855 participants aged 65 years or older from the North Manhattan Aging Project across three follow-up timepoints across ~5 years	Social Isolation: including lack of social contact and participation in social activities	Episodic memory decline: immediate recall from the Selective Reminding verbal list	Sociodemographic: Sex, age, education	Social isolation was associated with worse episodic memory function overtime (β=-2.66; 95% CI: -3.72, -1.59).

Golden et al.[163], 2009	Social Support Network Structure in Older People: Underlying Dimensions and Association with Psychological and Physical Health	Cross-sectional	1,334 participants aged 65 years or older	Social engagement: Wenger social support network type assessment	Cognitive impairment: Mini-Mental State Examination A score <24 indicated cognitive impairment	Sociodemographic: Age and gender	High social engagement was associated with a decreased odds of cognitive impairment (OR=0.68 p<0.001)
Green et al.[181], 2008	Influence of Social Network Characteristics on Cognition and Functional Status with Aging	Longitudinal	874 participants (mean age=47.3 years) from the Baltimore Epidemiologic Catchment Area (ECA) study over ~10 years of follow-up	Structural support: Social network size and frequency of contact	Cognitive function: MMSE and delayed recall task	Sociodemographic: Age, sex, race, education, household income Health status: CVD or risk, depressive symptoms, activities of daily living Lifestyle behaviours: alcohol abuse or dependence	More frequent social contact and were counterintuitively associated with worse MMSE performance overtime (β=-0.008; 95% CI: -0.080,0.064)

Harling et al.[55], 2020	Social Contact, Social Support, and Cognitive Health in a Population-based Study of Middle-aged and Older Men and Women in Rural South Africa	Cross-sectional	5,059 participants aged 40 years or older from the Health and Aging in Africa: A Longitudinal Study of an INDEPTH community in South Africa (HAALSI)	Structural support: Social contact (number of network members and frequency of contact)	Cognitive impairment: Scores of cognition including orientation in time, episodic memory (immediate and delayed recall task), and ability to follow counting patterns dichotomized into 'cognitively impaired' and 'not cognitively impaired'	Sociodemographic (childhood): country of origin, education, self-reported literacy, self-rated childhood health, and father's occupation Sociodemographic (current): marital status, household size and wealth, and employment status	Smaller, denser social networks were associated with cognitive impairment
James et al.[179], 2011	Late-Life Social Activity and Cognitive Decline in Old Age	Longitudinal	1,138 participants from the Rush Memory and Aging Project (mean age=79.6 years) follow-up over 12 years	Social activity: frequency of participation in six common types of social activities	Cognitive function: combination of tests of episodic memory working memory, perceptual speed, semantic memory, and visuospatial ability	Sociodemographic: age, sex, education, race Health status: depression, chronic conditions, disability Social network size Neuroticism, extraversion Cognitive and physical activity	Social activity was associated with slower cognitive decline Frequent compared to infrequent social activity was associated with a 70% reduction in global cognitive decline

Kim & Park[175], 2023	Prolonged Social Isolation and Cognitive Function in Older Adults: Lack of Informal Social Contact versus Formal Social Activity as the Source of Social Isolation	Longitudinal	2,740 participants ('social contact' sample) and 2,785 participants ('social activity' sample) aged 45 years or older at baseline across 7 waves of data over 12 years from the Korean Longitudinal Study of Aging (KLoSA)	Social contact: Frequency of contact with network members (dichotomized into 'frequent' and 'infrequent' social contact groups) Social activity: Participation in 7 social activities (dichotomized into 'no social activity' and 'otherwise'	Cognitive function assessed by the Korean version of the Mini-Mental State Examination (K-MMSE) on a scale from 0-30 with higher scores indicating better cognitive function.	Sociodemographic: Age, Sex, Education, Income, Religious Affiliation, Marital status, Residence (Urban/Rural) Lifestyle Behaviours: Smoking, Drinking, Exercise Health Status: Instrumental activities of daily living, Depressive symptoms (CES-D10)	Absence of social contact was linked to declines in cognitive function until wave 3 (β=-2.135; p<0.001) Absence of social activity was associated with cognitive decline up to wave 5 (β=-3.073; p<0.001)
Kotwal et al.[54], 2016	Social Function and Cognitive Status: Results from a US Nationally Representative Survey of Older Adults	Cross-sectional	3,310 participants between the ages of 62-90 years from the National Social life Health and Aging Project (NSHAP)	Structural support: network structure (size and density), social engagement (community involvement and socializing)	Mild Cognitive Impairment (MCI): (Montreal Cognitive Assessment (MoCA) >22 points=normal 18-22 points=MCI <18 points=Dementia)	Sociodemographic: Age, sex, education, race, marital status Health status: Self-rated health, depressive symptoms Lifestyle factors: Alcohol consumption, smoking, physical activity	Smaller network size and increased density was associated with risk for MCI Less community involvement was also more highly correlated in those who screen positive for MCI

LaFleur & Salthouse[165], 2017	Which Aspects of Social Support Are Associated with Which Cognitive Abilities for Which People?	Cross-sectional	2,613 cognitively normal adults stratified into three age groups (18-39, 40-59, 60-99) from the Virginia Cognitive Aging Project.	Structural support: Social embeddedness (Frequency of contact with family and friends)	Cognitive ability: Vocabulary (Wechsler Adult Intelligence Scale, a picture naming task, and synonym and antonym matching), Speed (comparison task and digit symbol task), Reasoning (letter sets task, Shipley's Abstraction, and matrix reasoning) , Space (form boards task, paper folding task, and a spatial relations task) and Memory (Wechsler Memory Scale-Logical memory task, free recall task, and paired associates' task)	Sociodemographic: age, sex, education Health status: self-related health General intelligence	Increased social contact with friends but not family was positively associated with memory function ($\hat{\beta}$=0.06; p<0.01) however, this association was not significant after the inclusions of covariates
Lara et al.[185], 2019	Are Loneliness and Social Isolation Associated with Cognitive Decline	Longitudinal	1,691 participants aged 50 years or older from "Edad con Salud" over ~ 3 years of follow-up	Social isolation: marital status, living arrangement, contact with friends, family, and children, and participation in social activities	A global composite cognition score and subtypes of cognition: word list immediate and delayed verbal recall from the Consortium to Establish a Registry for Alzheimer's disease (CERAD), digit span forward and backwards from the Wechsler Adult Intelligence scale, and an animal naming test	Sociodemographic: Age, sex, education Lifestyle behaviours: Physical activity, alcohol consumption Health status: Disability, chronic conditions, depression	Increased social isolation was associated with lower cognitive scores over time (β=-0.85; 95% CI: -.55, -0.14)

Park et al.[180], 2017	Life Course Trajectories of Later-Life Cognitive Functions: Does Social Engagement in Old Age Matter?	Longitudinal	7,374 participants 65 years or older from the Health and Retirement study from seven waves of data over 12 years	Social engagement: frequency of contact with social network members (0 to 2, with higher scores representing more engagement) and volunteer work (0=no and 1=yes)	Cognitive function: Telephone Interview for Cognitive Status scored from 0-35 with score of 0-12=low cognitive function, 13-24=moderate cognitive function, and 25-35=high cognitive function	Sociodemographic: age, sex, race, education, poverty status, childhood health, income, marital status Health status: chronic conditions, instrumental activities of daily living and activities of daily living	As social engagement increased overtime, participants were more likely to have high to moderate cognitive function (RRR=1.24) and those who became less engaged were less likely to have high stable levels of cognitive function (RRR=0.78)
Piolatto et al.[57], 2022	The Effect of Social Relationships on Cognitive Decline in Older Adults: An Updated Systematic Review and Meta-Analysis of Longitudinal Cohort Studies	Systematic Review and Meta-Analysis	34 articles in systematic review/31 articles in meta-analysis – in which 17 investigated structural aspects of support Participants were an average of 67.7 years of age. The average study timeframe was 11 years. The average sample size was 5,672 (ranging from 529-19,832)	Social activity (i.e., participation in social clubs, religious organizations, volunteer work), Network size, Social engagement (based on indices)	Cognitive function or decline assessed by neuropsychological test data including the MMSE and the Wechsler scale		The cumulative meta-analysis odds ratio was estimated to be 1.12 (95% CI:1.05, 1.20) confirming previous reports that low structural social support is associated with cognitive decline

Shankar et al.[187], 2013	Social Isolation and Loneliness: Relationships with Cognitive Function During 4 Years of Follow-up in the English Longitudinal Study of Ageing	Longitudinal	6,034 participants (mean age at baseline=65.6 years) from the English Longitudinal Study of Ageing (ELSA) at baseline to 4 year follow-up	Social isolation: index based on marital status, living arrangement, frequency of contact with children, family, and friends, and participation in social activities	Memory: immediate and delayed recall task Executive function: verbal fluency via an animal naming task	Sociodemographic: age and sex, education, wealth, working status Health status: Depression, chronic conditions Lifestyle: Smoking and physical activity Loneliness	Baseline social isolation predicted a decrease in verbal fluency (β=-0.32, p<0.05), immediate recall (β=-0.14, p<0.001), and delayed recall at follow-up (β=-0.15, p<0.001)
Son and Sung[176], 2022	The Reciprocal Relationship Between Social Engagement and Cognitive Function Among Older Adults in South Korea	Longitudinal	4,731 participants aged 45 years or older at baseline across 7 waves of data over 12 years from the Korean Longitudinal Study of Aging (KLoSA)	Informal Engagement: Frequency of contact with familiar persons (from 1 = Almost never to 10 =Almost every day) Formal Engagement: Number of associations in 7 memberships (from 0 to 7), Frequency of organizational activities (from 1 = Almost never to 10 =Almost every day)	Cognitive function assessed by the Korean version of the Mini-Mental State Examination (K-MMSE) on a scale from 0-30 with higher scores indicating better cognitive function.	Sociodemographic: Age, Sex, Education, Income, Religious Affiliation, Marital status, Residence (Urban/Rural) Lifestyle Behaviours: Smoking, Drinking, Exercise Health Status: Instrumental activities of daily living, Depressive symptoms (CES-D10)	Participation in organizational activities is more robustly associated with cognitive function (β=0.060; p<0.001) compared to frequency of contact with network members (β=0.057; p<0.001) or the number of association memberships (β=0.042; p<0.001) over 12 years of follow-up. No significant bidirectional association between cognitive function and any form of social engagement was found.

Sörman et al.[171], 2017	Social Network Size and Cognitive Functioning in Middle-Aged Adults: Cross-Sectional and Longitudinal Associations	Longitudinal	804 Swedish adults between the ages of 40-60 years cross-sectionally, 604 participants at 5-year follow-up, and 255 participants at 10-year follow-up	Social network size: number of contacts and frequency of interaction	Episodic memory: Free and cued recall tasks Semantic memory: verbal fluency and correctly identifying synonyms Visuospatial ability: WALS-R Block Design Test	Sociodemographic: age and sex, education Health status: Self-rated health, depressive symptoms Lifestyle: Alcohol consumption, physical activity	Social network size was positively associated with semantic memory (β=0.099, $p<0.01$), episodic memory(β=0.074, $p<0.05$), and visuospatial ability (β=0.088, $p<0.05$) at baseline At five year follow-up, baseline social network size was associated with semantic memory (β=0.058, $p<0.05$) At 10 year follow-up social network size was associated with semantic and episodic memory (β=0.010, $p<0.05$ and β=0.088, $p<0.088$ respectively) After reversing the association at 10-year follow-up, no relationship was found between any cognitive domain and network size

Yu et al.[183], 2021	Social Isolation, rather than Loneliness, is Associated with Cognitive Decline in Older Adults: The China Health and Retirement Longitudinal Study	Longitudinal	7761 participants aged 50 and older from the China Health and Retirement Longitudinal Study (CHARLS) across two waves of data over 4 years	Social Isolation score from 0-3 including: Marital status, social contact frequency with children, and participation in social activities, with higher scores indicating a higher level of social isolation	Episodic memory: Immediate and delayed recall memory test with scores from 0-10 with higher scores indicating better function Mental status: Telephone Interview for Cognitive Status (TICS) with scores from 0-10 with higher scores indicating better function	Sociodemographic: Age, gender, education, residence (urban/rural) Lifestyle habits: smoking status and alcohol consumption Health status: Activities of daily living and instrumental activities of daily living, depressive symptoms (CES-D10), Chronic diseases	Social Isolation was significantly associated with declines in episodic memory (β=-0.05; $p<0.001$) and mental status (β=-0.03; $p<0.01$) after 4 years

Zhou et al.[58], 2020	Prospective Association between Social Engagement and Cognitive Impairment among Middle-Aged and Older Adults: Evidence from the China Health and Retirement Longitudinal Study	Longitudinal	6920 participants from the China Health and Retirement Longitudinal Study (CHARLS) aged 45 and older at baseline, followed-up every 2 years over four waves of data	Social engagement including frequency of participation in social activities and interactions with friends categorized into 4 levels of engagement with higher levels indicating greater social engagement	Global cognition based on episodic memory (measured by an immediate and delayed recall task on a scale from 0-20) and mental intactness (measured through numerical ability, time orientation, and picture drawing scored on a scale from 0-10) Scores were summed from 0-30 and dichotomized such that a score of ≤ 11 indicated the presence of cognitive impairment	Demographic: Age, Sex, Education, Marital status, Residence (Urban/Rural) Lifestyle: Smoking and Alcohol use Health status Chronic conditions, Self-reported depressive symptoms, Instrumental activities of daily living and Activities of daily living Depressive symptoms: CES-D10	Having a higher level of social engagement was associated with lower risk of cognitive impairment in a dose response fashion

Table A-3. Summary of the Literature on the Association between Functional Social Support and Cognitive Function

Author(s)	Title	Study Design	Study Population	Predictor Measures	Outcome Measures	Covariates	Conclusions and Findings
Du et al.[191], 2022	Source of Perceived Social Support and Cognitive Change: An 8-Year Prospective Cohort Study	Longitudinal	1,319 participants aged 65 years or older from three waves of data (2006, 2010, and 2014) from the HRS	FSS: 4-items regarding perceived availability of support	Cognitive function: measured by the Telephone Interview Cognitive Screen (TICS) on a scale from 0-35 with higher scores indicating better cognitive function	Sociodemographic: Age, sex, race, education, wealth Health status: Physical health, depressive symptoms	Perceived levels of support were not significantly associated with changes in cognitive function however, support from children was positively associated with changes in cognitive function over time ($\hat{\beta}$=0.05, p<0.01) whereas, support from other family members were negatively associated with cognitive change over time ($\hat{\beta}$=-0.07, p<0.01)

Freak-Poli et al.[192], 2022	Loneliness, Not Social Support, Is Associated with Cognitive Decline and Dementia Across Two Longitudinal Population-Based Cohorts	Longitudinal	4,514 participants aged ≥ 55 from the Rotterdam Study (RS) follow-up every 4-5 years over 14 years 2,112 participants ≥55 years from the Swedish National Study on Aging Care in Kungsholmen (SNAC-K) with 3 follow-up timepoints over 10 years	FSS (RS): 5-items modified from the Health and Lifestyle Survey regarding perceived availability of support FSS (SNAC-K): 5-items regarding satisfaction with support	Cognitive function (RS): Delayed learning task, the Stroop 3 test, Letter-Digit Substitution Task, Purdue Pegboard test, and Word Fluency Cognitive function (SNAC-K): Pattern Comparison, free recall, vocabulary, letter fluency, and animal fluency Dementia (RS): an MMSE score <26 or a Geriatric Mental Schedule (GMS) score >0 Dementia (SNAC-K): diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV)	Sociodemographic: Age, sex, education Health status: Chronic conditions, Activities of Daily Living, BMI, Depressive symptoms Lifestyle behaviours: Smoking status, alcohol consumption	Perceived levels of social support were not found to have an association with cognitive decline or risk of dementia in either cohort.

Ma et al.[95], 2024	Social Support and Cognitive Activity and their Associations with Incident Cognitive Impairment in Cognitively Normal Older Adults	Longitudinal	9,394 participants aged 65 or over from 4 waves of data collected from the China Health and Retirement Longitudinal Study	FSS: Perceived availability of emotional, informational, and instrumental support	Cognitive impairment: Measured by the MMSE, cutoff score for impairment was based on level of education received	Sociodemographic: Age, sex, urban/rural living status, education, household income, marital status, and living arrangement Health status: Physical activity score, diet score activities of daily living, chronic conditions Lifestyle behaviours: Smoking status and alcohol consumption	Social support was associated with reduced risk of incident cognitive impairment (HR: 0.956; 95% CI: 0.932, 0.980)

Mogic et al.[18], 2023	Functional Social Support and Cognitive Function in Middle- and Older-Aged Adults: A Systematic Review of Cross-sectional and Cohort studies	Systematic Review	85 studies (44 cross-sectional and 41 cohort) of participants aged 40 years or older from any residential setting Sample sizes ranged from 20 to 30,029 participants.	FSS: Overall FSS or subtypes (emotional/informational support, tangible support, affectionate support, and positive social interactions)	Cognitive function: assessed globally (38 articles) or by domain (e.g., memory, executive function [20 articles]) Dementia: all-cause or Alzheimer's disease diagnosis (19 articles) See Table 1 [pp. 4 to 14] in the published review for a list of instruments		Positive associations were generally found between overall FSS and subtype specific FSS, and cognitive function High levels of affectionate support and positive support were associated with decreased risk for neurocognitive outcomes
Oh et al.[193], 2022	Association of Low Emotional and Tangible Support with Risk of Dementia Among Adults 60 Years or older in South Korea	Longitudinal	5,852 community-dwelling adults from the Korean Longitudinal Study on Cognitive Aging and Dementia (KLOSCAD) follow-up every 2 years over 8 years	FSS: Emotional and Tangible support based on the MOS-SSS Low FSS classified as below the 25th percentile	Dementia: Diagnosis based on the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease	Sociodemographic: Age, sex, education, economic status Health status: Chronic conditions and depressive symptoms Lifestyle behaviours: alcohol consumption, smoking, and level of physical activity	Low emotional support was associated with an increased risk of all-cause dementia and Alzheimer's disease (HR:1.42; 95% CI: 1.04,1.93 and HR: 1.45 95% CI: 1.00, 2.11 respectively) Low tangible support was associated with an increased risk of all-cause dementia and Alzheimer's disease (HR:0.79; 95% CI: 0.57,1.09 and HR: 0.99 95% CI: 0.69,1.44 respectively)

Ohman et al.[97], 2023	Subtypes of Social Support Availability are not Differentially Associated with Memory: A Cross-Sectional Analysis of the Comprehensive Cohort of the Canadian Longitudinal Study on Aging	Cross-Sectional	24,719 participants aged 45 to 85 years from the Comprehensive Cohort of the CLSA	FSS: Overall FSS and affectionate, emotional/informational, positive, and tangible support subtypes measured by the MOS-SSS	Episodic memory: immediate and delayed recall memory measured by a modified version of the RAVLT I and II	Sociodemographic: Age, sex, province, education, household income, marital status, and urban/rural living status Health status: self-rated health, depressive symptoms, and number of chronic conditions Lifestyle behaviours: Smoking status and alcohol consumption	Overall and subtypes of FSS were positively, and significantly associated with immediate and delayed recall memory expect for positive support and delayed recall memory ($\hat{\beta}$=0.02 95% CI:0.00, 0.04)
Peng et al.[94], 2022	Cognitive function and cognitive decline among older rural Chinese adults: the roles of social support, pension benefits, and medical insurance	Longitudinal	5,135 participants aged 45+ 3 waves of data collected (2013, 2015, 2018) from the China Health and Retirement Longitudinal Study	FSS: A single item regarding perceived availability of future support	Episodic memory: immediate & delayed word recall	Sociodemographic: Age, gender, education, marital status, household consumption, Health status: Activities of daily living	Perceived availability of support was associated with higher memory function at baseline ($\hat{\beta}$=0.25, p<0.05) and slower memory decline over time ($\hat{\beta}$=0.32, p<0.01)

Wang et al.[194], 2023	Relationship between Social Support and 7-Year Trajectories of Cognitive Decline: Results from the China Health and Retirement Longitudinal Study	Longitudinal	6,795 participants aged 60 or over from 4 waves of data collected from the China Health and Retirement Longitudinal Study	FSS: A single item regarding perceived availability of future support	Cognitive function: measured by immediate and delayed recall, time orientation, and executive function	Sociodemographic: Age, Sex, Urban/Rural status, Education Health status: BMI, depression, activities of daily living, chronic conditions Lifestyle behaviours: Smoking status and alcohol consumption	Perceived availability of support was associated with higher memory function at baseline ($\hat{\beta}$=0.442; 95% CI: 0.207, 0.678) and but increased memory decline over time ($\hat{\beta}$=-0.068; 95% CI: -0.123, -0.013)
Yoo et al.[96], 2023	The Association between Functional Social Support and Memory in Middle-Aged and Older Adults: A Prospective Analysis of the Canadian Longitudinal Study on Aging's Comprehensive Cohort	Longitudinal	12,011 participants aged 45 to 85 years at baseline from the Comprehensive Cohort of the CLSA	FSS: Overall FSS and affectionate, emotional/informational, positive, and tangible support subtypes measured by the MOS-SSS	Episodic memory: change scores from a combined score of immediate and delayed recall memory measured by a modified version of the RAVLT I and II	Sociodemographic: Age, sex, province, education, household income, marital status, and living arrangement Health status: functional status, number of chronic conditions, depressive symptoms Lifestyle behaviours: Smoking status and alcohol consumption	Although positive associations were found between overall and subtypes of FSS and memory, only tangible support was significantly associated with changes in memory function over three years ($\hat{\beta}$=0.07; 95% CI: 0.01, 0.14)

Table A-4. Summary of the Literature on the Association between Structural and Functional Social Support, and Cognitive Function

Author(s)	Title	Study Design	Study Population	Predictor Measures	Outcome Measures	Covariates	Conclusions and Findings
Chen & Chang[44], 2016	Developmental Patterns of Cognitive Function and Associated Factors among the Elderly in Taiwan	Longitudinal	3,155 participants aged 65 years or older from the Taiwan Longitudinal Study on Aging (TLSA) over 15 years of follow-up	Structural support: Social interaction (playing games and socializing with others) Functional support: Emotional support (being cared for when ill and being listened to by friends or relatives)	Cognitive function: The Short Portable Mental Status Questionnaire (SPMSQ)	Sociodemographic: Age, sex, education Lifestyle: physical activity, smoking, alcohol consumption Health status: BMI, self-rated health, chronic conditions, depressive symptoms, activities of daily living and instrumental activities of daily living	Emotional support reduced the odds of cognitive decline in individuals who previously has low cognitive function (OR=0.77; 95% CI: 0.60 to 0.99) No association was found between social interaction and odds of cognitive trajectory Analyses included all social variables simultaneously

DiNapoli et al.[45], 2014	Social Isolation and Cognitive Function in Appalachian Older Adults	Cross-sectional	267 community-dwelling older adults in West Virginia, 70 to 94 years (mean = 78.5 years)	Structural support: LSNS-6 - SI (network size and frequency of contact) Functional support: LSNS-6 - Perceived isolation and perceived confidence in network	Memory: Rey-Osterrieth Complex Figure and California Verbal Learning Test-2nd edition Short From (CVLT-II) Executive functioning: Trail making B and Controlled Oral Word Association Test Attention: Trail Making A Language: Boston Naming Test Cognitive function: a score from all six tests with higher scores indicating higher cognitive function	Sociodemographic: Age, sex, education, marital status, annual income Health status: vascular risk factors, depressive symptoms	For overall cognitive function, when both aspects of structural and functional support were included in the same model, perceived support accounted for 10.2% of variance in cognitive functioning while social isolation accounted for 5.7%

Fan et al.[112], 2021	Reduced Social Activities and Networks, but not Social Support are associated with Cognitive Decline among Older Chinese Adults: A Prospective Study	Longitudinal	3,314 participants between the ages of 65-110 years at baseline from the Chinese Longitudinal Healthy Longevity Survey (CLHLS) over 3 years of follow-up	Structural support: Social activity (engaging in group discussions, fieldtrips, and attendance of social groups) Social network (marital status, number of visits from children and siblings, living arrangements) Functional support: Social support (perception of the availability of emotional and instrumental support)	Cognitive function: Scores of overall cognitive functions assessed by the Chinese version of the MMSE (scored from 0-30 with higher scores indicating better cognitive function)	Sociodemographic: age, sex, education, residence Lifestyle: smoking status, alcohol consumption, and physical exercise Health status: Chronic conditions and self-reported health	In a mutually adjusted model including social activity, social networks, and social support only the associations between social activity (OR=0.80; 95% CI:0.65-0.98) and social networks (OR=0.70 95% CI: 0.56-0.87) and incident cognitive decline remained significant such that high social activity and larger networks protected against cognitive decline
Gow et al.[210], 2013	Which Social Network or Support Factors are Associated with Cognitive Abilities in Old Age?	Cross-sectional	1,091 individuals from the Lothian Birth Cohort 1936 (LBC1936), at age 70	Structural support: Contact with friends/family, marital status and living arrangement Functional support: Adapted from the Social Support Questionnaire-support received and level of satisfaction regarding received support	Cognitive ability: Memory (Wechsler Adult Intelligence Scale-III UK and Wechsler Memory Scale-III UK) and Processing speed (reaction and inspection time tests)	Sociodemographic: Social class, sex Health status: symptoms of depression Age-11 IQ	No associations were found between objective and subjective measures of social support and general cognitive ability Only processing speed was significantly associated with living alone after adjusting for covariates ($\hat{\beta}$=0.006; p<0.05) Analyses included all social variables simultaneously

Hughes et al.[36], 2008	The Association Between Social Resources and Cognitive Change in Older Adults: Evidence from the Charlotte County Healthy Aging Study	Longitudinal	Charlotte County Healthy Aging Study 217 participants (mean age=72.5 SD=6.2) 5-year follow-up	Structural support: LSNS-6 (network size and frequency of contact with friends, family, and other relatives) Functional support: LSNS-6 (perception and satisfaction with support)	Cognitive function: General cognitive ability (MMSE), Perceptual speed (Trail making test A and B), Attention (Stroop test), and Episodic memory (Hopkins Verbal Learning Test [delayed free recall, cued recall, and recognition])	Sociodemographic: age, gender, education, marital status, residence Personality	At baseline, increased negative social interactions and greater satisfaction of support were associated with higher global cognitive function ($\hat{\beta}$=0.42; p=0.03 and $\hat{\beta}$=0.45; p=0.02 respectively) however, these association were not significant at follow-up Analyses included all social variables simultaneously

Krueger et al.[132], 2009	Social Engagement and Cognitive Function in Old Age	Cross-sectional	Rush Memory and Aging Project in Chicago (n=838, mean age= 80.2, SD=7.5)	Structural support: Network size, frequency of contact, and frequency of social activity Functional support: Multidimensional Scale of Perceived Social Support	Cognitive function: Episodic memory (Word list memory, Recall and Recognition, and immediate and delayed recall from the Wechsler Memory Scale-Revised), Working memory (Digit Span Forward and Digit Span Backward), Semantic memory (15-item version of the Boston Naming Test, Verbal Fluency, and a 15-item version of the National Adult Reading Test), Perceptual speed (Symbol Digit Modalities Test, Number comparison, Stroop test), Visuospatial ability (Judgement of line orientation, Standard Progressive Matrices)	Sociodemographic: age, sex, education Health status: depressive symptoms, chronic conditions, disability, Lifestyle behaviours: physical activity Personality traits	When social network, social activity, and social support were included in the same model, only social activity and social support were significantly associated with global cognitive function ($\hat{\beta}$=0.161; p<.001 and $\hat{\beta}$=0.069; p=.003 respectively)

Li & Dong[204], 2018	Is Social Network a Protective Factor for Cognitive Impairment in US Chinese Older Adults? Findings from the PINE Study	Cross-sectional	Population Study of Chinese Elderly (PINE) in the US aged 60 and older, with a sample size of 3,157	Structural support: Network size, volume of contact, proportion kin, proportion female, and proportion co-resident Functional support: Quality of social relationship (emotional closeness)	Cognitive function: General cognition (MMSE), Episodic memory (Immediate recall of the East Boston Memory Test (EBMT) and delayed recall of East Boston Memory Test (EBDR) of brief stories in the East Boston Memory Test), Executive function (Symbol Digit Modalities Test), Working memory (Digit span backwards)	Sociodemographic: age, gender, education, annual income, years in the US, years in the community Health status: medical comorbidities, overall health status, health change in the last year	General cognition was positively, significantly associated with emotional closeness ($\hat{\beta}$=0.076; p<0.01) and network size ($\hat{\beta}$=0.049; p<0.001) Analyses included all social variables simultaneously

Paiva et al.[201], 2023	The Interrelationships between Social Connectedness and Social Engagement and its relation with Cognition: A Study using SHARE Data	Cross-sectional	66,504 non-working individuals aged 50 years or older from the Survey of Health, Ageing and Retirement in Europe (SHARE)	Structural support: Social Engagement (participation in three types of social activities including volunteering, club membership, and community organization membership and the frequency of participation. Scores were summed on a scale from 0-9 and categorized into four levels: 0, 1, 2, and 3 or more) Functional support: Social Connectedness (Number of and frequency of contact with close confidants and level of emotional closeness)	Cognitive function: sum of five cognitive test scores ranging from 12.53 to 40.48 including (1) Verbal Fluency (2) Immediate recall (3) Delayed recall (4) Numeracy (5) Orientation	Sociodemographic: Age, gender, living arrangement, education, perception of financial distress, income Health status: grip strength, self-reported health, chronic conditions, depressive symptoms	Higher levels of social engagement ($\hat{\beta}$=0.83; p<0.001) and social connectedness ($\hat{\beta}$=0.23; p<0.001) were associated with higher overall cognitive function The interaction between social engagement and connectedness was associated with higher cognitive function compared to when one of these aspects was lacking Analyses included all social variables simultaneously

Seeman et al.[34], 2001	Social Relationships, Social Support, and Patterns of Cognitive Aging in Health, High-Functioning Older Adults: MacArthur Studies of Successful Aging	Longitudinal	1,189 participants between the ages of 70-79 years from the MacArthur Studies of Successful Aging over 7.5 years	Structural support: marital status, number of close contacts (friends, relatives, and friends), participation in religious or other groups Functional support: emotional and instrumental support	Cognitive function: Brief test of adult cognition by telephone (BTACT) with higher scores indicating higher cognitive function	Sociodemographic: Age, sex, education, ethnicity, income Health status: chronic conditions, depressive symptoms, self-efficacy Lifestyle behaviours: physical activity Baseline cognitive function	Higher baseline emotional support was associated with higher cognitive scores at follow-up ($\hat{\beta}$=1.20; p=0.05) Analyses included all social variables simultaneously
Yeh & Liu[33], 2003	Influence of Social Support on Cognitive Function in the Elderly	Cross-sectional	4,993 city-dwelling adults from Taiwan aged 65 years or older	Structural support: Marital status, Living arrangement Functional support: perceived support from friends	Cognitive function: Higher Short Portable Mental Status Questionnaire (SPMSQ)	Sociodemographic: Age, gender, religion, occupation, education Health status: self-rated health, activities of daily living and instrumental activities of daily living, self-reported functional status, chronic conditions	Marital status ($\hat{\beta}$=0.13; p<0.005) and perceived support (β=0.11; p<0.001) were positively associated with higher scores on the SPMSQ Analyses included all social variables simultaneously

Table A-5. Summary of the Literature on the Association between Structural and Functional Social Support & Memory

Author(s)	Title	Study design	Study population	Predictor measures	Outcome measures	Covariates	Conclusions and Findings
DiNapoli et al.[45], 2014	Social Isolation and Cognitive Function in Appalachian Older Adults	Cross-sectional	267 community-dwelling older adults in West Virginia, 70 to 94 years (mean = 78.5 years)	Structural support: LSNS-6 - SI (network size and frequency of contact) Functional support: LSNS-6 - Perceived isolation and perceived confidence in network	Memory: Rey-Osterrieth Complex Figure and California Verbal Learning Test-2nd edition Short From (CVLT-II) Executive functioning: Trail making B and Controlled Oral Word Association Test Attention: Trail Making A Language: Boston Naming Test Cognitive function: a score from all six tests with higher scores indicating higher cognitive function	Sociodemographic: Age, sex, education, marital status, annual income Health status: vascular risk factors, depressive symptoms	Lower SI was associated with better memory function ($\hat{\beta}$=0.25; 95% CI: 0.11, 0.39) Higher perceived support was positively associated with memory ($\hat{\beta}$=0.28; 95% CI: 0.16, 0.40)
Gow et al.[210], 2013	Which Social Network or Support Factors are Associated with Cognitive Abilities in Old Age?	Cross-sectional	1,091 individuals from the Lothian Birth Cohort 1936 (LBC1936), at age 70	Structural support: Contact with friends/family, marital status and living arrangement Functional support: Adapted from the Social Support Questionnaire-support received and level of satisfaction regarding received support	Cognitive ability: Memory (Wechsler Adult Intelligence Scale-III UK and Wechsler Memory Scale-III UK) and Processing speed (reaction and inspection time tests)	Sociodemographic: Social class, age, sex Health status: symptoms of depression Age-11 IQ	No associations were found between objective and subjective measures of social support and memory Analyses included all social variables simultaneously

Hughes et al.[36], 2008	The Association Between Social Resources and Cognitive Change in Older Adults: Evidence from the Charlotte County Healthy Aging Study	Longitudinal	Charlotte County Healthy Aging Study 217 participants (mean age=72.5 SD=6.2) 5-year follow-up	Structural support: LSNS-6 (network size and frequency of contact with friends, family, and other relatives) Functional support: LSNS-6 (perception and satisfaction with support)	Cognitive function: General cognitive ability (MMSE), Perceptual speed (Trail making test A and B), Attention (Stroop test), and Episodic memory (Hopkins Verbal Learning Test [delayed free recall, cued recall, and recognition])	Sociodemographic: age, gender, education, marital status, residence Personality	No association was found between network size or frequency of contact and memory function Less satisfaction with support was marginally associated with memory decline ($\hat{\beta}$=0.18; p=0.06) Analyses included all social variables simultaneously
Hülür[31], 2022	Structural and Functional Aspects of Social Relationships and Episodic Memory: Between-Person and Within-Person Associations in Middle-Aged and Older Adults	Longitudinal	Health and Retirement Study (HRS), 50 years or older (mean age at baseline = 66 years, SD = 10, range = 50–104), 3 waves of data collected from 19,297 participants	Structural support: Social network size and contact frequency Functional support: Social support and social strain	Episodic memory: immediate and delayed recall test	Sociodemographic: Age, gender, education Health status: functional health and depressive symptoms	Being married/partnered ($\hat{\beta}$= 0.04; p< 0.01) and having more social contacts ($\hat{\beta}$= 0.02; p< 0.01) was associated with less episodic memory decline Low social strain ($\hat{\beta}$ = −0.16; p<0.01) and high social support ($\hat{\beta}$ = 0.19; p<0.01) buffered memory decline, however, the associations were no longer significant after inclusion of covariates Analyses included all social variables simultaneously

Krueger et al.[132], 2009	Social Engagement and Cognitive Function in Old Age	Cross-sectional	Rush Memory and Aging Project in Chicago (n=838, mean age= 80.2, SD=7.5)	Structural support: Network size, frequency of contact, and frequency of social activity Functional support: Multidimensional Scale of Perceived Social Support	Cognitive function: Episodic memory (Word list memory, Recall and Recognition, and immediate and delayed recall from the Wechsler Memory Scale-Revised), Working memory (Digit Span Forward and Digit Span Backward), Semantic memory (15-item version of the Boston Naming Test, Verbal Fluency, and a 15-item version of the National Adult Reading Test), Perceptual speed (Symbol Digit Modalities Test, Number comparison, Stroop test), Visuospatial ability (Judgement of line orientation, Standard Progressive Matrices)	Sociodemographic: age, sex, education Health status: depressive symptoms, chronic conditions, disability, Lifestyle behaviours: physical activity Personality traits	Increased social activity was positively associated with episodic memory after controlling for covariates ($\hat{\beta}$=0.171; 95% CI: 0.091, 0.251) FSS was positively related to higher levels of function in working memory ($\hat{\beta}$=0.11; 95% CI: 0.03, 0.18), but not in episodic or semantic memory
Li & Dong[204], 2018	Is Social Network a Protective Factor for Cognitive Impairment in US Chinese Older Adults? Findings from the PINE Study	Cross-sectional	Population Study of Chinese Elderly (PINE) in the US aged 60 and older, with a sample size of 3,157	Structural support: Network size, volume of contact, proportion kin, proportion female, and proportion co-resident Functional support: Quality of social relationship (emotional closeness)	Cognitive function: General cognition (MMSE), Episodic memory (Immediate recall of the East Boston Memory Test (EBMT) and delayed recall of East Boston Memory Test (EBDR) of brief stories in the East Boston Memory Test), Executive function (Symbol Digit Modalities Test), Working memory (Digit span backwards)	Sociodemographic: age, gender, education, annual income, years in the US, years in the community Health status: medical comorbidities, overall health status, health change in the last year	Network size was positively associated with episodic memory ($\hat{\beta}$=0.059; p<0.001) however, no significant association was found between emotional closeness and memory Analyses included all social variables simultaneously

Meister & Zahodne[212], 2022	Associations Between Social Network Components and Cognitive Domains in Older Adults	Longitudinal	2,553 participants from the Health and Retirement Study (HRS) 65 years or older in the Harmonized Cognitive Assessment Protocol (HCAP)	Structural support: Network size, marital status, contact frequency Functional support: Perceived support and perceived strain	Cognitive outcomes: Episodic memory (Measured using four indicators from the Consortium to Establish a Registry for Alzheimer's Disease [CERAD]), Executive function (Number series test, Raven's standard progressive matrices, Trail making test B), Visuoconstruction (CERAD), Language (TICS and visual confrontation naming and sentence writing from the MMSE), Processing speed (Symbol Digit Modalities Test, Trail making test A, a backwards counting task, and a letter cancellation task)	Sociodemographic: sex/gender, race/ethnicity, income, wealth, and education	Contact frequency with children ($\hat{\beta}$=0.12; p<0.05) and friends ($\hat{\beta}$=0.22; p<0.05) were positively related to episodic memory Social strain ($\hat{\beta}$=-0.30; p<0.05) and perceived social support ($\hat{\beta}$=-0.30; p<0.05) were negatively related to episodic memory overtime Analyses included all social variables simultaneously
Peng et al.[94], 2023	Cognitive function and cognitive decline among older rural Chinese adults: the roles of social support, pension benefits, and medical insurance	Longitudinal	China Health and Retirement Longitudinal Study. 5,135 participants aged 45+ 3 waves of data collected (2013, 2015, 2018)	Structural support: Living arrangements, financial transfers from adult children and frequency of contact Functional support: Perceived availability of future support	Episodic memory: immediate & delayed word recall	Sociodemographic: age, gender, education, marital status, household consumption Health status: activities of daily living Participation in social activities	Living alone was associated with an increased risk of memory decline ($\hat{\beta}$=-0.37; p<0.01) Perceived availability of support was associated with higher memory function at baseline ($\hat{\beta}$=0.25; p<0.05) and slower memory decline over time ($\hat{\beta}$=0.32; p<0.01) Analyses included all social variables simultaneously

Seeman et al.[211], 2011	Histories of Social Engagement and Adult Cognition: Midlife in the U.S. Study	Longitudinal	4,963 participants aged 35–85 years using data from the national Midlife in the U.S. (MIDUS) study First wave - 1994/1995 second wave - 2005/2006	Structural: Social contacts (frequency of contact) Functional: Social support (perceived support) Social Strain (perceived strain)	Cognitive function (Brief Test of Adult Cognition by Telephone (BTACT): Episodic memory (immediate and delayed word recall), Working memory (digits backward), Executive function and semantic memory (category fluency), Reasoning (number series completion), and Processing speed (backward counting)	Age, sex, race, education, health conditions (chronic conditions, reported disabilities, and depressive symptoms), and health behaviors	Greater social contact was associated with better episodic memory function overtime ($\hat{\beta}$=0.0493; p<0.01) Social support was cross-sectionally associated with episodic memory ($\hat{\beta}$=0.0513; p<0.01) but not over time Analyses included all social variables simultaneously

Zahodne et al.[46], 2019	Social Relations and Age-Related Change in Memory	Longitudinal	Health and Retirement Study (HRS) 10,390 participants (mean age = 69, SD = 9.53 at baseline) 4 follow-up time points over 6 years	Structural support: Marital status, network size, frequency of contact with social network members Functional support: Quality of social relations (social support and strain from social network members)	Episodic memory: Consortium to Establish a Registry for Alzheimer's Disease (CERAD) list learning task	Sociodemographic: Age, sex, race/ethnicity, education Health status: depressive symptoms, chronic conditions, self-rated health	Being married/partnered ($\hat{\beta}$=0.08; p=0.02) and reporting more contact frequency with friends ($\hat{\beta}$=0.10; p=0.01), but not children or other relatives, was associated with higher memory at baseline and slower episodic memory decline Greater support from spouses ($\hat{\beta}$=0.05; p<0.001) or friends ($\hat{\beta}$=0.09; p<0.001) was associated with better memory function at baseline; no longitudinal association was found between functional support and memory No evidence of bidirectionality was found, such that baseline memory did not predict subsequent changes in social relations Analyses included all social variables simultaneously

Zuelsdorff et al.[214], 2019	Social support and verbal interaction are differentially associated with cognitive function in midlife and older age	Cross-sectional	Wisconsin Registry for Alzheimer's Prevention (WRAP) study 1,052 participants (40-65 years)	Structural support: Quantity of social interactions (Low, moderate, high, very high) Functional support: Medical Outcomes Study-Social Support Survey (MOS-SSS)	Cognitive domains: Episodic memory (RAVLT, Visual Learning and Memory, and Weschler Memory Scale -Revised immediate and delayed recall) and Executive function (Trail making test A and B, Stroop test, Digit Span forwards and backwards, and Letter-Number sequencing)	Sociodemographic: age, gender, race, study site, education, partner status APOE-E4 carrier status Lifestyle behaviours: smoking status, alcohol consumption, caffeine consumption, physical activity Health status: BMI	"High" but not "very high" levels of verbal interactions was significantly associated with higher verbal learning and memory function ($\hat{\beta}$=0.16; 95% CI: 0.02, 0.30) A positive but not significant association was found between high perceived support and memory Analyses included all social variables simultaneously

Appendix B. Social Isolation Index

CLSA Module	Questions	Measurement
Social Networks	When did you last get together with: 1) any of your children who live outside of your household? 2) any of your siblings who live outside of your household? 3) any of your close friends who live outside of your household? 4) any of your neighbours?	Within the last day or two Within the last week or two Within the past month Within the past 6 months Within the past year More than 1 year ago
	How many people, not including yourself, currently live in your household?	Provide a number
	How many people do you consider close friends?	Provide a number
	How many of your neighbours do you know?	Provide a number
	How many children do you have?	Provide a number
	How many, if any, living siblings do you have?	Provide a number
	About how many living relatives do you have?	Provide a number
Social Participation	In the past 12 months, how often did you participate: 1. in family or friendship-based activities outside the household? 2. Sports or physical activities that you do with other people 3. Educational and cultural activities	At least once a day At least once a week At least once a month At least once a year Never

	4. Church or religious activities such as services, committees, or choirs 5. Service club or fraternal organizational activities 6. Volunteer or charity work 7. Neighbourhood, community, or professional association activities 8. 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 Married/living with a partner in a common-law relationship Widowed Divorced Separated
Retirement Status	At this time, do you consider yourself to be completely retired, partly retired, or not retired?	Completely retired Partly retired Not retired

This social isolation index is based on previous work by Menec et al.[24]

[1]The index is scored on a scale from 0-5. Each of the following criteria yields one point:

1) Lives alone and is not married or in a common-law relationship.
2) Has gotten together with friends or neighbours less frequently than 'within the last month' or reported having no friends or neighbours.
3) Has gotten together with relatives/siblings less frequently than 'within the last month' or reported having no relatives or siblings.
4) Has gotten together with children less frequently than 'within the last month' or has no children.
5) Is retired and participates in no more than one of eight social activities at least once a month or more often.

Appendix C. Medical Outcomes Study – Social Support Survey (MOS–SSS) [30]

	Questions	Type of Functional Social Support
1	Someone you can count on to listen to you when you need to talk	Emotional/Informational
2	Someone to give you advice about a crisis	
3	Someone to give you information in order to help you understand a situation	
4	Someone to confide in or talk to about yourself or your problems	
5	Someone whose advice you really want	
6	Someone to share your most private worries and fears with	
7	Someone to turn to for suggestions about how to deal with a personal problem	
8	Someone who understands your problems	Tangible
9	Someone to help you if you were confined to bed	
10	Someone to take you to the doctor if you needed it	
11	Someone to prepare your meals if you were unable to	
12	Someone to help you with daily chores if you were sick	
13	Someone who shows you love and affection	Affectionate
14	Someone who hugs you	
15	Someone to love you and make you feel wanted	
16	Someone to get together with for relaxation	Positive social interaction
17	Someone to do something enjoyable with	
18	Someone to have a good time with	
19	Someone to do things with to help you get your mind off	Additional item

Appendix D. Covariates

	Covariate	Measurement	Variable Name
Sociodemographic	Sex	Male Female	SEX_ASK_TRM
	Age	45-54 years 55-64 years 65-74 years 75 years or older	AGE_GRP_TRM
	Education	Less than high school High school diploma Some post-secondary education Post-secondary degree/diploma	ED_UDR04_TRM
	Province of residence	One of the ten provinces	WGHTS_PROV_TRM
	Total annual household outcome	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 $150,000 or more	INC_TOT_TRM
Health status	Functional status	0 (no assistance required for any activity) 1 (assistance required for at least one activity)	ADL_DCLS_TRM
	Chronic conditions	0 (no chronic condition) 1 (one or more chronic conditions)	CCT_F2_TRM
	Depressive symptoms (Center for Epidemiological Studies Short Depression Scale [CES-D10])	Score from 0-30 0= not severe (less than 10) 1=Severe (10 or more)	DEP_CESD10_TRM

Lifestyle Behaviours	Smoking status	0=Non-user (did not smoke in the past 30 days) 1=Occasional user (at least one cigarette in the past 30 days, but not every day) 2= Daily user (at least one cigarette every day for the past 30 days)	SMK_CURRCG_TRM
	Alcohol consumption	0= Non-user (Did not drink in the last 12 months) 1= Occasional drinker 2=Regular drinker (At least once a month)	ALC_TTM_TRM

Variables utilized in analysis as covariates – variable names based on original CLSA questionnaires and derived variables[234,235,289–293].

[1]The suffix "TRM" indicates variable at t_0

Appendix E. Plots Describing the Relationship Between Baseline and Follow-up Memory

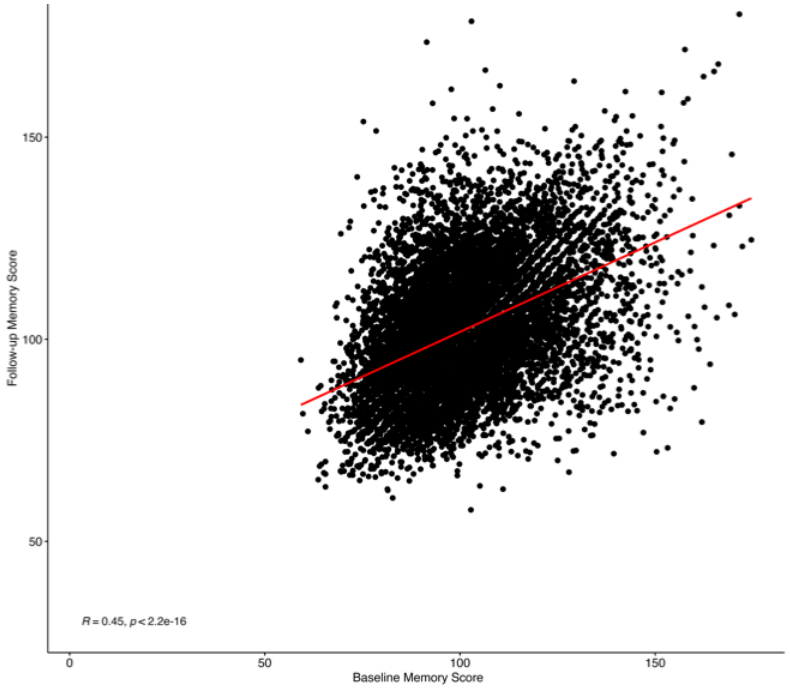


Figure E-1 Scatterplot - Relationship between Baseline and Follow-up Memory Scores

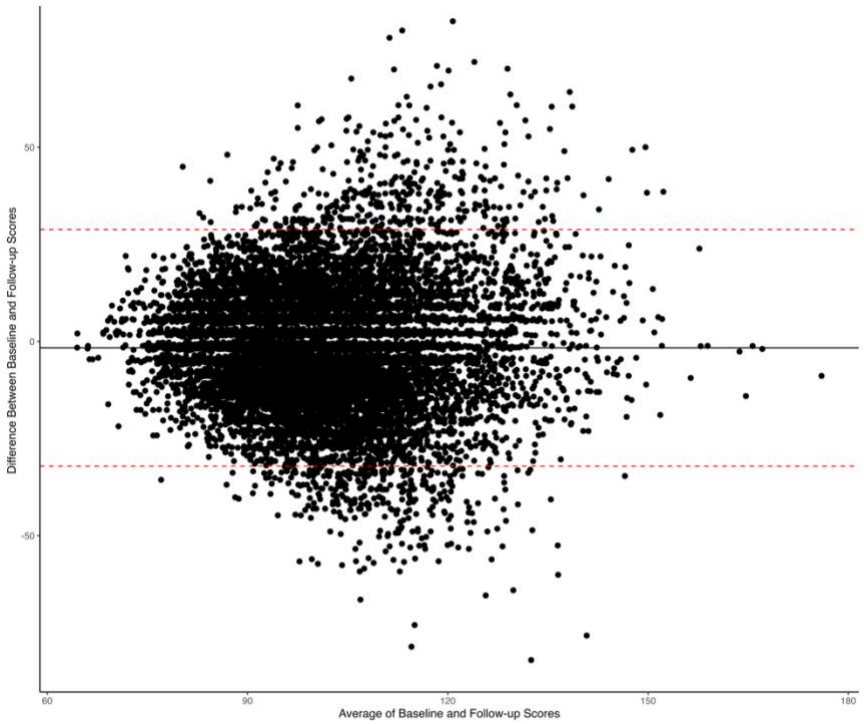


Figure E-2 Bland-Altman Plot - Agreement Between Baseline and Follow-up Memory Scores and 95% Confidence Interval (represented by the red dotted lines)

Appendix F. Regression Analyses: Base and Adjusted Models for the Association Between Social Isolation and Memory

	Base Model $\hat{\beta}$ (95% CI)	Adjusted Model $\hat{\beta}$ (95% CI)
Exposure		
Social Isolation Status		
(Ref: Not socially isolated)		
Socially isolated	**-0.75 (-1.32, -0.18)**	-0.13 (-0.68, 0.45)
Sociodemographic		
Sex		
(Ref: Male)		
Female	0.28 (-0.17, 0.74)	**0.69 (0.23, 1.16)**
Age Group		
(Ref: 45-54 years)		
55-64 years	-0.25 (-0.82, 0.32)	0.15 (-0.43, 0.73)
65-74 years	**-0.76 (-1.40, -0.12)**	0.03 (-0.66, 0.72)
75 years +	**-3.90 (-4.62, -3.17)**	**-2.91 (-3.69, -2.12)**
Province		
(Ref: Ontario)		
Alberta	-0.17 (-1.04, 0.69)	-0.18 (-1.05, 0.69)
British Columbia	-0.63 (-1.45, 0.20)	-0.40 (-1.22, 0.43)
Manitoba	**-1.17 (-2.15, -0.19)**	**-1.02 (-2.00, -0.05)**
New Brunswick	**-1.09 (-2.10, -0.08)**	-0.70 (-1.71, 0.31)
Newfoundland and Labrador	-0.53 (-1.61, 0.54)	-0.25 (-1.32, 0.82)
Nova Scotia	-0.37 (-1.32, 0.58)	-0.10 (-1.05, 0.85)
Prince Edward Island	-0.75 (-1.84, 0.34)	-0.64 (-1.73, 0.45)
Quebec	0.18 (-0.54, 0.90)	0.51 (-0.21, 1.24)
Saskatchewan	-0.75 (-1.75, 0.25)	-0.63 (-1.63, 0.37)
Education		
(Ref: Less than secondary)		
Completed secondary		0.49 (-0.40, 1.37)
Some post-secondary		0.53 (-0.16, 1.22)
Post-secondary degree or diploma		**1.46 (0.52, 2.39)**
Income		
(Ref: Less than $20,000)		
< $20,000		0.81 (-0.38, 2.00)
$20,000 to < $50,000		**2.38 (1.18, 3.59)**
$50,000 to < $100,000		**2.75 (1.45, 4.05)**
$100,000 to < $150,000		**3.15 (1.78, 4.52)**
Missing		0.64 (-0.85, 2.12)
Health Status		
Functional Status		
(Ref: No assistance required for any activity)		
Assistance required for ≥ 1 activity		**-2.47 (-3.30, -1.65)**
Missing		-2.73 (-6.16, 0.70)

Chronic Conditions		
(Ref: No chronic conditions)		
≥ 1 chronic condition(s)		-0.46 (-1.24, 0.31)
Missing		0.23 (-4.50, 4.95)
Depressive Symptoms		
(Ref: Not Severe)		
Severe		**-0.72 (-1.39, -0.05)**
Missing		-2.52 (-7.75, 2.71)
Lifestyle Behaviours		
Smoking		
(Ref: Not at all)		
Occasionally		-0.19 (-1.97, 1.59)
Daily		0.20 (-0.70, 1.10)
Missing		**1.03 (0.52, 1.55)**
Alcohol Consumption		
(Ref: Not at all)		
Occasionally		**0.92 (0.01, 1.83)**
Regularly		0.64 (-0.11, 0.14)
Missing		0.90 (-0.60, 2.39)
Functional social support (t_0)		
(Ref: Low)		
High	0.39 (-0.12, 0.89)	0.17 (-0.33, 0.68)
Functional social support (t_1)		
(Ref: Low)		
High	**0.90 (0.39, 1.40)**	**0.59 (0.09, 1.10)**
Memory (t_0)	**0.44 (0.42, 0.45)**	**0.43 (0.42, 0.45)**

Notes: $\hat{\beta}$=Regression Coefficient; CI=Confidence Interval; Ref=Reference Category; t_0=baseline, t_1=follow-up

Appendix G. Mediation Model

Table G-1 Regression Analyses: "a" and "b" Paths of the Mediation Model

	"a" Path $\hat{\beta}$ (95% CI)	"b" Path $\hat{\beta}$ (95% CI)
Exposure		
Social Isolation Status (Ref: Not socially isolated)		
Socially isolated	**-0.06 (-0.08, -0.04)**	-0.13 (-0.68, 0.45)
Functional social support (Ref: Low)		
High		**0.59 (0.09, 1.10)**
Sociodemographic		
Sex (Ref: Male)		
Female	**-0.02 (-0.04, -0.01)**	**0.69 (0.23, 1.16)**
Age Group (Ref: 45-54 years)		
55-64 years	**0.03 (0.01, 0.05)**	0.15 (-0.43, 0.73)
65-74 years	0.02 (0.00, 0.05)	0.03 (-0.66, 0.72)
75 years +	0.00 (-0.03, 0.03)	**-2.91 (-3.69, -2.12)**
Province (Ref: Ontario)		
Alberta	**-0.05 (-0.08, -0.02)**	-0.18 (-1.05, 0.69)
British Columbia	-0.01 (-0.04, -0.01)	-0.40 (-1.22, 0.43)
Manitoba	0.02 (-0.02, 0.05)	**-1.02 (-2.00, -0.05)**
New Brunswick	0.03 (-0.01, 0.06)	-0.70 (-1.71, 0.31)
Newfoundland and Labrador	0.01 (-0.03, 0.05)	-0.25 (-1.32, 0.82)
Nova Scotia	0.00 (-0.03, 0.04)	-0.10 (-1.05, 0.85)
Prince Edward Island	0.00 (-0.04, 0.04)	-0.64 (-1.73, 0.45)
Quebec	0.00 (-0.02, 0.03)	0.51 (-0.21, 1.24)
Saskatchewan	0.02 (-0.02, 0.06)	-0.63 (-1.63, 0.37)
Education (Ref: Less than secondary)		
Completed secondary	0.07 (-0.08, 0.22)	0.49 (-0.40, 1.37)
Some post-secondary	**0.16 (0.04, 0.28)**	0.53 (-0.16, 1.22)
Post-secondary degree or diploma	**0.22 (0.06, 0.38)**	**1.46 (0.52, 2.39)**
Income (Ref: Less than $20,000)		
< $20,000	**0.07 (0.03, 0.12)**	0.81 (-0.38, 2.00)
$20,000 to < $50,000	**0.13 (0.08, 0.18)**	**2.38 (1.18, 3.59)**
$50,000 to < $100,000	**0.18 (0.13, 0.23)**	**2.75 (1.45, 4.05)**
$100,000 to < $150,000	**0.19 (0.14, 0.25)**	**3.15 (1.78, 4.52)**
Missing	**0.08 (0.03, 0.14)**	0.64 (-0.85, 2.12)

Health Status		
Functional Status		
(Ref: No assistance required for any activity)		
Assistance required for ≥ 1 activity	-0.01 (-0.04, 0.02)	**-2.47 (-3.30, -1.65)**
Missing	-0.05 (-0.18, 0.07)	-2.73 (-6.16, 0.70)
Chronic Conditions		
(Ref: No chronic conditions)		
≥ 1 chronic condition(s)	**-0.04 (-0.06, -0.01)**	-0.46 (-1.24, 0.31)
Missing	-0.01 (-0.18, 0.16)	0.23 (-4.50, 4.95)
Depressive Symptoms		
(Ref: Not Severe)		
Severe	**-0.09 (-0.12, -0.07)**	**-0.72 (-1.39, -0.05)**
Missing	-0.17 (-0.37, 0.02)	-2.52 (-7.75, 2.71)
Lifestyle Behaviours		
Smoking		
(Ref: Not at all)		
Occasionally	-0.14 (-0.46, 0.17)	-0.19 (-1.97, 1.59)
Daily	-0.06 (-0.21, 0.10)	0.20 (-0.70, 1.10)
Missing	0.03 (-0.06, 0.12)	**1.03 (0.52, 1.55)**
Alcohol Consumption		
(Ref: Not at all)		
Occasionally	0.03 (-0.13, 0.19)	**0.92 (0.01, 1.83)**
Regularly	0.06 (-0.07, 0.19)	0.64 (-0.11, 0.14)
Missing	0.08 (-0.17, 0.34)	0.90 (-0.60, 2.39)
Functional social support (t_0)		
(Ref: Low)		
High	**0.36 (0.35, 0.38)**	0.17 (-0.33, 0.68)
Memory (t_0)	0.00 (0.00, 0.00)	**0.43 (0.42, 0.45)**

Notes: $\widehat{\beta}$ = Regression Coefficient; CI = Confidence Interval; Ref = Reference Category; t_0 = baseline, t_1 = follow-up.
The "a" path represents the association between social isolation and functional social support.
The "b" path represents the association between functional social support and memory.

```
Causal Mediation Analysis

Quasi-Bayesian Confidence Intervals

               Estimate 95% CI Lower 95% CI Upper p-value
ACME            -0.0323      -0.0649        -0.01   0.014 *
ADE             -0.1321      -0.6844         0.45   0.652
Total Effect    -0.1644      -0.7159         0.41   0.576
Prop. Mediated   0.0707      -1.4594         1.41   0.586
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

Figure G-1 Output from Mediation Package in "R"

Notes: CI = Confidence Interval; ACME = “ab” path; ADE = “c-prime” path; Prop = Proportion; Signif = Significance.

Appendix H. Sensitivity Analysis

Table H-1 Regression Analyses: Social Isolation and Memory - Main versus Sensitivity Analyses

		Base Model $\hat{\beta}$ (95% CI)	Adjusted Model $\hat{\beta}$ (95% CI)
Exposure			
Social Isolation Status (Ref: Not socially isolated)	Sensitivity*	-0.07 (-1.02, 0.33)	-0.05 (-1.04, 0.34)
Socially isolated	Main	**-0.75 (-1.32, -0.18)**	-0.13 (-0.68, 0.45)

Notes: $p < 0.05$ in bolded font; Adjusted for baseline functional social support, baseline memory score, sociodemographic factors, health status, and lifestyle behaviours. $\hat{\beta}$ = regression coefficient value; CI = confidence interval.
*Analysis where participants with missing covariates were removed from the model.

Table H-2 Mediation Effects of Functional Social Support on Social Isolation and Memory: Main versus Sensitivity Analyses

Path	**$\hat{\beta}$ (95% CI)**

a		
	Sensitivity*	**0.05 (-0.08, -0.02)**
	Main	**-0.06 (-0.08, -0.04)**
b		
	Sensitivity*	0.43 (-0.18, 1.03)
	Main	**0.59 (0.09, 1.10)**
ab		
	Sensitivity*	-0.02 (-0.06, 0.01)
	Main	**-0.03 (-0.06, -0.01)**
c-prime		
	Sensitivity*	0.34 (-0.33, 1.03)
	Main	-0.13 (-0.71, 0.46)
c		
	Sensitivity*	0.32 (-0.36, 1.01)
	Main	-0.17 (-0.78, 0.42)
PM		
	Sensitivity*	-0.04 (-0.77, 0.67)
	Main	0.07 (-0.58, 4.70)

Notes: $p < 0.05$ in bolded font; Adjusted for baseline functional social support, baseline memory score, sociodemographic factors, health status, and lifestyle behaviours. $\hat{\beta}$ = regression coefficient value; CI = confidence interval; PM = proportion mediated.
The "a" path represents the association between social isolation and functional social support.
The "b" path represents the association between functional social support and memory.
The "ab" path represents the indirect effect of social isolation on memory through functional social support as a mediator
The "c-prime" path represents the direct effect of social isolation on memory
The "c" path represents the total effect of social isolation on memory
*Analysis where participants with missing covariates were removed from the model.

Table H-3 Moderated Mediation: Main versus Sensitivity Analysis

	a $\hat{\beta}$ (95% CI)	b $\hat{\beta}$ (95% CI)	ab $\hat{\beta}$ (95% CI)	c-prime $\hat{\beta}$ (95% CI)	c $\hat{\beta}$ (95% CI)	PM $\hat{\beta}$ (95% CI)
Male						
Sensitivity*	**-0.06 (-0.48, -0.17)**	0.38 (-0.46, 1.22)	-0.02 (-0.08, 0.03)	0.72 (-0.23, 1.68)	0.70 (-0.25, 1.64)	-0.02 (-0.40, 0.27)
Main	**-0.05 (-0.08, -0.02)**	0.44 (-0.28, 1.17)	-0.05 (-0.13, 0.03)	0.15 (-0.70, 0.98)	0.10 (-0.75, 0.93)	-0.03 (-1.88, 1.93)
Female						
Sensitivity*	**-0.05 (-0.09, -0.02)**	0.46 (-0.41, 1.33)	-0.02 (-0.08, 0.02)	-0.17 (-1.02, 0.97)	-0.04 (-1.06, 0.94)	0.01 (-0.82, 0.80)
Main	**-0.06 (-0.09, -0.03)**	**0.76 (0.06, 1.47)**	-0.08 (-0.16, 0.00)	-0.35 (-1.19, 0.46)	-0.43 (-1.27, 0.39)	0.12 (-1.63, 1.76)
45-54 years						
Sensitivity*	-0.05 (-0.1, 0.00)	0.50 (-0.57, 1.57)	-0.03 (-0.12, 0.03)	1.31 (-0.20, 2.84)	1.29 (-0.18, 2.81)	-0.01 (-0.14, 0.03)
Main	**-0.05 (-0.09, -0.01)**	0.36 (-0.53, 1.22)	-0.04 (-0.13, 0.05)	1.03 (-0.27, 2.12)	0.99 (-0.20, 2.08)	-0.03 (-0.40, 0.17)
55-64 years						
Sensitivity*	**-0.10 (-0.14, -0.05)**	0.19 (-0.81, 1.20)	-0.02 (-0.11, 0.07)	0.08 (-1.03, 1.18)	0.06 (-1.04, 1.16)	-0.002 (-1.00, 1.06)
Main	**-0.10 (-0.14, -0.06)**	0.45 (-0.40, 1.30)	-0.06 (-0.19, 0.05)	-0.46 (-1.46, 0.52)	-0.52 (-1.51, 0.45)	0.08 (-1.15, 1.45)
65-74 years						
Sensitivity*	**-0.07 (-0.13, -0.02)**	0.80 (-0.58, 2.18)	-0.05 (-0.18, 0.04)	0.15 (-1.38, 1.69)	0.10 (-1.41, 1.62)	-0.007 (-1.24, 1.16)
Main	**-0.06 (-0.11, -0.02)**	0.80 (-0.39, 2.00)	-0.09 (-0.24, 0.04)	-0.38 (-1.71, 0.92)	-0.47 (-1.80, 0.84)	0.08 (-1.65, 1.80)
75+ years						
Sensitivity*	0.04 (-0.03, 0.11)	0.73 (-0.98, 2.44)	0.03 (-0.06, 0.16)	-0.63 (-2.50, 1.18)	-0.61 (-2.46, 1.22)	-0.006 (-0.56, 0.51)
Main	-0.03 (-0.06, 0.08)	1.30 (-0.10, 2.71)	-0.01 (-0.11, 0.06)	-1.01 (-2.46, 0.42)	-1.03 (-2.49, 0.41)	0.007 (-0.23, 0.24)

Notes: $p < 0.05$ in bolded font; Adjusted for baseline functional social support, baseline memory score, sociodemographic factors, health status, and lifestyle behaviours. $\hat{\beta}$ = regression coefficient value; CI = confidence interval.
The "a" path represents the association between social isolation and functional social support.
The "b" path represents the association between functional social support and memory.
The "ab" path represents the indirect effect of social isolation on memory through functional social support as a mediator
The "c-prime" path represents the direct effect of social isolation on memory
The "c" path represents the total effect of social isolation on memory
*Analysis with participants with missing covariates removed from the model

Appendix I. Model Diagnostics

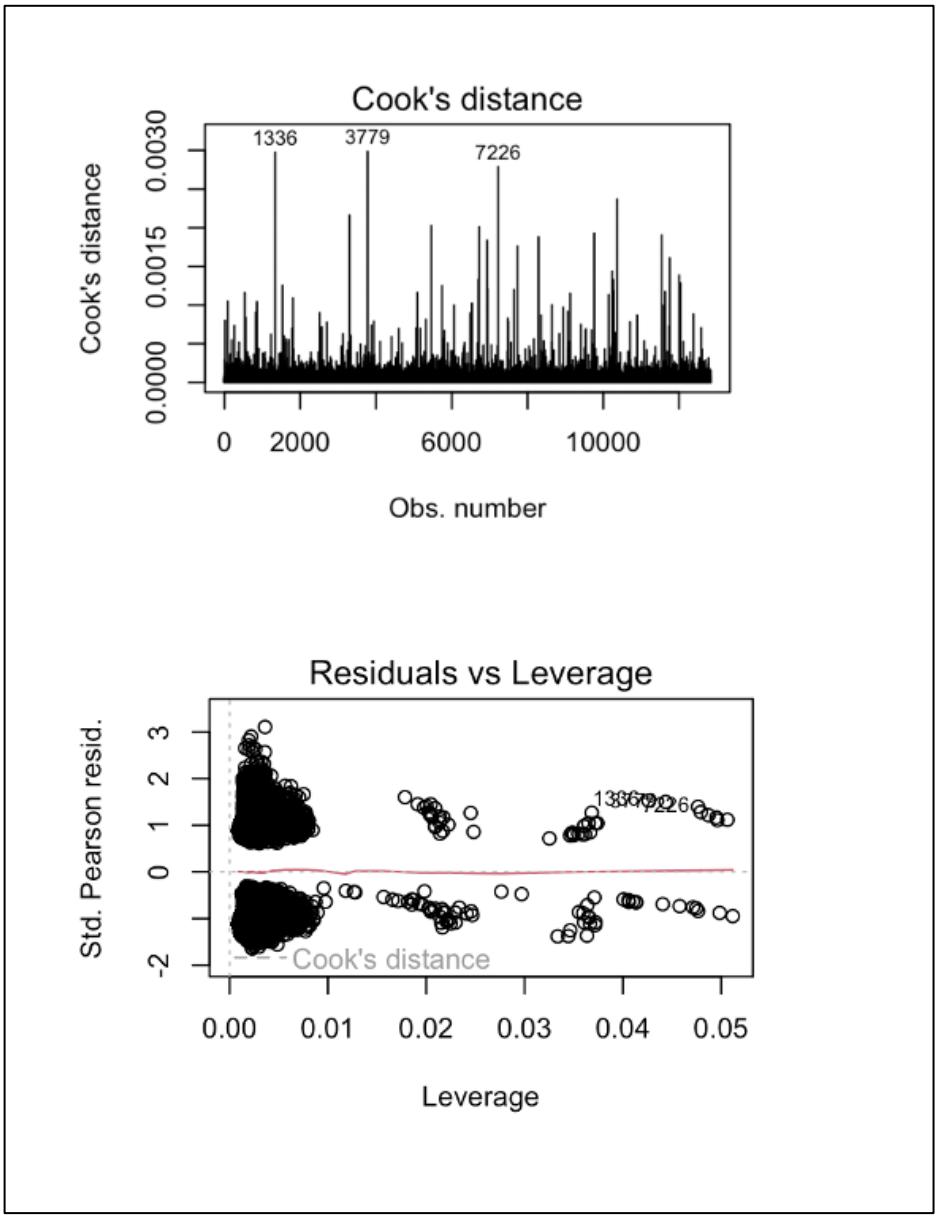


Figure I-1 Model Diagnostics for Logistic Regression of the "a" Path

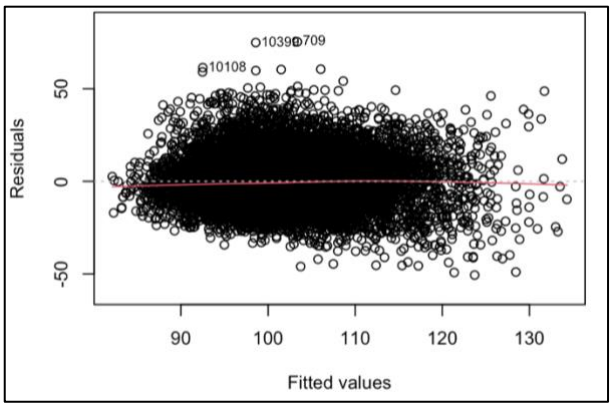


Figure I-2 Model Diagnostics for Linear Regression of the "b" Path - Residuals versus Fitted

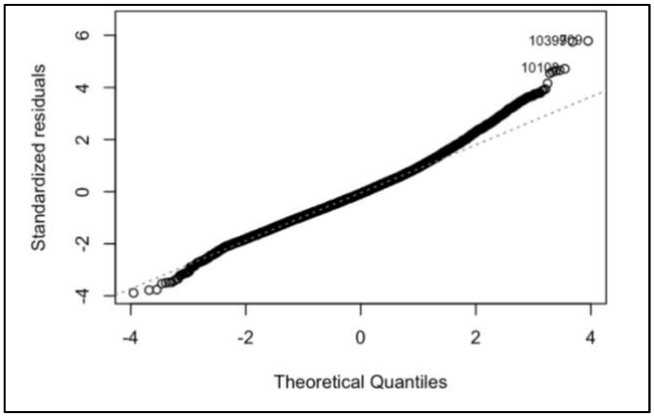


Figure I-3 Model Diagnostics for Linear Regression of the "b" Path - Q-Q Residuals

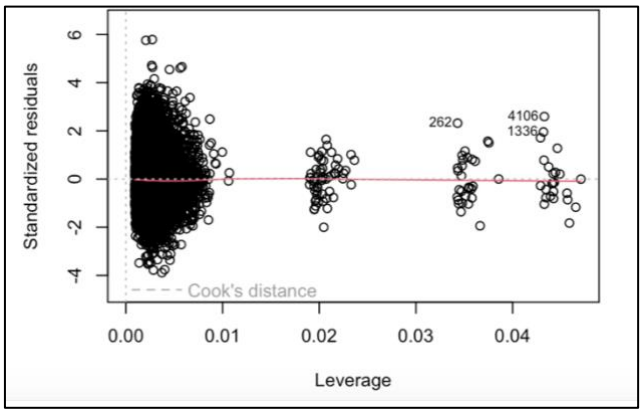


Figure I-4 Model Diagnostics for Linear Regression of the "b" Path - Residuals versus Leverage