

Aging Under Pressure: Stress, Inflammation, and Cognitive Change in Immigrant and Non-Immigrant Canadians

by

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Examining Committee Membership

The following members served on the Examining Committee for this thesis. The decision of the Examining Committee is by majority vote.

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Author's Declaration

This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the 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.

Statement of Contributions

This thesis consists in part of three manuscripts written for publication.

Exceptions to sole authorship of material are as follows:

Chapter 4: Shorey, C.L., Mielke, J.G., Maxwell, C.J., & Tyas, S.L. Physical health conditions, inflammation, and cognitive function in aging immigrant and non-immigrant Canadians: Findings from the CLSA.

Chapter 5: Shorey, C.L., Mishra, A.A., Mielke, J.G., Maxwell, C.J., & Tyas, S.L. Examining psychosocial stress, inflammation, and cognitive function in aging immigrants and non-immigrants: Findings from the CLSA.

Chapter 6: Shorey, C.L., Maxwell, C.J., Mielke, J.G., & Tyas, S.L. Psychological distress, inflammation, and cognitive function in aging immigrant and non-immigrant Canadians: Findings from the CLSA.

As lead author of these three chapters, I was responsible for conceptualizing the study design and methodology. I performed the literature review, analyzed the data, led the interpretation of findings, and drafted the manuscripts under the direction of Dr. Suzanne Tyas. My co-authors provided guidance in interpretation, analytic methods, and feedback on draft manuscripts.

Note: There may be overlap in the contents of this dissertation, particularly the description of methods, because the research was designed as three separate manuscripts for journal submission according to university guidelines.

Abstract

Background

Cognitive impairment and its risk factors are a growing global concern, particularly among understudied populations such as immigrants. Physical health, psychosocial, and mental health stressors (“stress”) are all linked to poorer cognitive function. While immigrants are more likely than non-immigrants to experience adverse effects of stress, likely due to greater exposure to stressors, they may also experience unique psychosocial and mental health stressors. At the same time, they may benefit from physical health protective factors such as the “healthy immigrant effect”. However, whether their distinct stress profile increases their vulnerability to cognitive impairment remains unclear and was therefore the key focus of this dissertation. Further, because stress can elevate systemic inflammation, this research examined whether inflammation mediated the association between stress and cognitive function. The role of sex in this association was also explored, as immigrant women often experience higher levels of stress, which may amplify inflammatory responses and contribute to worse cognitive outcomes compared to immigrant men and non-immigrants.

Methods

All studies used data from the Canadian Longitudinal Study on Aging’s (CLSA) Comprehensive cohort, a prospective, population-based study of Canadians aged 45-85 at baseline (n = 30,097, including 5,449 immigrants). Structural equation models examined the association between baseline physical health (measured by physical health conditions), psychosocial (measured by barriers to social activities, financial need, and housing problems), and mental health (measured by psychological distress) stressors with executive function and memory at baseline and three-year follow-up. Analyses were stratified by immigrant status and sex, with inflammation (measured by C-reactive protein; CRP) tested as a potential mediator. Models were adjusted for age, education, and congruence between the participant’s first language learned and the language of the cognitive testing.

Results

Study 1: Physical health stress. Negative associations of physical health conditions with executive function and episodic memory were more consistent among non-immigrants than immigrants. In non-immigrants, significant negative associations were observed at both baseline and follow-up, whereas among immigrants, effects varied by sex. While immigrant women showed no association between physical health conditions and baseline episodic memory, they exhibited significant associations with all other cognitive outcomes. In contrast, for immigrant men, physical health conditions were only associated with baseline episodic memory and not with any other cognitive outcomes. These findings suggest that stress related to physical health conditions had a more limited role in cognitive outcomes for immigrant men compared to immigrant women and non-immigrant women and men. Although CRP significantly mediated some associations, the effects were clinically negligible.

Study 2: Psychosocial stress. Associations of psychosocial stress with executive function and episodic memory were observed in both immigrants and non-immigrants.

However, immigrant women were the least likely to show significant associations between psychosocial stress and cognitive outcomes, while immigrant men were the most likely, showing stronger associations than immigrant women and non-immigrant women and men across all of the cognitive domains and time points. This pattern highlights the disproportionate impact of psychosocial stress on cognitive outcomes among immigrant men. While there were statistically significant mediations by CRP, they were clinically negligible.

Study 3: Mental health stress. Negative associations of psychological distress with executive function and episodic memory were observed in both immigrants and non-immigrants. However, immigrant women and men experienced more pronounced associations between psychological distress and baseline executive function than non-immigrant women and men. Notably, immigrant men also showed a strong association with baseline episodic memory, further emphasizing their susceptibility to the effects of mental health stress on cognition. While there were statistically significant mediations by CRP, they were clinically negligible.

Contribution

To our knowledge, no previous studies globally have measured the complex effects of stress and inflammation on cognition in aging immigrants. The findings align with the “healthy immigrant effect” as, despite physical health conditions being generally similar between immigrants and non-immigrants, their impact on cognition was greater among non-immigrants. This suggests that while stress related to physical health conditions was less strongly linked to cognition in immigrants, psychosocial and mental health stress may be more strongly associated with cognitive outcomes in this group. Notably, immigrant men were the most likely to show significant negative associations of psychosocial and mental health stressors with cognition, highlighting their particular vulnerability and a potential area for targeted intervention. While stress-related cognitive vulnerabilities were evident across all of the groups, the strength and consistency of these associations varied, suggesting that certain subgroups may be more vulnerable to stress and may benefit from targeted support. Although CRP significantly mediated some associations across all categories of stressors, the effects were consistently negligible, suggesting that systemic inflammation, as measured by baseline CRP, was not the primary mechanism linking chronic stress to cognition in these studies. By providing much-needed data on a diverse immigrant population—unlike much of the existing literature, which focuses on more homogeneous groups—these studies contribute to a broader global understanding of how stress impacts cognitive function in aging adults, with implications for public health and policy across different immigration contexts.

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And finally, recognizing that a PhD in normal times can be an isolating experience, but completing one during a pandemic often required an extra measure of inner strength, I'll close with the words of the great Snoop Dogg: “Last but not least, I want to thank me for believing in me, I want to thank me for doing all this hard work, I want to thank me for having no days off, I want to thank me for never quitting...”.

Table of Contents

Examining Committee Membership	ii
Author's Declaration.....	iii
Statement of Contributions	iv
Abstract	v
Acknowledgements	vii
List of Figures	xi
List of Tables	xii
List of Abbreviations	xiii
Chapter 1 Introduction	1
1.1 Stress	2
1.2 Stress and Cognitive Outcomes.....	2
1.2.1 Physical Health Stress and Cognitive Outcomes.....	3
1.2.2 Psychosocial Stress and Cognitive Outcomes	4
1.2.3 Mental Health Stress and Cognitive Outcomes	4
1.2.4 Sex Differences in Cognitive Outcomes	5
1.3 Inflammation and Cognitive Outcomes	6
1.4 Stress and Inflammation.....	6
1.4.1 Physical Health Stress and Inflammation	8
1.4.2 Psychosocial Stress and Inflammation	8
1.4.3 Mental Health Stress and Inflammation	9
1.4.4 Sex Differences in Stress and Inflammation	9
1.5 Immigration.....	10
1.5.1 Historical and Structural Context of Immigration in Canada.....	11
1.5.2 Stress, Inflammation, and Cognitive Outcomes.....	13
1.5.3 Physical Health Stress, Inflammation, and Cognitive Outcomes in Immigrants ...	13
1.5.4 Psychosocial Stress, Inflammation, and Cognitive Outcomes in Immigrants.....	15
1.5.5 Mental Health Stress, Inflammation, and Cognitive Outcomes in Immigrants.....	16
1.5.6 Gaps in the Existing Literature on Stress and Cognitive Outcomes in Immigrants	16
1.6 Conclusion.....	17
Chapter 2 Research Questions and Hypotheses.....	18
2.1 Research Questions for Study 1	19
2.1.1 Study 1 Hypotheses	19
2.2 Research Questions for Study 2	20
2.2.1 Study 2 Hypotheses	20
2.3 Research Questions for Study 3	21
2.3.1 Study 3 Hypotheses	21
Chapter 3 Methodology	22
3.1 Introduction to Structural Equation Modeling	22
3.2 Factor Analysis.....	22
3.3 Path Diagrams	23
3.4 Factor Loadings.....	24
3.5 First- and Second-Order Factors	24
3.6 Missing Data and MAR Assumptions.....	26

3.7 Data Source: Canadian Longitudinal Study on Aging (CLSA)	27
Chapter 4 Physical Health Stress	29
4.1 Background	30
4.2 Methods	31
4.2.1 Study Design and Population	31
4.2.2 Measures	32
4.2.2.1 Independent Variable	32
4.2.2.2 Dependent Variable	32
4.2.2.3 Mediation Variable	33
4.2.2.4 Covariates	33
4.2.3 Data Analysis.....	34
4.2.3.1 Descriptives.....	34
4.2.3.2 Measurement Models.....	34
4.2.3.3 Structural Equation Modeling.....	35
4.3 Results	36
4.3.1 Descriptive Analyses	36
4.3.2 Measurement Model	39
4.3.3 Structural Equation Models: Examining Differences by Immigrant Status	39
4.3.4 Structural Equation Models: Examining Sex Differences Within Immigrant Status	42
4.4 Discussion	45
4.4.4 Conclusion	51
Chapter 5 Psychosocial Stress	52
5.1 Background	53
5.2 Methods	55
5.2.1 Study Design and Population	55
5.2.2 Measures	56
5.2.2.1 Independent Variable	56
5.2.2.2 Dependent Variable	56
5.2.2.3 Mediation Variable	57
5.2.2.4 Covariates	57
5.2.3 Data Analysis.....	58
5.2.3.1 Descriptives.....	58
5.2.3.2 Measurement Models.....	58
5.2.3.3 Structural Equation Models	60
5.3 Results	61
5.3.1 Descriptive Analyses	61
5.3.2 Measurement Models	62
5.3.3 Structural Equation Models: Examining Differences by Immigrant Status	64
5.3.4 Structural Equation Models: Examining Sex Differences Within Immigrant Status	66
5.4 Discussion	69
5.4.1 Strengths	72
5.4.2 Limitations.....	73
5.4.3 Future Directions	74
5.4.4 Conclusion	74

Chapter 6 Mental Health Stress	76
6.1 Background	77
6.2 Methods	79
6.2.1 Study Design and Population	79
6.2.2 Measures	79
6.2.2.1 Independent Variable	79
6.2.2.2 Dependent Variable	80
6.2.1.1 Mediation Variable	81
6.2.1.2 Covariates	81
6.2.3 Data Analysis	82
6.2.3.1 Descriptives	82
6.2.3.2 Measurement Models	82
6.2.3.3 Structural Equation Models	83
6.3 Results	84
6.3.1 Descriptive Analyses	84
6.3.2 Measurement Model	85
6.3.3 Structural Equation Models: Examining Differences by Immigrant Status	87
6.3.4 Structural Equation Models: Examining Sex Differences Within Immigrant Status	89
6.4 Discussion	91
6.4.1 Strengths	94
6.4.2 Limitations	95
6.4.3 Future Directions	96
6.4.4 Conclusion	97
Chapter 7 Conclusion	98
7.1 Summary of Findings	98
7.2 Consistencies and Inconsistencies with Literature	101
7.3 Interpretation of Findings	104
7.3.1 Acute versus Longer-Term Effects of Stress on Cognition	104
7.3.2 Limited Evidence for CRPs as a Mediator of Cognitive Associations	105
7.3.3 An Overlooked Pattern? Mental Health–Related Cognitive Vulnerability in Immigrant Men	107
7.4 Strengths and Limitations	109
7.5 Future Directions	112
7.6 Implications	114
7.7 Conclusion	115
References	116
Appendix A: Supplementary Material for Chapter 3 Methodology	154
Appendix B: SEM Specification Across All Studies	158
Appendix C: Supplementary Material for Study 1 Physical Health Stress	159
Appendix D: Supplementary Material for Study 2 Psychosocial Stress	165
Appendix E: Supplementary Material for Study 3 Mental Health Stress	167

List of Figures

Figure 1. Conceptual map of the association between stress and cognitive function, with inflammation as a mediator and immigration status and sex as moderators.....	18
Figure 2. Factor sub-model.	23
Figure 3. Path analysis sub-model.	23
Figure 4. First- and second-order factor models.	25
Figure 5. Path diagrams for displaying structural sub-models.	33
Figure 6. Path model for follow-up analysis illustrating the mediation model tested using a structural equation model.....	35
Figure 7. Path diagrams for displaying structural sub-models.	57
Figure 8. Path model for follow-up analysis illustrating the mediation model tested using a structural equation model.....	59
Figure 9. Percentage of absence or presence of stressors by immigrant status and sex.	61
Figure 10. Path diagrams for displaying structural sub-models.	81
Figure 11. Path model for follow-up analysis illustrating the mediation model tested using a structural equation model.....	83
Figure 12. Associations between stress measures and cognitive outcomes across three studies, stratified by immigrant status and sex.	100
Figure 13. Conceptual overlap across the three studies among immigrants.	101
Figure C1. Median baseline and follow-up executive function tasks by immigrant status...160	
Figure C2. Median baseline and follow-up episodic memory tasks by immigrant status. 160	
Figure C3. Factor loading for physical health conditions.	163
Figure C4. Factor loading for A. baseline and B. follow-up executive function in Study 1.	163
Figure C5. Factor loading for A. baseline and B. follow-up episodic memory in Study 1.	164
Figure D1. Factor loading for psychosocial stress.	165
Figure D2. Factor loading for A. baseline and B. follow-up executive function in Study 2.	165
Figure D3. Factor loading for A. baseline and B. follow-up episodic memory in Study 2.	166
Figure E1. Factor loading for psychological distress.	168
Figure E2. Factor loading for A. baseline and B. follow-up executive function in Study 3.	168
Figure E3. Factor loading for A. baseline and B. follow-up episodic memory in Study 3.	169

List of Tables

Table 1. Descriptive characteristics by immigrant status (N = 30,093).....	38
Table 2. Distribution of first language(s) learned by immigrant status.	39
Table 3. Effect of baseline physical health conditions on baseline and follow-up executive function and episodic memory by immigrant status, mediated by baseline ln-CRP.	41
Table 4. Effect of baseline physical health conditions on baseline and follow-up executive function and episodic memory by immigrant status and sex, mediated by baseline ln-CRP.	43
Table 5. Descriptive characteristics by immigrant status and sex (N = 30,093).	63
Table 6. Effect of baseline psychosocial stress on baseline and follow-up executive function and episodic memory by immigrant status, mediated by baseline ln-CRP.....	65
Table 7. Effect of baseline psychosocial stress on baseline and follow-up executive function and episodic memory by immigrant status and sex, mediated by baseline ln-CRP.	67
Table 8. Descriptive characteristics by immigrant status and sex (N = 30,093).	86
Table 9. Effect of baseline psychological distress on baseline and follow-up executive function and episodic memory by immigrant status, mediated by baseline ln-CRP.	88
Table 10. Effect of baseline psychological distress on baseline and follow-up executive function and episodic memory by immigrant status and sex, mediated by baseline ln-CRP.	90
Table A1. Summary of variables used in analyses and measurement source in the CLSA.	154
Table A2. Summary of cognitive variables used in analyses.	157
Table C1. Chronic health conditions included in the construction of latent variables physical health conditions.	159
Table C2. Association of first language learned and age at arrival in Canada with cognition (executive function and episodic memory) among immigrants.....	162

List of Abbreviations

AFT Animal Fluency Test
CFA Confirmatory Factor Analysis
CFI Comparative Fit Index
CLSA Canadian Longitudinal Study on Aging
COPD Chronic Obstructive Pulmonary Disease
COWAT Controlled Oral Word Association Test
CRP C-reactive protein
EFA Exploratory Factor Analysis
FIML Full Information Maximum Likelihood
HPA Hypothalamus, Pituitary Gland, and Adrenal Cortex
IL-6 Interleukin-6
K10 Kessler Psychological Distress Scale
ln-CRP Natural Log-Transformed CRP
MAR Missing at Random
MAT Mental Alternation Test
MCI Mild Cognitive Impairment
REY 1 Rey Auditory Verbal Learning Test Immediate Word Recall
REY 2 Rey Auditory Verbal Learning Test Delayed Word Recall
RMSEA Root Mean Square Error of Approximation
SEM Structural Equation Modelling
Stroop Victoria Stroop Neurological Screen Test
T₀ Baseline
T₁ Follow-Up
TIA Transient Ischemic Attack
TMT Time-based Prospective Memory Test
TNF- α Tumor Necrosis Factor Alpha

Chapter 1

Introduction

Cognitive impairment, a measurable decline in one or more cognitive domains, limits independence, increases morbidity, and reduces quality of life (Harada et al, 2013). To support the health of older immigrant and non-immigrant Canadians, we need to understand the factors that put them at risk for cognitive impairment. Adversity throughout the lifespan (e.g., discrimination, socioeconomic strains) increases vulnerability for poorer physical and mental health (Matheson et al., 2008), and increases risk for dementia in later life (Rajan et al., 2015). Such adverse exposures affect immigrants at disproportionately higher rates compared to non-immigrant Canadians. With advancing age, we become more vulnerable to the deleterious effects of chronic stress—frequently repeated or continuous exposure to physical health (e.g., cardiovascular disease), psychosocial (e.g., social isolation), or mental health (e.g., psychological distress) stressors—which can disrupt regulatory systems and contribute to poorer cognitive function. Given that many immigrants experience cumulative stressors across their lifespan, these vulnerabilities may be further compounded in later life, making them particularly susceptible to cognitive decline.

Chronic stress can dysregulate the immune system leading to increased systemic inflammation (Morey et al., 2015). Although inflammation has been implicated in both poorer physical and cognitive health (Kinney et al., 2018), little is known about the inter-relationships between chronic stress, inflammation, and cognitive function in aging immigrant Canadians. While immigrants, at a population level, may initially exhibit better health outcomes—a phenomenon known as the “healthy immigrant effect”—they also face different patterns of stress exposure compared to non-immigrants. The cumulative effects of chronic stress may contribute to differences in cognitive function over time. Therefore, these three studies examined whether chronic stress, categorized as physical health, psychosocial, or mental health stress, was associated with cognitive function in older immigrant and non-immigrant Canadians. Additionally, this study assessed whether systemic inflammation measured by C-reactive protein (CRP), a marker of inflammation linked to various health outcomes, mediated these associations and whether they varied by sex.

1.1 Stress

Chronic stress is a key pathway linking adversity to aging-related changes in health and cognition. Stress is a physiological and behavioural response to an internal or external threat (Chrousos & Gold, 1992; Russell & Lightman, 2019). Central to the stress response, the brain assesses and determines what is a threat and to what extent it should be deemed stressful (McEwen et al., 2015). These threats can range from daily hassles to life-threatening emergencies; however, just the anticipation of a threat can be enough to activate a stress response (Russell & Lightman, 2019). The hypothalamus, pituitary gland, and adrenal cortex (HPA) axis initiates the stress response, releasing glucocorticoids (e.g., cortisol). The stress response mobilizes cognitive, immunological, cardiovascular and metabolic functions to perform at optimal capacity towards ensuring survival (Russell & Lightman, 2019).

Dysregulation of the HPA axis is one mechanism linking chronic stress with poor health. This dysregulation often results in chronically elevated cortisol levels when exposed to stressors (Khoury et al., 2019; McEwen et al., 2015). With prolonged exposure, glucocorticoid resistance may also develop, whereby impaired signal transduction reduces the ability of cortisol to regulate physiological processes (Silverman & Sternberg, 2012). If this occurs for too long, cortisol may become depleted, producing a blunted cortisol response to stressors (Russell & Lightman, 2019). Prolonged hyper- or hypoactivation of the HPA axis reflects allostatic overload, when the body is no longer able to cope with chronic stress (McEwen, 1998). Both hyper- and hypoactive responses can have an enduring impact leading to poor health outcomes, including cardiometabolic disorders and poorer mental health (Russell & Lightman, 2019).

1.2 Stress and Cognitive Outcomes

Cognitive abilities, performance in executive function and episodic memory, become increasingly susceptible to the effects of chronic stress with age, making them a key outcome of interest in later life. Even mild cognitive impairment (MCI), also referred to as minor neurocognitive disorder, can affect decision making, limit independence and reduce quality of life; more severe cognitive decline, including dementia or major neurocognitive disorder, leads to further loss of independence and increased morbidity. Three brain regions are

especially vulnerable to cognitive decline: the prefrontal cortex, hippocampus, and amygdala (Lupien et al., 2009). These regions are important for controlling executive function and language, managing spatial and episodic memory, and processing emotions. Understanding the ways in which stress affects these cognitive domains provides critical insight into how cognitive aging progresses.

Exposure to chronic stress can impact brain regions important for cognition. The prefrontal cortex, hippocampus, and amygdala influence how the HPA axis responds to stress (McEwen et al., 2015; McEwen & Morrison, 2013). For instance, following an emotionally stressful event, heightened activity of the amygdala can stimulate the hypothalamus, activating the HPA axis (Khoury et al., 2019). Repeated stress exposure can lead to sustained cortisol elevation, which has been associated with structural and functional changes in these brain regions (Khoury et al., 2019). Prolonged cortisol exposure has been linked to reduced hippocampal volume and impaired memory function (McEwen & Morrison, 2013). Beyond structural changes, chronic stress also affects neuronal plasticity and cognitive processing. Stress can reduce the production of new neurons in the hippocampus, contribute to the loss of neurons over time, and alter neurotransmitter levels that regulate mood and cognitive function (Lupien et al., 2009). These disruptions can make it harder to form and retrieve memories, as well as to process new information effectively.

1.2.1 Physical Health Stress and Cognitive Outcomes

In addition to the direct effects of stress on the brain, chronic stress can also contribute to physical health conditions that are known to affect cognition. Physical health stress plays a role in the development and progression of these conditions, as prolonged activation of the HPA axis and sustained glucocorticoid exposure can impair vascular function, increase oxidative stress, and promote neuroinflammation (Juster et al., 2010; McEwen & Morrison, 2013). These stress-related physiological changes can contribute to metabolic dysregulation, vascular damage, and systemic inflammation—factors that are also implicated in cognitive decline (Juster et al., 2010; McEwen & Morrison, 2013). Cardiovascular disease, diabetes, and metabolic disorders have been consistently linked to poorer cognitive performance (Livingston et al., 2024). High blood pressure is associated with reduced blood flow to the brain, affecting executive function and memory (Gottesman et

al., 2017). Insulin resistance associated with type 2 diabetes has been implicated in slower processing speed and increased risk for memory impairment (Arvanitakis et al., 2020). Chronic conditions such as hypertension and diabetes may further accelerate age-related cognitive changes by contributing to reduced cerebral blood flow, vascular damage, and metabolic dysregulation, all of which have been linked to poorer executive function and memory performance (Iadecola et al., 2016; Ogoh, 2017).

1.2.2 Psychosocial Stress and Cognitive Outcomes

While physical health conditions represent one pathway linking stress and cognition, psychosocial stressors such as financial strain, social isolation, and caregiving burden also show strong negative associations with memory and executive function (James et al., 2020). Economic hardship has been associated with increased stress-related cognitive difficulties, particularly in memory and processing speed (Lee et al., 2003). Neighbourhood stressors, such as housing insecurity, overcrowding, and poor living conditions, have been associated with higher levels of chronic stress, which may negatively impact cognitive function over time (Muñoz et al., 2021; Pevalin et al., 2008). Additionally, lack of social engagement is a known risk factor for cognitive decline, independent of other health factors (Livingston et al., 2024).

1.2.3 Mental Health Stress and Cognitive Outcomes

In addition to external stressors, mental health-related responses to chronic stress can also affect cognition through biological changes in the brain. Abnormal increases in cortisol can lead to dendritic atrophy in the prefrontal cortex and hippocampus, and hypertrophy of the amygdala (McEwen & Morrison, 2013). This results in a reduced ability to regulate emotions, with fear and anxiety remaining after an event or experience is gone, potentially leading to affective and anxiety disorders (McEwen et al., 2015). Further, these effects are moderated by sex. Men, when exposed to chronic stress, have shown prefrontal cortex atrophy, which may increase vulnerability to cognitive difficulties such as executive dysfunction (Lupien et al., 2009; McEwen & Morrison, 2013). Women exhibit dendritic growth of the amygdala, heightening emotional reactivity and risk for affective disorders

(McEwen & Morrison, 2013). These changes, particularly to the amygdala, promote a maladaptive emotional response to chronic stress.

Psychological distress, a measure of mental health stress, refers to emotional suffering in response to stressful life events and interpersonal difficulties; dose-response relationships have been found between this form of distress and cognitive outcomes (Mirowsky & Ross, 2002). Individuals experiencing high psychological distress were seven times more likely to report subjective memory complaints (Paradise et al., 2011), while those who were prone to distress—measured through neuroticism, an indicator of the tendency to experience psychological distress—had more than double the risk of developing Alzheimer’s disease (Wilson et al., 2006). Further, older adults with MCI and symptoms of psychological distress had a higher likelihood of progressing to Alzheimer’s disease than those with MCI and no distress (Apostolova & Cummings, 2008).

1.2.4 Sex Differences in Cognitive Outcomes

Patterns of cognitive performance also vary by sex and gender, reflecting both biological (e.g., hormonal influences, brain structure) and socially constructed roles and expectations. Men often outperform women in tasks requiring spatial awareness, such as abstract reasoning and route memory (Asperholm et al., 2019; Maeda & Yoon, 2013). Women typically perform better than men on verbal episodic memory tasks, including remembering words, phrases, and locations (Asperholm et al., 2019). Moreover, women generally show advantages on most verbal fluency and comprehension tasks (Asperholm et al., 2019), which may be linked to more effective processing strategies during cognitive tasks (Weiss et al., 2006). Given that most neuropsychological assessments favour verbal tasks, it is unsurprising that women often achieve higher scores than men in standard cognitive assessments. Although individual differences exist, men and women show distinct patterns of cognitive strengths and vulnerabilities across multiple domains. These cognitive differences may influence how individuals respond to stress, both in the context of acute stress responses and in the effects of chronic stress, given that the neurobiological systems affected by stress such as the hippocampus and prefrontal cortex are involved in the domains where men and women show relative cognitive strengths (Asperholm et al., 2019; Lupien et al., 2009; McEwen & Morrison, 2013).

Age-associated effects on cognitive function, particularly executive function and episodic memory, are well established (Harada et al., 2013; Kramer et al., 2003). Although highly influenced by education and disease states, generally men's and women's executive function and episodic memory peak in early adulthood. Both men and women see a progressive decline in executive function and episodic memory throughout life, with longitudinal studies suggesting modest but measurable decreases beginning in midlife and accelerating in older age; however, women's episodic memory stays relatively stable throughout adulthood until menopause (Harada et al., 2013). Women's relative advantage in verbal episodic memory is thought to be partially influenced by estrogen's neuroprotective effects, which contribute to differences in memory function and processing efficiency (Kramer et al., 2003). Meanwhile, men's strengths in spatial cognition may be linked to difference in brain organization and task-specific strategies (Graves et al., 2017).

1.3 Inflammation and Cognitive Outcomes

A predictor of numerous age-related conditions, systemic inflammation has detrimental effects throughout the body; in particular, it may impact cognitive decline. Although neuroinflammation during an immune response is evolutionarily adaptive, prolonged neuroinflammation is damaging. Systemic inflammation, as indicated by elevated CRP levels, has been associated with cognitive decline in older adults (Kinney et al., 2018; Singh-Manoux et al., 2014). While neuroinflammation plays a role in conditions such as Alzheimer's disease, evidence suggests that chronic systemic inflammation may also contribute to cognitive aging and performance through pathways related to vascular health, metabolic function, and stress-related immune dysregulation (Singh-Manoux et al., 2014). Given that chronic stress contributes to systemic inflammation, which has been linked to cognitive outcomes, understanding this relationship can help identify factors that influence cognitive health.

1.4 Stress and Inflammation

In addition to its direct effects on the brain and indirect effects through physical and mental health conditions, chronic stress may also affect cognitive health through biological pathways such as systemic inflammation. Inflammation is the body's immune response to an

internal (e.g., bacteria) or external (e.g., injury) trigger. A successful immune response recruits many immune system cells that are both pro-inflammatory and anti-inflammatory (Campos-Rodríguez et al., 2013). Pro-inflammatory cytokines signal the activation of immune-related cells that fight infection, clear damaged cells, and provide tissue repair. This response is generally short-lived, ending when the inflammatory response is no longer needed. Acting on the immune cells, cortisol and catecholamines (e.g., adrenaline), which are released as part of the body's response to stress, regulate inflammation by suppressing pro-inflammatory activity and promoting resolution of the immune response (Tian et al., 2014; Zhang & An, 2007).

The immune response can be dysregulated by chronic stress (McEwen, 1998). Prolonged cortisol exposure can impair the hormone's ability to regulate inflammation, a phenomenon often described as glucocorticoid resistance, in which immune cells become less responsive to cortisol's anti-inflammatory effects (Tian et al., 2014; Ravi et al., 2021). While acute inflammation is typically short-lived, chronic stress can lead to repeated immune activation, increasing the risk of persistent systemic inflammation. Chronic systemic inflammation is marked by a two- to three-fold increase in inflammatory markers such as CRP (Petersen & Pedersen, 2005). CRP, which is produced by the liver in response to pro-inflammatory signaling, is a well-established marker of chronic stress-related immune dysregulation. Prolonged systemic inflammation has been linked to cognitive decline and an increased risk of age-related diseases (Finger et al., 2022). Further, mechanisms that were meant to be adaptive become maladaptive, contributing to systemic inflammation that negatively affects cognition and increases risk for cardiovascular and metabolic disorders (Ravi et al., 2021).

CRP is a widely used marker of systemic inflammation. Elevated CRP levels have been linked to cardiovascular disease, which often involves inflammatory processes, as well as mental health conditions such as depression (Vaccarino et al., 2007; Valkanova et al., 2013). Chronic psychosocial stress, particularly stressors related to conditions out of one's control, has also been associated with increased CRP levels (Hamer, 2012; Hamer et al., 2006). Given its role as an indicator of systemic inflammation, CRP may provide insight into how chronic stress contributes to long-term health outcomes, including cognitive decline. While CRP reflects the presence of systemic inflammation, it does not capture the timing,

duration, or severity of stress exposure. However, as a stable and a well-validated biomarker, CRP remains useful for examining longer-term physiological changes associated with chronic stress, particularly over the multi-year timeframe of this study.

1.4.1 Physical Health Stress and Inflammation

To better understand how stress contributes to systemic inflammation, it is useful to consider how physical health conditions and physiological strain interact over time. The relationship between chronic stress and physical health conditions is bidirectional: while chronic stress can contribute to the development of chronic conditions, these conditions can also act as persistent sources of physiological strain on the body. Prolonged and repeated stressors, especially among vulnerable groups, can significantly elevate inflammatory levels, increasing risk of poorer physical and mental health. For instance, elevated cortisol increases risk for high blood pressure, heart disease, stroke, and diabetes mellitus (Lob & Steptoe, 2019). However, the immune response has also been found to activate aspects of the stress response. Persistent or recurrent inflammation from the inability to fully heal chronic conditions puts stress on the immune system, further exacerbating chronic inflammation and increasing risk for more chronic conditions and for death (Glaser & Kiecolt-Glaser, 2005; Kyrou & Tsigos, 2009). A meta-analysis of prospective observational studies found that individuals with high CRP levels had nearly twice the risk of cardiovascular mortality and all-cause mortality (Li et al., 2017). These links between chronic stress, inflammation, and health outcomes suggest that systemic inflammation may serve as a key pathway through which different types of stress, including not only physical health but also psychosocial stressors, contribute to long-term disease risk.

1.4.2 Psychosocial Stress and Inflammation

Psychosocial stress is the consequence of an imbalance between the adverse events we experience in our everyday lives, such as discrimination due to race or sexuality, and our ability to cope with them. Strain from psychosocial stress often arises from common life experiences, including work overload and interpersonal conflicts such as marital strain (Pearlin, 1983). Like other stressors, psychosocial stressors have been found to stimulate and fatigue the HPA axis (Glaser & Kiecolt-Glaser, 2005; Haley et al., 2010; Nazmi & Victora,

2007; Ong & Williams, 2019). This over-stimulation contributes to increased systemic inflammation through the dysregulation of the immune system's pro-inflammatory response (Hänsel et al., 2010; Johnson et al., 2013). Further, psychosocial stress throughout the lifespan may act cumulatively to promote inflammation (Brydon et al., 2009; Chen & Lacey, 2018; Levine et al., 2015). This may be because traumatic experiences in childhood, such as abuse, alter the body's long-term stress regulation systems, including inflammatory processes, increasing sensitivity to stress later in life (Atkinson et al., 2023). As a result, individuals with heightened sensitivity to stress may be more vulnerable to psychological distress, further exacerbating the link between psychosocial stress, inflammation, and long-term health outcomes.

1.4.3 Mental Health Stress and Inflammation

Psychological distress increases vulnerability to mental health disorders (Phillips, 2009). Not only is psychological distress a key symptom of depression and anxiety (Kessler et al., 2003), but it is relatively common with up to 11-15% of adults reporting at least moderate levels of distress (Enticott et al., 2018; Mojtabai & Jorm, 2015). Growing evidence suggests that psychological distress can upregulate inflammatory processes, leading to elevated levels of systemic inflammation and increasing the risk for further health problems (Goldman-Mellor et al., 2010). Although some studies in adolescents and young adults have reported inverse or non-significant associations—where higher psychological distress is linked to lower or unchanged levels of inflammation (Goldman-Mellor et al., 2010; O'Toole et al., 2018)—psychological distress has been more consistently associated with elevated inflammation in older adults (Baek et al., 2018; Kim et al., 2016; Puustinen et al., 2011).

1.4.4 Sex Differences in Stress and Inflammation

The effects of stress and inflammation on health may also vary depending on biological sex, which shapes physiological and immune responses across the lifespan. Briefly and simplistically, sex refers to a biological classification typically determined by chromosomes and assigned at birth, females having two X chromosomes, while males have one X and one Y chromosome. Both women's and men's sex hormones (estrogen and progesterone, and testosterone, respectively) moderate the HPA axis (Bale & Epperson,

2015). For men, testosterone and the HPA axis interact through a bidirectional feedback loop, where each influences the regulation of the other; thus, when chronic stress interferes with this system, testosterone levels are no longer controlled, resulting in increases in cortisol (Stanojević et al., 2018). Unlike men, women are regularly vulnerable to stress impacts because of the variability of the menstrual cycle. Moreover, declining levels of testosterone and estrogen with age further disrupt the ability to regulate the stress response (Bale & Epperson, 2015). This reduced influence on the HPA axis often leads to poorer physical health outcomes in men and poorer mental health outcomes in women (Khoury et al., 2019).

Clear sex-specific differences have also been found in the immune response (Di Florio et al., 2020; Yang & Kozloski, 2011). Sex hormones influence regulation of the inflammatory response, resulting in clear distinctions in the various diseases women and men are at greatest risk for. Expressing a more robust immune system than men (Márquez et al., 2020), women account for 80% of all autoimmune disorders (where a hyperactive immune system attacks its own organs and tissues; Klein & Flanagan, 2016). On the other hand, men experience an immunosuppressive response, doubling their risk of malignant cancer diagnoses (Klein & Flanagan, 2016). Gendered differences in behaviour also influence health outcomes. Behavioural changes to attenuate chronic stress, such as a greater consumption of alcohol and calorie-dense foods and a decrease in physical activity, contribute to weight gain and abnormalities of lipid and glucose metabolism. The maladaptive behavioural responses associated with chronic stress differ by sex, with women more likely to have poorer eating habits and men less likely to engage in physical activity (Taylor et al., 2018).

Hormonal and immune changes that occur with aging can reduce the body's ability to regulate inflammation. As immune function declines, inflammation can become more persistent, contributing to increased susceptibility to infection, poorer immune response to vaccines, and elevated risk of chronic disease (Klein & Flanagan, 2016). These age-related immune changes, when combined with prolonged stress, may have consequences for brain health, particularly through the effects of systemic inflammation on cognitive function.

1.5 Immigration

Among diverse populations, immigrants may face distinct patterns of chronic stress exposure shaped by their migration histories, settlement experiences, and structural barriers

in the host country. These experiences can influence long-term health outcomes, including inflammation and cognition. Understanding how immigration intersects with stress and aging provides important context for evaluating the cognitive health of older immigrant populations in Canada.

1.5.1 Historical and Structural Context of Immigration in Canada

Canada is a nation shaped by immigration. However, only recently has research begun to recognize that immigrants' diverse life experiences influence health and cognitive outcomes in distinct ways. Historically, Canada's immigration policies were restrictive, favouring European settlers. Major immigration policy changes in the mid-20th century, such as the removal of explicitly race-based selection criteria in 1962, the introduction of a merits-based system in 1967, and the adoption of multiculturalism in 1971, transformed the country's immigrant demographics (Liston & Carens, 2008). By the 1980s, economic migration became a key focus, and along with family sponsorship and refugee admission, it became one of the main pathways to immigrate to Canada. These changes led to an increasingly diverse immigrant population, with more recent arrivals primarily from Asia, the Middle East, and Africa (Elrick, 2022; Statistics Canada, 2001).

While economic migration created opportunities, many immigrants have faced marginalization, social isolation, financial strain, employment barriers, and lower socioeconomic status, challenges that have historically affected various immigrant groups regardless of admission category (Arat-Koc, 1999; Reitz, 2001). In recent decades, temporary migration pathways such as those for international students, temporary foreign workers, and caregivers have played a growing role in Canada's immigration system (Miller, 2023). While these pathways expanded in the 2000s and 2010s, recent policy shifts have introduced caps and restrictions in response to housing and labour concerns (Immigration, Refugees and Citizenship Canada, 2024). These streams typically offer limited access to permanent residency and are associated with greater economic and social precarity. One longstanding barrier remains the demand for "Canadian experience," which limits labour market access even for highly skilled newcomers (Bhuyan et al., 2017). More recently, immigrants are increasingly represented in precarious and low-wage employment, including platform-based gig work, which often emerges as a constrained choice when stable,

commensurate employment is unavailable (Lam & Triandafyllidou, 2024). Together, these structural barriers such as restrictive policy changes, temporary work pathways, and exclusion from stable employment may contribute to chronic stress exposures and long-term health risks that are unlikely to be reflected in earlier cohorts like the Canadian Longitudinal Study on Aging's (CLSA).

Despite the growing recognition of stress-related health disparities, research on the long-term impact of chronic stress in aging immigrant populations remains limited. However, the available limited evidence suggests that young adult immigrants may exhibit heightened physiological stress responses when exposed to acute stressors, increasing their risk for stress-related disorders such as anxiety and depression (Fischer et al., 2017; Goreis et al., 2022). This response in immigrants may indicate increased susceptibility to health conditions related to psychosocial and psychological stressors. Most existing research on immigrant health and cognition has focused on Latin American immigrants in the U.S., given their large representation in that population (Black et al., 1999; Casanova & Aguila, 2020; Garcia et al., 2017, 2021, 2022; Hill, Angel, Balistreri, et al., 2012; Muñoz et al., 2021; Rote & Angel, 2021; Sheffield & Peek, 2009). However, Canada's immigration system and demographic composition differ significantly. Historically, most immigrants to Canada were of European origin, but since the mid-20th century, immigration has increasingly come from Asian countries, including India, China, and the Philippines. By 2021, the top countries of origin for immigrants were India (18.6%), the Philippines (11.4%), China (8.9%), Syria (4.8%), and Nigeria (3.0%) (Statistics Canada, 2001, 2022a). Unlike the U.S., where immigration has been largely shaped by regional proximity, Canada's policies have prioritized skilled labour migration from a broad range of source countries. These demographic and policy distinctions shape the kinds of stressors immigrants are exposed to, which are increasingly recognized as relevant to long-term cognitive health. As a result, Canada's immigrant population is more diverse in terms of national origins and migration experiences, leading to varying exposures to stress and differing pathways to integration. These differences suggest that findings based on U.S. immigrants may not fully capture the health trajectories of Canada's aging immigrant communities. While Canada's immigration context is distinct, similar shifts in migration policy and increasing diversity have also occurred in parts of Europe, suggesting that findings from Canada may offer insights for other aging, migrant-receiving societies.

1.5.2 Stress, Inflammation, and Cognitive Outcomes in Immigrants

Prolonged exposure to chronic stress, experienced by many immigrants, may increase risk for cognitive health problems later in life. Although immigrants tend to arrive in their new host country in good health, this advantage may diminish over time due to accumulated stressors, socioeconomic barriers, and limited healthcare access (De Maio & Kemp, 2010; Vang et al., 2017). Immigrants have significantly higher odds of developing cognitive impairment and dementia than their host country counterparts (Kovaleva et al., 2021; Moon et al., 2019; Parlevliet et al., 2016). These studies suggest that disparities in cognitive health may be linked to factors such as lower educational attainment, social isolation, financial strain, and higher rates of depressive symptoms, all of which have been associated with increased dementia risk in immigrant populations. Further, immigrants who develop Alzheimer's disease tend to be younger and more likely to be male than their non-immigrant counterparts (Segers et al., 2013). This pattern may reflect differences in health-seeking behaviours, as men are generally less likely to access healthcare services, leading to later diagnoses and potentially more severe disease progression (Ssendikaddiwa et al., 2023). However, few studies have assessed longitudinal cognitive function in immigrants, making it difficult to determine how cognition changes over time. A Canadian study assessing dementia incidence and prevalence over a decade found that more recent immigrants had lower odds of developing dementia compared to non-immigrants, which may reflect the healthy immigrant effect (Wong et al., 2021). However, this advantage diminished among long-term immigrants, suggesting that prolonged exposure to stressors, socioeconomic disadvantages, and healthcare barriers over time may contribute to an increased dementia risk. These patterns raise questions about how physical health stress and chronic disease risk may evolve over time in immigrant populations, particularly as initial health advantages decline.

1.5.3 Physical Health Stress, Inflammation, and Cognitive Outcomes in Immigrants

Immigrants who first arrive in their host country tend to be healthier than individuals born in the host country (Blair & Schneeberg, 2014; Vang et al., 2017). The 'healthy immigrant effect' is often seen amongst immigrants who arrive due to their own self-

selection as well as selection by host countries favouring healthier individuals (Matlin et al., 2018). Immigrants, for instance, are less likely to have physical health conditions such as asthma or cardiovascular disease than their host country counterparts (Newbold, 2006; Vyas et al., 2024). However, this health advantage for immigrants declines over time. With longer duration of residence, immigrants often align with the host country's lifestyle and health behaviours, which results in a deterioration of health and increased risks of cardiovascular and metabolic diseases (Fennelly, 2008). The decline in health over time has important implications for cognitive health, as cardiovascular and metabolic conditions are known risk factors for cognitive decline, including Alzheimer's disease and vascular dementia. For example, older Mexican-born immigrants in the U.S. who had been in the country for less than 15 years had a more favourable inflammatory profile than those who had lived in the U.S. for over 15 years, illustrating how health can decline with longer duration of residence.

Systemic inflammation, which has been linked to both chronic disease and cognitive decline, may contribute to this increased risk. Prolonged exposure to metabolic dysfunction and vascular damage can promote systemic inflammation, further accelerating cognitive decline in aging immigrant populations. While recent immigrants may have lower dementia rates than long-term residents, this difference decreases with longer residency (Wong et al., 2021). A meta-analysis found that certain immigrant populations in Europe, particularly those from Asia and Africa, may face higher risk of dementia in their host countries compared to non-immigrants (Selten et al., 2020). The authors suggest this may be driven by post-migration factors such as reduced cognitive reserve, socioeconomic disadvantage, and limited access to healthcare including underdiagnosis in their countries of origin. While differences in diagnostic practices or surveillance in countries of origin may also contribute to observed patterns, Selten et al. (2020) note that dementia prevalence in countries of origin is generally not higher, supporting the role of host-country factors. These cumulative social, economic, and environmental challenges may contribute to chronic stress and inflammation, which can erode the initial health advantage observed through the healthy immigrant effect and increase risk for cognitive decline over time. In addition to physical health stressors tied to chronic disease risk, psychosocial stress may also play a critical role in shaping inflammation and cognitive health in immigrant populations.

1.5.4 Psychosocial Stress, Inflammation, and Cognitive Outcomes in Immigrants

Beyond physical health factors, immigrants face unique psychosocial stressors that may contribute to inflammation and cognitive decline, particularly in memory performance and executive function (James et al., 2020; Muñoz et al., 2021). These stressors often fall into social, economic, and cultural domains, including challenges related to financial strain, discrimination, language barriers, and limited support networks. Financial strain, precarious employment, and economic hardship are common challenges, especially for recent immigrants, and have been associated with increased stress-related cognitive difficulties, particularly in memory and processing speed (Fabio et al., 2022; Muñoz et al., 2021). Immigrants are also more likely to experience particular psychosocial stressors, such as discrimination due to being a visible minority (Alemi & Stempel, 2018), not speaking English as a first language, and lack of family supports (Toselli et al., 2014), all of which can result in greater psychological distress (Tong et al., 2020). These stressors may compound over time, leading to chronic stress exposure that negatively impacts cognitive function. Studies suggest that limited proficiency in the host country's language may not only hinder communication but also affect cognitive test performance, particularly on tasks involving verbal fluency and processing speed and especially when assessments are conducted in a language in which the individual is not fully proficient (Garcia et al., 2021). Limited social networks among immigrants may exacerbate stress exposure, creating additional barriers to cognitive resilience.

In addition to day-to-day stressors, broader life-course and resettlement experiences can also shape immigrants' exposure to psychosocial stress and inflammation. While resettlement holds the potential for greater economic or work opportunities, the process of resettlement comes with a multitude of challenges, increasing exposure to stressors and seemingly impacting immigrants more strongly the younger they are when they immigrate. Evidence suggests that there is a cumulative effect of adversity throughout the lifespan significantly increasing inflammatory levels in late life (Chen & Lacey, 2018; Hostinar et al., 2015; Levine et al., 2015). Among immigrants experiencing psychosocial stressors post-migration (e.g., job instability, financial stress), inflammatory levels were significantly higher than in those not experiencing such stressors (Steffen et al., 2016). However, greater acculturation (i.e., adaption to culture) saw associated with decreased inflammation and

better self-rated health in immigrants (Lommel et al., 2019). These findings underscore the relevance of psychosocial stress and inflammation in shaping long-term health trajectories among immigrants, highlighting potential pathways through which chronic stress may contribute to cognitive outcomes in later life. Among the most common outcomes of sustained psychosocial stress is psychological distress, which may also contribute to inflammatory processes and cognitive decline.

1.5.5 Mental Health Stress, Inflammation, and Cognitive Outcomes in Immigrants

Psychological distress, a result of overwhelming psychosocial stress, tends to occur at higher levels among immigrants than non-immigrants, potentially contributing to differences in inflammation and cognitive outcomes. Although the same factors that contribute to the general population's risk for psychological distress are found within the immigrant community, accumulation of psychosocial stress factors such as pre-migration trauma and experiences of discrimination post-migration increase immigrants' risk of distress (Li & Anderson, 2016). Additional factors that have been found to be protective against distress, such as family cohesion and support and a sense of control over lives, are less likely to occur in immigrants (Drapeau et al., 2011). Sex differences also shape experiences of psychological distress; for example, women are more likely to report psychological distress than men (Ryan et al., 2008), in part because women may be more affected by the loss of social support following migration. These differences in psychological distress may also have physiological consequences, as immigrant populations may exhibit distinct inflammatory profiles influenced by acculturation stress and health behaviours, which could affect levels of CRP and other inflammatory markers (Scholaske et al., 2021). Despite growing evidence linking stress, inflammation, and cognition in immigrant populations, important gaps remain in how these relationships have been studied.

1.5.6 Gaps in the Existing Literature on Stress and Cognitive Outcomes in Immigrants

While there are many studies on immigrant health, few investigate the long-term implications of differing types of chronic stress on immigrant cognition. First, many studies assume all immigrants' experiences are homogeneous. Although some individuals choose to migrate voluntarily, others are forced to leave their countries due to war, persecution, or

economic necessity and their experiences upon arrival can be quite diverse. These distinctions shape exposure to stressors, yet studies often fail to account for these differences.

Additionally, many studies assessing immigrant health do not include appropriate comparison groups, limiting the ability to determine how immigrant health trajectories differ from those of non-immigrants. Many studies also focus on younger immigrant populations, making it difficult to assess cognitive change in aging immigrants. Further, many studies rely on cross-sectional designs, which restrict analyses to single time points and prevent researchers from examining how stress-related factors affect cognition over time.

Moreover, very few studies measure cognitive function rather than dementia outcomes in immigrants and, to my knowledge, no published studies have assessed the relationship between chronic stress, inflammation, and cognitive decline outcomes among immigrants. This is a significant shortfall given that chronic exposure to physical health, psychosocial, and mental health stressors can alter our stress response system and contribute to cognitive decline. Supporting this, Canadian evidence suggests that increased chronic stress among aging racialized populations is associated with poorer cognitive outcomes (Stinchcombe & Hammond, 2021).

1.6 Conclusion

The literature indicates a robust and persistent association between chronic stress, inflammation, and reduced cognitive function, modified by sex. The stress response is a complex system, and its dysregulation can result from the type, duration, or intensity of stressors. Chronic stress and inflammation may be particularly detrimental to cognition as individuals age. However, research assessing these associations in aging Canadians has remained limited. This is especially true for immigrant populations, who may experience greater cumulative stress exposure across the life course than non-immigrants. Therefore, the present studies examined whether exposure to physical health, psychosocial, and mental health stressors is associated with cognitive function in older immigrant and non-immigrant Canadians. Additionally, the analyses assessed whether systemic inflammation (measured by CRP) mediated these associations, and whether the relationships varied by sex.

Chapter 2

Research Questions and Hypotheses

Chronic exposure to physical health, psychosocial, and mental health stressors can disrupt the body's ability to regulate stress, increasing vulnerability and poorer cognitive performance. Stress-related disruptions can impair memory, executive function, and other cognitive processes, with long-term exposure linked to an increased risk of dementia. Therefore, these studies investigated the impact of physical health (physical health conditions), psychosocial (e.g., social isolation), and mental health stressors (psychological distress) on cognition in older adults (**Figure 1**). Additionally, while systemic inflammation—measured by CRP—has been proposed as a pathway linking stress to cognitive decline, these studies assessed whether CRP mediated these associations and whether the relationships varied by sex.

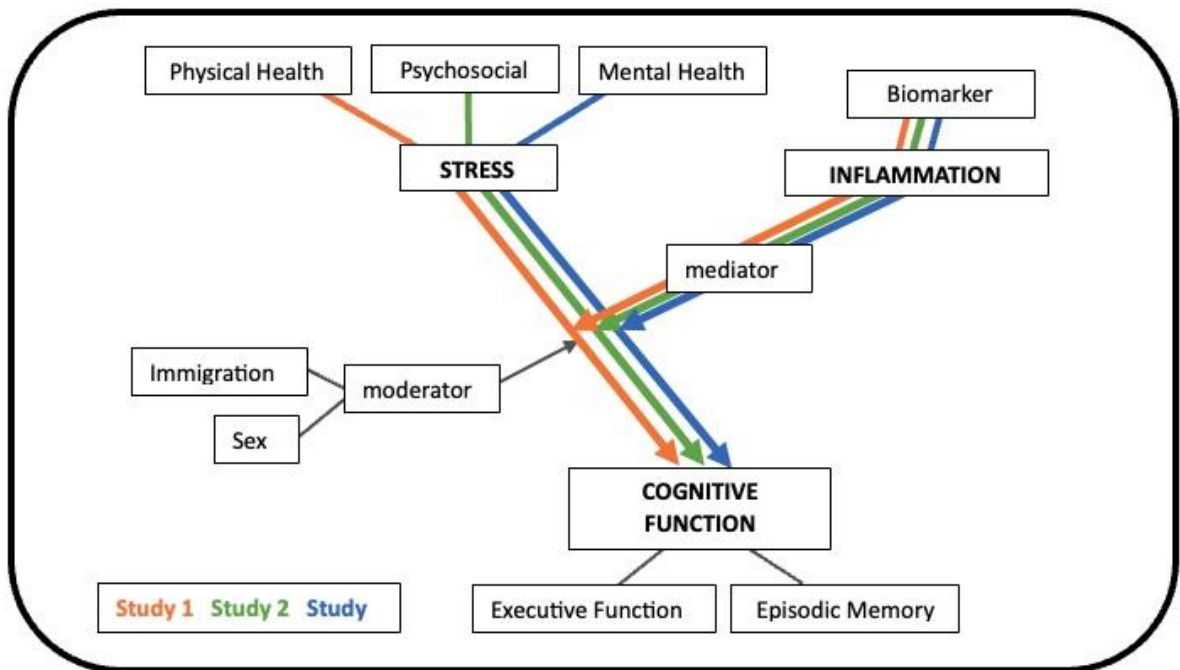


Figure 1. Conceptual map of the association between stress and cognitive function, with inflammation as a mediator and immigration status and sex as moderators

2.1 Research Questions for Study 1

Physical health stress, often driven by chronic physical health conditions, can place prolonged strain on the body and activate the inflammatory process. This study examined whether physical health conditions are a predictor of poorer cognitive performance at two timepoints in aging immigrant and non-immigrant Canadian adults. Additionally, given the interconnectedness between physical health conditions and inflammation, and the known impact that physical health has on cognition, inflammation was assessed as a mediator between physical health conditions and cognitive function.

The research questions for Study 1 were:

1. Do baseline measures of physical health conditions differ in aging immigrant and non-immigrant Canadians?
2. Does the association between baseline physical health conditions and follow-up cognitive performance (executive function and memory) differ across immigrant and non-immigrant Canadians?
3. Does inflammation mediate the association between physical health conditions and cognitive performance, and does this differ across immigrant and non-immigrant Canadians?
4. Does sex modify the above associations?

2.1.1 Study 1 Hypotheses

1. Given that immigrants in this sample have been residing in Canada long-term, their physical health conditions and cognitive outcomes will be similar to those of non-immigrants.
2. Both immigrant and non-immigrant women will have poorer physical health outcomes compared to their male counterparts.
3. Levels of inflammation will be higher in immigrants, particularly in immigrant women, reflecting a heightened vulnerability to the cumulative effects of chronic stress.

2.2 Research Questions for Study 2

Chronic psychosocial stress can dysregulate the immune system, resulting in increased pro-inflammatory responses and higher levels of inflammation. Examining the association between psychosocial stressors and cognitive aging among populations with heightened exposure to stressors (i.e., immigrants) provides a unique opportunity to study the inter-relationships between stress, inflammation and cognition in aging. Therefore, Study 2 examined the associations between psychosocial stressors and cognition in aging immigrant and non-immigrant Canadian adults and assessed whether inflammation mediated that association.

The research questions for Study 2 were:

1. Do baseline and three-year follow-up measures of psychosocial stressors differ in aging immigrant and non-immigrant Canadians?
2. Does the association between baseline psychosocial stressors and follow-up cognitive performance (executive function and memory) differ across immigrant and non-immigrant Canadians?
3. Does inflammation mediate the association between number of psychosocial stressors and cognitive performance, and does this differ across immigrant and non-immigrant Canadians?
4. Does sex modify the above associations?

2.2.1 Study 2 Hypotheses

1. Immigrants, particularly women, will report a higher number of psychosocial stressors compared to non-immigrants.
2. Psychosocial stressors will have a stronger negative association with cognitive function among immigrants, particularly women, due to disproportionate exposure to financial strain, caregiving burden, and social isolation.
3. Levels of inflammation will be higher in immigrants, particularly in immigrant women, reflecting a heightened vulnerability to the cumulative effects of chronic psychosocial stress.

2.3 Research Questions for Study 3

Psychological distress, which includes symptoms of anxiety and depression, is a common response to chronic stress and may influence cognitive function in later life. Immigrants are more likely to report higher levels of psychological distress than non-immigrants, which may be due to cumulative stress exposure across the life course. This study examined whether psychological distress was associated with cognitive performance in aging immigrant and non-immigrant Canadian adults and whether inflammation mediated that association.

The research questions for Study 3 were:

1. Do baseline and three-year follow-up measures of mental health stressors differ in aging immigrant and non-immigrant Canadians?
2. Does the association between baseline mental health stressors and follow-up cognitive performance (executive function and memory) differ across immigrant and non-immigrant Canadians?
3. Does inflammation mediate the association between mental health stressors and cognitive performance, and does this differ across immigrant and non-immigrant Canadians?
4. Does sex modify the above associations?

2.3.1 Study 3 Hypotheses

1. Immigrant women and non-immigrant women will report a higher number of mental health stressors than non-immigrant men.
2. Mental health stressors will have a stronger negative association with cognitive function in immigrants, particularly in immigrant women, compared to non-immigrants.
3. Levels of inflammation will be higher in immigrants, particularly immigrant women, indicating a heightened vulnerability to the cumulative effects of mental health stress.

Chapter 3

Methodology

3.1 Introduction to Structural Equation Modeling

A structural equation model (SEM) is a comprehensive statistical framework that allows researchers to test complex relationships between observed and latent variables while simultaneously analyzing multiple pathways (Bollen, 1989). It combines elements of factor analysis and multiple regression, making it particularly useful for modeling both direct and indirect relationships. SEM has become widely adopted across fields including psychology and epidemiology (Amorim et al., 2010; Beran & Violato, 2010; Foong et al., 2018; Tomás et al., 2012) due to its ability to study latent constructs, such as psychological traits or socioeconomic status, which are not directly measurable but can be inferred through multiple observed indicators. The model specifies hypothesized relationships among these variables through a system of equations, enabling researchers to evaluate how well their theoretical model fits the data (Amorim et al., 2010). This approach also allows for the estimation of measurement error, offering a more nuanced understanding of the underlying processes compared to traditional regression methods.

3.2 Factor Analysis

Factor analysis, a theory-driven specialized application of SEM, is used to test the fit of hypothesized measurement models and measure difficult-to-quantify concepts such as psychosocial stress and cognitive domains (**Figure 2**; Brown & Moore, 2012). There are two types of factor analysis: Exploratory Factor Analysis (EFA) and Confirmatory Factor Analysis (CFA). Both EFA and CFA aim to identify underlying latent variables that explain the relationships between indicator variables and their factors, but while EFA is data-driven and seeks to uncover potential factor structures, CFA tests predefined hypotheses about those structures. The observed indicators are intercorrelated because they share a common construct. For example, depression is not directly measurable, but it is inferred from symptoms, such as persistent sadness and loss of interest, that indicate its presence. CFA ensures that each indicator meaningfully contributes to the latent construct, resulting in a more theoretically sound measurement model (Brown & Moore, 2012).

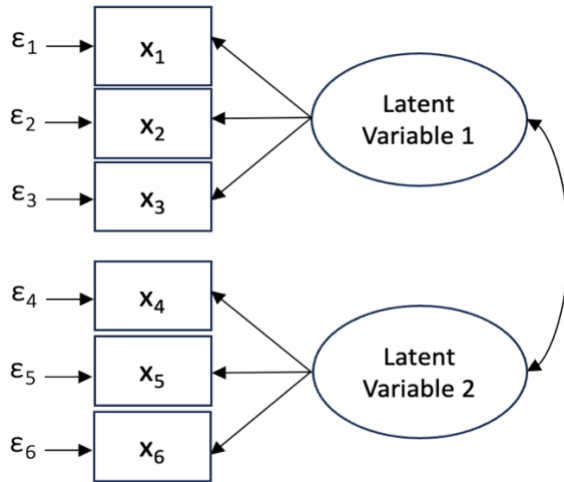


Figure 2. Factor sub-model.

Note: An unanalyzed association is often represented by curved arrows, with circles for latent variables and rectangles for observed variables. While x represents indicator variables, ϵ indicates the error attributed to each indicator variable.

3.3 Path Diagrams

Path diagrams, another component of SEM, visually represent relationships between variables, connected by arrows to show direction and strength (**Figure 3**; Bollen, 1989).

These diagram act as sub-models within SEM, integrating multiple interconnected models to examine direct, indirect, and total effects. Path diagrams help clarify complex relationships and provide a simplified view of the model's structure before testing it statistically (Amorim et al., 2010).

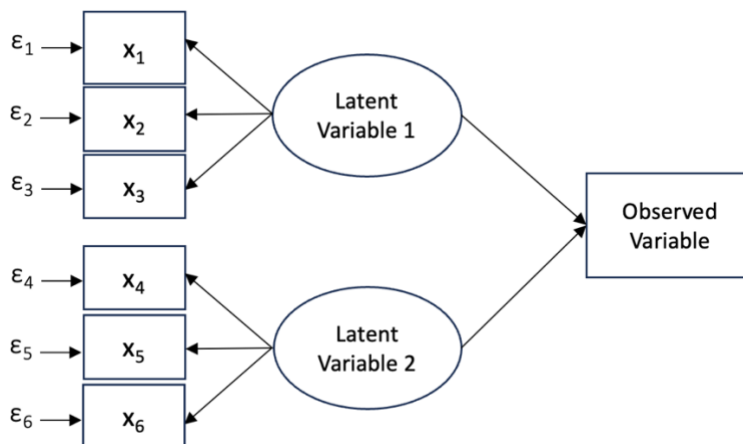


Figure 3. Path analysis sub-model.

In this research, SEM is used to examine multiple pathways through which stress may influence cognitive outcomes, considering the intricate interactions between biological, psychological, and social factors. Unlike traditional regression techniques, SEM integrates latent variables, such as psychosocial stress, allowing for a deeper understanding of how these stress dimensions contribute to poorer cognitive outcomes or resilience among immigrant and non-immigrant aging populations. SEM's ability to weigh indicators and account for measurement errors ensures that the theoretical constructs are reflected accurately in the data (Beran & Violato, 2010).

3.4 Factor Loadings

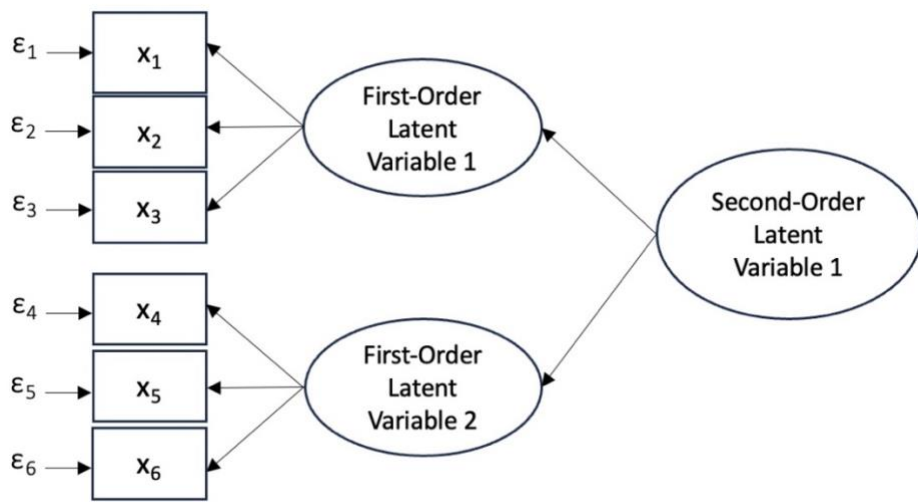
In SEM and CFA, path coefficients and factor loadings are critical. Path coefficients quantify the direct effects of one variable on another, while factor loadings describe relationships between observed variables and latent constructs. High factor loadings validate the indicators of stress and cognitive function used in this study, and analyzing both paths and loadings provides clarity on the causal mechanisms underlying these relationships, leading to more precise interpretations and conclusions.

In this study, CFA was used to construct latent factors representing physical health conditions, psychosocial stress, and psychological distress by selecting key indicators based on prior literature and retaining those with statistical significance. While the recommended threshold for factor loadings is 0.35 and above (Stevens, 2012), indicators with loadings below 0.35 that represent theoretically important constructs will also be retained, provided they are well supported by the literature. This ensures that even indicators with modest loadings contribute to the overall construct validity.

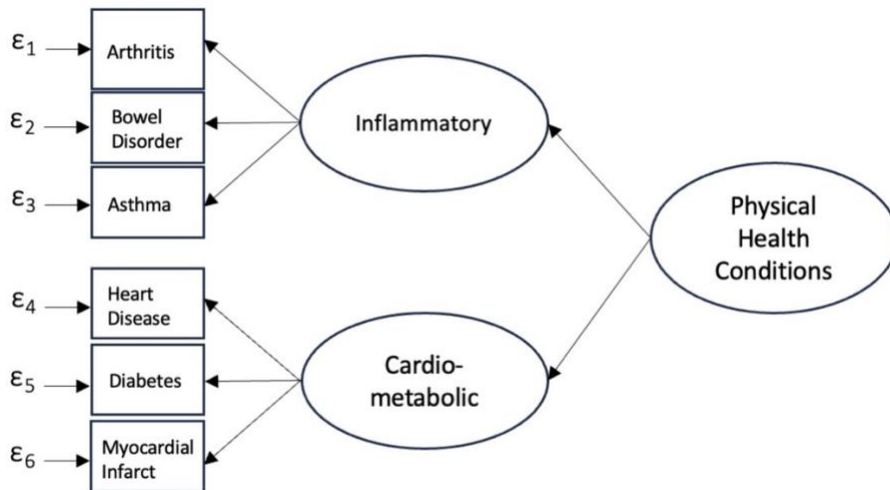
3.5 First- and Second-Order Factors

To improve model validity, a second-order factor may be introduced, which groups related first-order latent variables under a broader, higher-order construct (**Figure 4**; Brooks & Beard, 2006). This approach captures shared variance among the first-order factors and strengthens the overall model structure. For example, grouping specific chronic conditions, such as inflammatory diseases and cardiometabolic conditions under the broader latent variable of physical health conditions may be necessary to improve the factor structure in our

analysis (**Figure 4B**). Creating second-order factors provides a more nuanced understanding of how these complex constructs are structured. This approach balances theoretical expectations with empirical realities. It provides a clearer, more robust framework for interpreting the relationships between stress and cognition compared to models that only include first-order constructs.



A.



B.

Figure 4. First- and second-order factor models.

3.6 Missing Data and MAR Assumptions

Missing data in cognitive outcomes were assessed for both executive function and memory domains at baseline and follow-up. Executive function was measured using five tests: Animal Fluency Test (AFT); Mental Alternation Test (MAT), Controlled Oral Word Association Test (COWAT), Victoria Stroop Neurological Screen Test (Stroop), and Time-based Prospective Memory Test (TMT), and episodic memory was assessed using two tests: Rey Auditory Verbal Learning Test immediate word recall (REY1) and delayed word recall (REY2). At baseline, approximately 5.2% of executive function test scores and 3.5% of episodic memory test scores were missing across the full sample. At follow-up, 23.0% of executive function tests and 21.0% of episodic memory tests were missing. These rates refer to missing individual test scores, rather than participants missing all cognitive assessments. In other words, a participant may have completed some tests but not others within the same cognitive domain. Rates of missingness are consistent with patterns observed in other longitudinal analyses of cognitive aging using CLSA data (Best, 2024) as well as within the range observed in other longitudinal studies of aging and cognition (Hernandez et al., 2024). The increase in missingness from baseline to follow-up is consistent with expected patterns due to participant attrition, health deterioration, or continued difficulty completing computerized assessments, which may become more pronounced over time as cognitive or physical abilities decline (Hernandez et al., 2024; Katsuno et al., 2023).

Full information maximum likelihood (FIML) was used to handle missing data across all models (Enders & Bandalos, 2001). Under the assumption that the data are Missing at Random (MAR), FIML provides unbiased parameter estimates by using all available data from each participant without imputing values. Rather than excluding cases with any missing data, FIML retains participants with partial data and estimates parameters based on the likelihood of the data they did provide (Enders, 2022). This approach has also been applied in other CLSA studies examining longitudinal changes in cognition (Best, 2024).

To assess the plausibility of the MAR assumption required for FIML, Poisson regression analyses were conducted separately for executive function and episodic memory outcomes to determine whether missingness was associated with observed participant characteristics. These included sociodemographic characteristics (age, sex, education, immigrant status, first language learned), all of the physical health conditions examined in

Study 1 (e.g., stroke, heart disease) plus additional conditions available in the dataset (e.g., dementia), psychosocial stress variables (e.g., financial strain, barriers to social participation due to health), and psychological distress. Older age, being male, lower education, and physical health conditions such as stroke, heart disease, and diabetes were the strongest predictors of missing data. Financial strain and psychological distress were also associated with missingness, though their effects were smaller and less consistent. Other tested variables showed no meaningful associations with missingness. As an additional check, models were re-estimated using listwise deletion. Parameter estimates and patterns of association remained largely consistent with those obtained using FIML.

Although dementia was not included in the final models, its relationship with missingness warrants clarification. Dementia and memory impairment were associated with missingness. Dementia was excluded from the physical health latent variable in Study 1 due to its very weak factor loading and it was not included in the subsequent studies that focused on psychosocial and mental health constructs. However, the physical health construct in Study 1 still included a broad range of physical health conditions (e.g., stroke, heart disease, diabetes), that were also associated with missingness. As shown in earlier analyses (Rutter et al., 2025), missingness was not limited to any one condition or domain but reflects a broader set of health and social factors. Therefore, the exclusion of dementia is unlikely to meaningfully bias the results.

Taken together, these steps lend support to the plausibility of the MAR assumption. Predictors of missingness were included within each of the SEMs, and missingness was found to be associated with a range of observed characteristics rather than unobserved variables. The use of FIML is considered appropriate in this context and aligns with prior longitudinal analyses of CLSA cognitive data (Best, 2024). This approach allows participants with incomplete data to be retained in the analysis, thereby reducing bias and preserving statistical power relative to traditional approaches such as listwise deletion.

3.7 Data Source: Canadian Longitudinal Study on Aging (CLSA)

This research analyzed data from the Comprehensive cohort of the Canadian Longitudinal Study on Aging (CLSA), a population-based prospective cohort study of community-dwelling Canadian adults aged 45 to 85 at baseline (N = 30,093). Baseline data

were collected between 2011 and 2015, and follow-up data were collected between 2015 and 2018. Participants completed both in-home interviews and clinical assessments at 11 Data Collection Sites across 7 provinces (Raina et al., 2019).

Recruitment was originally stratified by age, sex, and province to ensure representativeness, with subsequent targeted oversampling of geographic regions associated with higher proportions of residents who had not completed high school, as identified using 2006 Canadian Census data (Canadian Longitudinal Study on Aging, 2020). Three primary sampling frames: the Canadian Community Health Survey-Healthy Aging (CCHS-HA), provincial health registration databases, and random-digit dialing (Canadian Longitudinal Study on Aging, 2020). An additional sampling frame was the Quebec Longitudinal Study on Nutrition and Aging (NuAge), with the same inclusion criteria applied as for CCHS-HA. Participants were eligible if they were English or French-speaking, non-institutionalized residents of the 10 Canadian provinces. Exclusion criteria included full-time members of the Canadian Armed Forces; individuals living in the three territories or on First Nations reserves; and individuals with signs of overt cognitive impairment, as determined by trained interviewers at recruitment. Further study details are available elsewhere (Canadian Longitudinal Study on Aging, 2020; Raina et al., 2019).

Measures collected included sociodemographic characteristics, physical health conditions, psychosocial stressors (e.g., barriers to social participation), psychological distress, executive function and episodic memory. Measures relevant to each study are described in their respective chapters, and the exact wording of CLSA questionnaire items is provided in **Appendix A: Supplementary Material for Chapter 3 Methodology**.

Chapter 4

Physical Health Stress

Physical health conditions, inflammation, and cognitive function in aging immigrants and non-immigrants: Findings from the Canadian Longitudinal Study on Aging

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4.1 Background

As a reflection of medical and health care advances, older adults are living longer. Despite this progress, chronic health conditions such as hypertension and diabetes remain highly prevalent among older adults. In Canada, a substantial portion of the population of adults are over 65 years of age (6.6 million or 17.5%; Public Health Agency of Canada, 2021). Two-thirds of those older adults live with at least one chronic health condition, with a disproportionate number of women reporting two or more chronic health conditions (multimorbidity). Having chronic health conditions elevates the risk of additional adverse health outcomes, including cognitive decline and dementia (Grande et al., 2021; Mayeda et al., 2013; Shorey, 2019; Vassilaki et al., 2015).

Inflammation is a potential factor explaining the link between chronic health conditions—also referred to as chronic physical health stress—and cognitive impairment (McEwen, 1998; Russell & Lightman, 2019). This relationship operates bidirectionally: chronic physical health stress contributes to a state of persistent or systemic inflammation, while systemic inflammation in turn exacerbates the progression of chronic health conditions. Heightened levels of systemic inflammation have been associated with increases in cognitive impairment among older adults (Marsland et al., 2015; Yaffe et al., 2003), especially in those with chronic health conditions (Miller & Spencer, 2014; Yaffe et al., 2004).

Chronic physical health stress and persistent inflammation may exacerbate the health risks experienced by vulnerable populations such as immigrants, who encounter additional stressors unique to their circumstances. Approximately 30% of Canadians aged 65 and older are immigrants (Employment and Social Development Canada, 2018). Senior immigrants in Canada are more likely to face challenges such as poverty and to have poorer health outcomes and greater difficulty accessing health services (Turcotte & Schellenberg, 2006). Factors such as social isolation, discrimination, and other challenges related to immigration status further compound the burden of chronic health conditions among immigrants (Commodore-Mensah et al., 2018; Commodore-Mensah et al., 2016; Constant et al., 2018). Limited health literacy and inadequate access to healthcare resources may result in delayed diagnosis and treatment, ultimately exacerbating systemic inflammation (Viruell-Fuentes et al., 2012).

Despite extensive research on immigrant health (Angel et al., 2001, 2012; Argeanu Cunningham et al., 2008; Commodore-Mensah et al., 2018; Commodore-Mensah et al., 2016; Reynolds et al., 2016; Rosenthal, 2014; Vang et al., 2017), including cognitive outcomes (Black et al., 1999; Casanova & Aguila, 2020; Garcia et al., 2017, 2022; Hill, Angel, & Balistreri, 2012; Hill, Angel, Balistreri, et al., 2012; Kindratt et al., 2022; Tang et al., 2019; Xu et al., 2017), no study to date has assessed the complex interplay between chronic physical health stress, inflammation, and cognition in aging immigrants. Therefore, the present study aimed to assess whether chronic physical health stress and cognitive performance differ between aging immigrant and non-immigrant Canadians. Moreover, given the bidirectional relationship between inflammation and chronic health conditions, both of which are associated with cognitive decline, we investigated whether inflammation mediates the relationship between chronic physical health stress and cognitive function. Additionally, we sought to examine whether these associations varied by immigrant status or sex.

4.2 Methods

4.2.1 Study Design and Population

This study analyzed data from the Comprehensive cohort of the CLSA (N = 30,093). The CLSA is a prospective, population-based panel study of non-institutionalized English and French-speaking Canadians aged 45 and 85 years at recruitment (Raina et al., 2019). Participant baseline (2011-2015) and follow-up (2015-2018) data were collected from both in-home interviews and clinical assessments at 11 Data Collection Sites across seven provinces. The immigrant subsample in this study represents a well-established population in Canada at the time of recruitment (mean years in Canada = 40.20 ± 16.28 SD).

At recruitment, CLSA excluded full-time members of the Canadian Armed Forces, First Nations Peoples living on federal reserves or other First Nations settlements, and residents of the three territories and some remote regions. Individuals with cognitive impairment were excluded if they were unable to provide informed consent, as determined by trained interviewers at recruitment. Additional study details are available elsewhere (Canadian Longitudinal Study on Aging, 2020; Raina et al., 2019).

4.2.2 Measures

4.2.2.1 Independent Variable

Using the Disease Symptoms questionnaire, participants were asked “Has a doctor ever told you that you have ____?” and provided “yes/no/I don’t know” answers. These conditions had to be long-term (i.e., lasting for more than six months) and diagnosed by a health professional (Canadian Longitudinal Study of Aging, 2014). In total, 15 physical health conditions at baseline were chosen to derive the latent variables *physical health conditions* (for full list see Appendix C, **Table C1**).

4.2.2.2 Dependent Variable

The dependent variables were baseline and follow-up executive function and episodic memory. Our analyses included the Animal Fluency Test (AFT; Goodglass & Kaplan, 1983; Read, 1987), Mental Alternation Test (MAT; Teng, 1995), Controlled Oral Word Association Test (COWAT; Benton & Hamsher, 1978), Victoria Stroop Neurological Screen Test (Stroop; Bayard et al., 2009, 2011; Moroni & Bayard, 2009; Troyer et al., 2006), and Time-based Prospective Memory Test (TMT; Lowenstein & Acevedo, 2001) for executive function (**Figure 5A**), and the Rey Auditory Verbal Learning Test (called REY in CLSA) 1 and 2 (immediate and delayed word recall, respectively) for episodic memory (**Figure 5B**; Rey, 1958). Tests were modified for use in the CLSA (Tuokko et al., 2017). For example, the lenient scoring of AFT, which gives points for each distinct animal, was used. In addition, the errors from the Stroop assessments and interference, and the learning trials from the REY, were not included in implementation of these tests in the CLSA. Scores for each test were standardized using z-scores and calculated separately for each cognitive domain in English and in French. These were then combined following published methods (Iacono et al., 2023; Oremus et al., 2019, 2020).

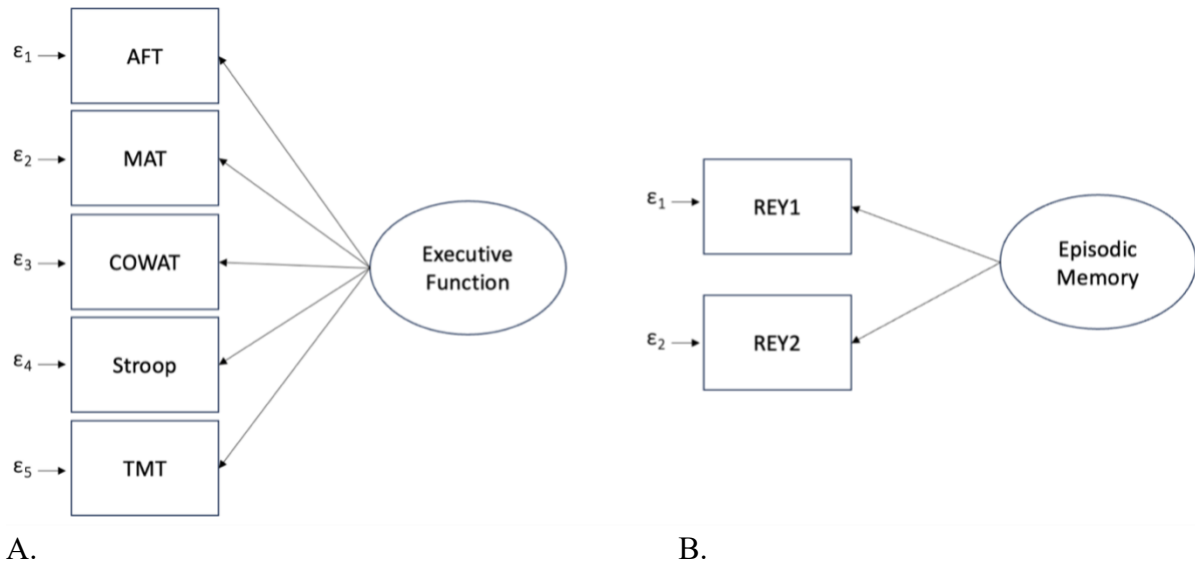


Figure 5. Path diagrams for displaying structural sub-models.

A. Executive function sub-model: Animal Fluency Test (AFT); Mental Alternation Test (MAT), Controlled Oral Word Association Test (COWAT), Victoria Stroop Neurological Screen Test (Stroop), and Time-based Prospective Memory Test (TMT).

B. Episodic memory sub-model: Rey Auditory Verbal Learning Test (REY)1 immediate word recall and REY2 delayed word recall.

4.2.2.3 Mediation Variable

Inflammation was measured using baseline serum CRP levels determined from venous blood samples collected at the Data Collection Sites (Canadian Longitudinal Study on Aging, 2015a, 2015b) and analyzed as a continuous variable.

4.2.2.4 Covariates

To assess immigrant status at baseline, participants were asked the open-ended question, “In what country were you born?”. The variable was then coded into a dichotomous variable: non-immigrant (born in Canada) and immigrant (born outside of Canada).

Baseline covariates included age (continuous), sex (at baseline, participants were asked “Are you male or female?”), education, and first language learned. First language learned was operationalized as the first official language(s) learned and still understood (“English or French; English and French; English and/or French and Other; Other”).

4.2.3 Data Analysis

4.2.3.1 Descriptives

Univariate analyses described means and standard deviations or medians with interquartile ranges for continuous variables, while frequencies and percentages were reported for categorical variables. Bivariate analyses used chi-square tests (χ^2) for categorical variables and Wald tests for group comparisons. Group comparisons were conducted using Wald tests but were limited to cases where both groups had statistically significant associations. Comparisons were not performed when effects were non-significant or in the same direction for both groups, as these did not indicate a meaningful difference to test.

4.2.3.2 Measurement Models

The conceptual model is depicted in

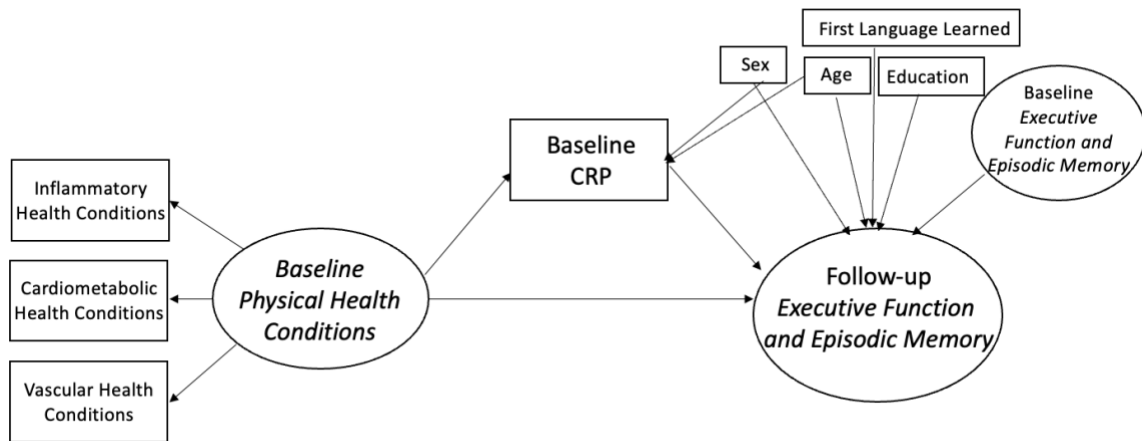


Figure 6. Standardized tests for executive function and episodic memory served as indicators for their respective latent variables (**Figure 5**). Pearson's correlation was used to determine which chronic health condition variables were related to each construct for grouping under the latent variables (Appendix C, **Table C1**). Consistent with correlation results, confirmed by our conceptual framework, diseases clustered by medical commonality (e.g., cardiometabolic diseases were correlated). Variables not correlated with clusters were included in models as single variables. Confirmatory factor analysis was used to construct the factors of *inflammatory, cardiometabolic, vascular, endocrine, and neurological health*

conditions. Given poor model fit, final models excluded *endocrine* and *neurological health conditions* as factors for the latent *physical health conditions* variable. Back pain, kidney disease and cancers were also excluded from final models due to poor fit. The final *physical health conditions* latent variable thus included inflammatory health conditions (bowel disorders [e.g., ulcerative colitis], asthma, chronic obstructive pulmonary disease [COPD], ulcers, rheumatoid arthritis, osteoarthritis, and allergies); cardiometabolic health conditions (heart disease and congestive heart failure, angina, myocardial infarct, diabetes, and hypertension); and vascular health conditions (peripheral vascular disease, transient ischemic attack [TIA], and stroke).

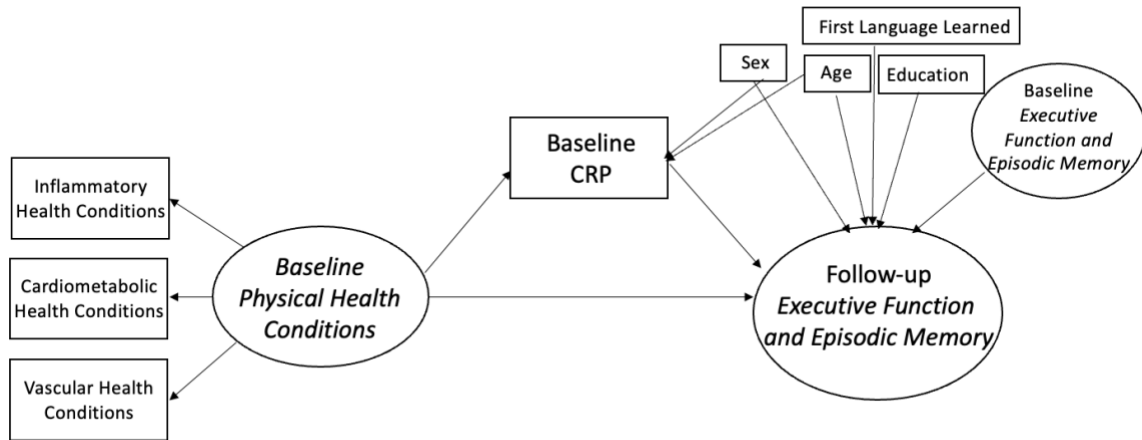


Figure 6. Path model for follow-up analysis illustrating the mediation model tested using a structural equation model.

The model includes latent variables for *physical health conditions* (comprising inflammatory, cardiometabolic, and vascular health conditions), *executive function* and *episodic memory*. Follow-up executive function and episodic memory models were run separately and were adjusted for their baseline counterparts (executive function or episodic memory).

Model fit was deemed acceptable when the Comparative Fit Index (CFI) exceeded 0.90 (Amorim et al., 2010; Bentler, 1990) and the Root Mean Square Error of Approximation (RMSEA) was below 0.08 (Barrett, 2007; Browne & Cudeck, 1993). However, while the chi-square test is commonly used to assess model fit, it can be overly sensitive in larger samples (Alavi et al., 2020; Kline, 2023). Given our large sample size, we interpreted the X^2 results

with caution, relying more on other fit indices to assess whether the model was adequate. Path coefficient significance was set at 0.05.

4.2.3.3 Structural Equation Modeling

SEM was used to explore the associations between the latent variable of *physical health conditions* and the separate outcomes of *executive function* and *episodic memory*. Multiple group SEM first tested for structural invariance and examined group-specific effects between immigrants and non-immigrants, adjusting for age (continuous), sex, education, and first language(s) learned. While all four covariates were initially included on CRP, only age and sex were retained in the final models, as education and first language(s) learned were not statistically significant and their inclusion worsened model fit. To further investigate potential sex-specific effects, models stratified by both immigrant status and sex were estimated. The models assessing follow-up executive function and episodic memory performance were also adjusted for their respective baseline cognitive scores. CRP was natural log-transformed (ln-CRP) to address a positively skewed distribution and was included in all models as the mediator. For interpretation, a one-unit increase in the ln-CRP is associated with approximately a 100% increase in untransformed CRP.

Missing data affected 23.0% of executive function tests at follow-up and 21.0% of episodic memory tests at follow-up, which is within the range of missingness commonly observed in longitudinal studies of aging and cognition (Hernandez et al., 2024). Four participants did not respond to the immigrant status question and were excluded from the analysis. FIML was used to account for missing data (Enders & Bandalos, 2001) under the assumption that the data are MAR. FIML does not impute missing values; instead, it estimates model parameters by maximizing the likelihood function for each individual based on the available observed data, thereby reducing bias associated with listwise deletion. Additional technical details regarding model specification, grouping strategy, and parameter constraints across studies are provided in Appendix B. Data were analyzed using Stata SE version 17 (StataCorp, 2021). Data access was approved by the Canadian Longitudinal Study on Aging (#2104054) and ethics approval was received for this project from the University of Waterloo Office of Research Ethics (#43403).

4.3 Results

4.3.1 Descriptive Analyses

Participants were aged 45 to 85 years (mean age 63 ± 10.25 SD) at recruitment, with immigrants (64.70 ± 10.53) slightly older on average than non-immigrants (62.57 ± 10.15). Less than half of immigrant participants were women (46.69%), whereas over half (51.83%) of non-immigrant participants were women. Most participants were non-immigrant Canadians (81.88%; **Table 1**). Immigrants were more likely than non-immigrants to have a university degree (54.36% vs. 43.12%, $p < .001$). Immigrants and non-immigrants had a similar number of physical health conditions (mean [SD] 1.38 [1.37] vs. 1.41 [1.41], $p = .26$); however, CRP levels for immigrants were lower than those of non-immigrants (2.41 [4.92] vs 2.60 [5.11], $p = .02$).

Non-immigrants generally showed better cognitive performance than immigrants. Mean executive function scores increased from baseline to follow-up for both immigrants (mean [SD] = -0.22 [3.77] to -0.09 [3.64]) and non-immigrants (0.13 [3.68] to 0.19 [3.58]), while episodic memory scores stayed stable for both groups (**Table 1**). Executive function and episodic memory scores are standardized z-scores based on CLSA procedures and are reported as medians and interquartile ranges. These reflect relative performance within the CLSA sample, with wider IQRs expected due to the composite nature of the scores (see Methods, Section 4.2.2.2).

While non-immigrants generally showed higher median baseline and follow-up scores for both executive function and episodic memory (**Table 1**), immigrants outperformed non-immigrants on one specific task of executive function: the Stroop test (Appendix A, Error! Reference source not found.). In contrast, although immigrants and non-immigrants performed similarly on tasks of baseline episodic memory, non-immigrants outperformed immigrants on tasks of follow-up episodic memory (Appendix C, **Table C2**). Furthermore, while 96.57% of non-immigrants' first language matched the testing language (English or French), only 61.09% of immigrants' first language did (**Table 2**).

Table 1. Descriptive characteristics by immigrant status (N = 30,093).

Baseline Characteristics	Immigrants n=5,449			Non-Immigrants n=24,644		
	M (SD)	Md (IQR)	n (%)	M (SD)	Md (IQR)	n (%)
Sex						
Female			2,544 (46.69)			12,774 (51.83)
Male			2,905 (53.31)			11,870 (48.17)
Age (years)	64.70 (10.53)	65 (17)		62.57 (10.15)	62 (16)	
First Language was English or French						
Yes			3,329 (61.09)			23,794 (96.56)
No			2,120 (38.91)			847 (3.44)
Education						
Up to High school/GED			961 (17.66)			5,779 (23.45)
Trade/College			1,523 (27.98)			8,235 (33.42)
University degree or higher			2,959 (54.36)			10,625 (43.12)
Number of Physical Health Conditions	1.38 (1.37)	1 (2)		1.41 (1.41)	1 (2)	
Inflammatory	0.59 (0.82)	0 (1)		0.63 (0.86)	0 (1)	
Cardiometabolic	0.71 (0.88)	0 (1)		0.70 (0.89)	0 (1)	
Vascular	0.09 (0.30)	0 (0)		0.09 (0.30)	0 (0)	
CRP (mg/L)	2.41 (4.92)	1.2 (1.9)		2.60 (5.11)	1.2 (2.1)	
Executive Function (T ₀)	-0.22 (3.77)	-0.19 (4.82)		0.13 (3.68)	0.23 (4.66)	
Executive Function (T ₁)	-0.09 (3.64)	-0.02 (4.61)		0.19 (3.58)	0.32 (4.67)	
Episodic Memory (T ₀)	-0.16 (1.84)	-0.27 (2.48)		0.04 (1.84)	0.00 (2.31)	
Episodic Memory (T ₁)	-0.17 (1.89)	-0.18 (2.55)		0.05 (1.88)	-0.14 (2.41)	

Note: CRP = C-reactive protein; IQR = interquartile range; M = mean; Md = median; mg/L = milligrams per litre; n = subsample size; pg/mL = picograms per millilitre; SD = standard deviation; T₀ = baseline and T₁ = follow-up; Trade/College = Trade/community college or university certificate. Executive function and episodic memory scores are standardized z-scores based on CLSA procedures and are reported as medians and interquartile ranges. These reflect relative performance within the CLSA sample, with wider IQRs expected due to the composite nature of the scores (see Methods, Section 4.2.2.2).

Table 2. Distribution of first language(s) learned by immigrant status.

Immigrant Status	English or French	English and French	English and/or French and Other	Other
Immigrant (n = 5,499)	58.40%	0.29%	2.40%	38.91%
Non-Immigrant (n = 24,644)	94.97%	0.81%	0.79%	3.44%

4.3.2 Measurement Model

The measurement model, which assess the relationships between observed variables and their underlying latent constructs, included *physical health conditions*, *executive function*, and *episodic memory* as latent variables. All measures significantly loaded onto physical health conditions ($\beta = 0.27\text{--}0.55$, $P < 0.001$ for all, Appendix C, **Figure C3**) baseline and follow-up executive function ($\beta = 0.08\text{--}0.66$, $P < 0.001$ and $\beta = 0.10\text{--}0.65$, $P < 0.001$ for all, respectively, Appendix C, **Figure C4**) and baseline and follow-up episodic memory ($\beta = 0.70\text{--}0.98$, $P < 0.01$ for all and $\beta = 0.79\text{--}0.98$, $P < 0.01$ for all, respectively, Appendix C, **Figure C5**), indicating that convergent validity was achieved. The measurement models depicted adequate fit indices for baseline and follow-up executive function (CFI = 0.81, RMSEA = 0.06 and CFI = 0.82, RMSEA = 0.06, respectively) and baseline and follow-up episodic memory (CFI = 0.86, RMSEA = 0.08 and CFI = 0.90, RMSEA = 0.08, respectively) which indicated that the construct validity was achieved. However, χ^2 indicated a lack of fit for all models. Despite this, the data aligned well with the hypothesized measurement model, and all measures that representing the four latent variables demonstrated high reliability. Additionally, all four main models, baseline and follow-up executive function ($R^2 = .62$ and $R^2 = .95$, respectively) and baseline and follow-up episodic memory ($R^2 = .59$ and $R^2 = .70$, respectively), had high predictive accuracy.

4.3.3 Structural Equation Models: Examining Differences by Immigrant Status

SEM was used to examine whether physical health conditions were associated with executive function and episodic memory at baseline and follow-up, stratified by immigrant status (**Table 3**). Among immigrants, physical health conditions were significantly associated with poorer executive function at baseline, but not at follow-up. In contrast, among non-immigrants

physical health conditions were associated with both baseline and follow-up executive function. There were no significant group differences for baseline executive function; however, a significant group difference was observed at follow-up ($\chi^2[1] = 6.16, p = 0.01$).

Moreover, physical health conditions were associated with baseline but not follow-up episodic memory for immigrants, whereas among non-immigrants, physical health conditions were associated with both poorer baseline and follow-up episodic memory performance (**Table 3**). While no group difference was observed for baseline episodic memory, a significant group difference was again observed at follow-up ($\chi^2[1] = 4.54, p = 0.03$).

The effect of physical health conditions on executive function and episodic memory mediated by CRP is summarized in **Table 3**. Although the effects were negligible, ln-CRP partially mediated the association between physical health conditions and baseline executive function among immigrants, as well as baseline episodic memory among immigrants and non-immigrants. Group comparisons indicated that the partial mediation effect of CRP on the association between physical health conditions and baseline episodic memory was stronger among immigrants than non-immigrants ($b = .03, p < 0.001$).

Table 3. Effect of baseline physical health conditions on baseline and follow-up executive function and episodic memory by immigrant status, mediated by baseline ln-CRP.

	Models							
	Executive Function (T₀)		Executive Function (T₁)		Episodic Memory (T₀)		Episodic Memory (T₁)	
	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>
Baseline Characteristics	<i>Immigrants</i>							
Physical Health Conditions	-.34***(-.49, -.19)	-.11	-.05 (-.16, .06)	-.02	-.13 (-.29, .02)	-.04	-.16 (-.32, .01)	-.05
ln-CRP	-.02*(-.05, -.00)	-.01	-.01 (-.03, .005)	-.003	-.03*(-.05, -.003)	-.01	-.01 (-.03, .02)	-.003
	<i>Non-immigrants</i>							
Physical Health Conditions	-.34***(-.41, -.27)	-.13	-.19***(-.24, -.14)	-.08	-.22***(-.29, -.14)	-.07	-.17***(-.24, -.10)	-.06
ln-CRP	-.02 (-.04, .01)	-.01	-.001(-.01, .01)	-.001	-.01*(-.21, -.000)	-.004	.004 (-.01, .02)	.001

Note. *b* = unstandardized regression coefficient value; *B* = standardized regression coefficient value; CI= 95% confidence interval; Covariates: age, sex, education, and first language learned; ln-CRP = natural log-transformed C-reactive protein; T₀ = baseline and T₁ = follow-up. **Bold** indicates a significant relationship * *p* < 0.05; ** *p* < .01; *** *p* < .001

4.3.4 Structural Equation Models: Examining Sex Differences Within Immigrant Status

Further analyses examined sex differences in the associations between physical health conditions and cognitive function among immigrants and non-immigrants (**Table 4**). Among immigrants, physical health conditions were significantly negatively associated with poorer baseline executive function in women, but not in men. In contrast, only immigrant men showed an association between physical health conditions and poorer episodic memory at baseline, while only immigrant women demonstrated this relationship at follow-up. There was no significant effect on follow-up executive function for either sex.

Among non-immigrants, physical health conditions were linked to poorer baseline executive function in both women and men. Additionally, physical health conditions predicted poorer episodic memory at both baseline and follow-up for both non-immigrant women and men. However, no significant relationship was found between physical health conditions and follow-up executive function for either sex.

Group comparisons showed significant differences in these associations by sex and immigrant status. There were no group differences for baseline or follow-up executive function. For baseline episodic memory, physical health conditions were associated with poorer performance in both non-immigrant women and men, but the association was slightly stronger in women ($\chi^2[1] = 12.29, p = 0.001$). There were no other group differences. At follow-up, differences emerged between immigrant and non-immigrant women, with a stronger negative association observed in immigrant women ($\chi^2[1] = 1322.87, p < 0.001$). Additionally, non-immigrant women showed a stronger association with poorer episodic memory at follow-up compared to non-immigrant men ($\chi^2[1] = 3510.09, p < 0.001$).

The effect of physical health conditions on executive function and episodic memory mediated by ln-CRP is summarized in **Table 4**. Among non-immigrant men, ln-CRP partially mediated the associations between physical health conditions and both baseline executive function and baseline episodic memory. While physical health conditions were not associated with baseline episodic memory for immigrant women, ln-CRP was linked to baseline episodic memory in this group. No significant group differences were observed for baseline episodic memory. No significant mediation was found for immigrant men and non-immigrant women.

Table 4. Effect of baseline physical health conditions on baseline and follow-up executive function and episodic memory by immigrant status and sex, mediated by baseline ln-CRP.

	Models							
	Executive Function (T₀)		Executive Function (T₁)		Episodic Memory (T₀)		Episodic Memory (T₁)	
	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>
Baseline Characteristics	<i>Immigrants</i>							
Females								
Physical Health Conditions	-.54***(-.77, -.32)	-.16	-.10 (-.35, .16)	-.02	-.01 (-.25, .23)	-.003	-.17*(-.32, -.02)	-.09
ln-CRP	-.03 (-.07, .02)	-.01	-.02 (-.07, .03)	-.01	-.05*(-.10, -.004)	-.02	.02 (-.02, .03)	.01
Males								
Physical Health Conditions	-.24 (-.48, .01)	-.07	.22 (-.07, .51)	.04	-.29*(-.53, -.04)	-.07	.10 (-.11, .32)	.04
ln-CRP	-.02 (-.05, .002)	-.01	-.01 (-.04, .02)	-.003	-.01 (-.03, .01)	-.001	-.02 (-.05, .01)	-.01
	<i>Non-immigrants</i>							
Females								
Physical Health Conditions	-.43***(-.53, -.33)	-.14	-.09 (-.21, .03)	-.02	-.26***(-.38, -.15)	-.07	-.11**(-.19, -.04)	-.06
ln-CRP	-.02** (-.04, -.005)	-.01	-.002 (-.03, .02)	-.002	-.01 (-.03, .02)	-.002	.01 (-.01, .03)	.001
Males								
Physical Health Conditions	-.32***(-.44, -.22)	-.10	-.07 (-.20, .05)	-.02	-.22***(-.33, -.10)	-.06	-.10*(-.19, -.01)	-.04
ln-CRP	-.04***(-.06, -.02)	-.02	-.01 (-.03, .01)	-.001	-.02**(-.04, -.01)	-.01	-.01 (-.02, .001)	-.001

Note. *b* = unstandardized regression coefficient value; *B* = standardized regression coefficient value; CI= 95% confidence interval; Covariates: age, sex, education, and first language learned; ln-CRP = natural log-transformed C-reactive protein; T₀ = baseline and T₁ = follow-up. **Bold** indicates a significant relationship * *p* < 0.05; ** *p* < .01; *** *p* < .001

Sensitivity Analysis

To assess potential age-related variation in associations, models were stratified by age using multiple approaches: as a continuous variable (ages 45–85), two broad groups (45–64 and 65–85), and four narrower categories (45–54, 55–64, 65–74, and 75–85). Across all stratifications, no consistent or significant differences in the pattern or magnitude of associations were observed.

4.4 Discussion

The current study examined whether physical health conditions were associated with poorer executive function and episodic memory performance at baseline and follow-up in aging immigrant and non-immigrant Canadians while also exploring whether CRP mediated these relationships. Physical health conditions were more likely to be associated with poorer cognitive performance among non-immigrants compared to immigrants. Once stratified by sex, a greater number of physical health conditions remained associated with poorer executive function and episodic memory at baseline than at follow-up among immigrant women and non-immigrant women and men; however, among immigrant men, these associations were less consistent. There was no meaningful mediation by CRP in any model.

This study explicitly examined whether there were differences in cognitive performance between older immigrant and non-immigrant Canadians. Overall, for executive function and episodic memory, non-immigrants had higher median scores compared to immigrants. However, further examination revealed that on specific tests of executive function, immigrants, many of whom were performing in a second or third language, scored lower on tests that were language-dependent, such as word generation (e.g., AFT and COWAT) and higher on tests of inhibition and cognitive flexibility (e.g., Stroop) than non-immigrants (Appendix C, **Figure C1**). On tests of immediate and delayed recall memory, immigrants and non-immigrants performed more similarly (Appendix C, **Figure C2**). These findings align with results of other studies that compared cognitive performance in those who speak English as a first language with those who do not (Boone et al., 2007; Kissner et al., 2012). While the immigrant group in this study was well established, on average residing in Canada for 40 years, multilingualism remains cognitively demanding throughout the lifespan, especially for those who continue to use multiple languages in daily life. Studies suggest that lifelong multilingualism may confer advantages in specific domains such as inhibition and cognitive flexibility (Antoniou, 2019), which may help explain the higher scores observed on Stroop tasks among immigrants. However, disadvantages may also coexist in other executive function skills such as language-dependent tasks, particularly when testing occurs in a non-dominant language.

We also sought to answer whether chronic physical health stress was directly associated with declines in cognitive function. We found that chronic physical health conditions were more likely to predict poorer cognitive function among non-immigrants than among immigrants. Physical health conditions were only associated with baseline cognition among immigrants, suggesting that they did not serve as predictors of longer-term cognition in this group. This pattern may reflect an acute or short-term effect of physical health burden on executive function among immigrants, rather than a sustained impact over time. One possibility is that protective factors, such as cognitive reserve, resilience, or lower baseline comorbidity, buffer against longer-term decline (Stern, 2009; Arenaza-Urquijo et al., 2017; Vang et al., 2017). This observation may also imply that acute stress exerts a more pronounced influence on cognition among immigrants than chronic stress.

Given the limited comparable evidence assessing the direct effect of multiple chronic health conditions on aging immigrant and non-immigrant cognition, it is difficult to compare our results with other studies. However, our results for the non-immigrant population are consistent with those of other studies, indicating a strong association between chronic health conditions and declines in cognition, particularly between cardiovascular and metabolic conditions (Baumgart et al., 2015; Bennett & Sauvé, 2003; Grodstein et al., 2001; Tuligenga et al., 2014), neurologic conditions (Kaffashian et al., 2013; Knopman et al., 2009), inflammatory disorders (Hopkins et al., 2021; Kaffashian et al., 2011), and multimorbidity (Shorey, 2019; Wei et al., 2020). To our knowledge there are no studies assessing the association between physical health and cognition in immigrants. While immigrants perform more poorly than non-immigrants on tests of cognitive function, our findings support prior research indicating that after adjusting for chronic health conditions, most immigrants exhibit lower cognitive dysfunction than non-immigrant Canadians (Kopec et al., 2001).

Upon immigrating, immigrants typically exhibit better health than non-immigrants, which has been attributed to positive selectivity factors such as higher education, better health, self-selection, and immigration policies. This ‘healthy immigrant effect’ (Chen et al., 1996), however, diminishes over time due to the adoption of behaviours and lifestyles more typical of the host country (Commodore-Mensah et al., 2018; Commodore-Mensah et al., 2016; Constant et al., 2018; Vang et al., 2017). Cognitive reserve, the brain’s ability to cope with damage or degeneration through existing cognitive networks (Stern, 2009), is enhanced

by positive selectivity factors, mitigating negative effects of chronic physical health conditions that are seen later in life (Arenaza-Urquijo et al., 2017; Cabeza et al., 2018). Thus, while immigrant and non-immigrant health may be similar, the presumed cognitive reserve that has been built years before may confer protective benefits against cognitive decline in aging immigrants.

Our results also highlight the importance of assessing whether there is a moderating effect of sex on cognition in older adults. When the non-immigrant group was stratified by sex, the association between physical health conditions and follow-up executive function was no longer significant. This may reflect a reduction in statistical power due to smaller subgroup sample sizes, as well as increased model complexity (Kline, 2023; Moshagen and Bader, 2024). The effect remained in the combined model, suggesting that the overall trend persisted but could not be reliably detected within sex-stratified subgroups. While test results did not produce clear sex patterns when we assessed the association between chronic physical health conditions and cognition, interesting trends were observed. The smallest effect between chronic physical health conditions and poorer cognitive function was found for immigrant females, with the greatest effect found in non-immigrant females. Among aging immigrants, many studies have shown a cognitive disadvantage for women compared to men (Garcia et al., 2017; Hill, Angel, Balistreri, et al., 2012; Tang et al., 2019). Where that was true for the mean cognitive scores, our results indicate immigrant females' cognition was generally less impacted by chronic physical health conditions, suggesting a resilience to decline.

Among all the models very few inflammatory mediating effects were found. Although there is increasing evidence that inflammatory mechanisms are associated with cognitive decline and dementia (Grande et al., 2021; Marsland et al., 2015; Yaffe et al., 2003), some studies have shown that CRP is not predictive of cognitive decline (Dik et al., 2005). CRP did not mediate any relationship among non-immigrants; however, it did partially mediate the association between chronic physical health conditions and baseline tests of executive function and episodic memory among immigrants. In a study of the direct association between CRP and cognition, Marsland et al. (2015) similarly found that CRP accounted for up to 5.0% of the variance of cognitive function in their sample of aging community volunteers. They further determined that the inverse relationship between CRP

and cognitive function was found in mid-life preceding the start of clinical impairment (e.g., memory loss), raising the possibility that increased inflammation may be a marker of accelerated cognitive aging. The fact that CRP was a mediator only in immigrant models may also indicate that CRP is more than just a by-product of chronic physical health conditions among immigrants: it may be an indicator of additional stressors (e.g., psychosocial) and contribute to poor cognitive performance in those with few to no chronic health conditions.

4.4.1 Strengths

We were able to tap into a rich source of CLSA biopsychosocial data from a large-scale sample of aging adults. The prospective nature of the CLSA allowed us to study cognitive change within and between immigrant groups over two timepoints, providing a more nuanced and complete analysis. Use of SEM allowed us to handle data with latent variables (unobserved variables), including multiple indicators for each construct as well as observed variables. Alternative approaches, such as summing indicators into one variable rather than creating a latent construct, run the risk of treating unequal indicators as equal and producing erroneous results. By treating indicators, such as cognitive tests for executive function, as unequal, they are weighted accordingly and receive their own measurement error. Using SEM also provided the opportunity to address missing values by using maximum likelihood, a method considered to be robust and efficient compared to other estimation methods (Grande et al., 2021; Marsland et al., 2015; Yaffe et al., 2003).

4.4.2 Limitations

A potential limitation of this study is the discrepancy between model fit and predictive accuracy across cognitive domains. The relationship between physical health conditions and executive function showed poorer model fit, yet high R^2 values indicated strong predictive accuracy. This suggests that while physical health conditions play a significant role in executive function, additional unmeasured factors may contribute to the underlying construct, which could explain the weaker model fit. In contrast, episodic memory demonstrated better model fit but lower R^2 values, indicating that while the included variables adequately captured the construct, physical health conditions may be less central to

memory performance. These differences may reflect the distinct ways in which physical health conditions influence executive function and episodic memory, with executive function potentially being more directly impacted by physical health burden whereas memory may be shaped by a broader range of psychosocial factors. Nonetheless, measurement models for both cognitive domains demonstrated adequate fit indices, supporting construct validity.

Although CLSA employs a stratified random sampling methodology, selection bias may still be present. It's possible that healthier and more cognitively intact older adults opted to participate in the study, potentially skewing the results (O'Connell et al., 2019).

Neurological conditions such as multiple sclerosis and Parkinson's disease, which are risk factors for cognitive decline, may not have been well represented if individuals with these conditions were less likely to enroll. Furthermore, those moderately to severely ill may have been disinclined to participate in the extensive research demands of the Comprehensive cohort, including multiple in-person assessments, follow-ups, and cognitive and biological evaluations.

CRP was only measured at baseline, which may have limited its ability to capture changes in systemic inflammation over time. The relatively healthier nature of the sample likely contributed to lower overall CRP levels, reducing its role as a mediator. If participants were generally healthier at study entry, CRP may not have been a sensitive marker for capturing the physical health effects of stress on cognition. Alternative biomarkers, such as cortisol, may better reflect stress-related mechanisms. However, the study was constrained by the biomarkers available in the CLSA full sample, limiting the ability to examine a broader range of inflammatory or stress-related pathways.

Another limitation of this study is that two cognitive assessments lacked some standard tasks in their scoring. Specifically, the Rey assessment omitted interference and learning trials, and the modified Victoria Stroop assessment did not measure errors; the adaptations are consistent with the streamlined scoring methods used in the CLSA neuropsychology battery (O'Connell et al., 2023). However, although our study's outcomes may not directly align with those of studies conducted outside the CLSA, we provide insights into between-group cognitive outcomes. Further, with cognitive testing conducted in a second language for many participants, particularly immigrants, test performance may reflect both cognitive ability and language proficiency. While immigrant participants in this study

were long settled in Canada, language and cultural differences may still influence performance on certain tasks, particularly those that rely heavily on verbal processing. This raises the possibility that observed cognitive differences between immigrant and non-immigrant groups may be shaped by factors beyond cognitive function alone.

Finally, stress related to physical health conditions may encompass more than physiological burden alone. Individuals managing chronic physical health conditions often experience psychological or emotional stress, which may interact with physical health stress in ways not fully captured in this analysis. Depression, anxiety, and mood disorders were tested in preliminary models but were not significantly associated with cognition, and their inclusion worsened model fit. Because they did not meaningfully contribute to the physical health construct or improve prediction, they were excluded from the final model. This pattern is not unexpected given the relatively healthy nature of the CLSA sample, in which mental health symptoms may have been low overall. Nonetheless, research suggests that chronic physical conditions can contribute to the onset of mental health stress (Scott et al., 2016), underscoring the complex interplay between physical and mental health in aging populations. It is also possible that unmeasured confounding variables, such as early-life adversity (Brown et al. 2022, cumulative stress exposure, or health behaviours not captured in the dataset, may have influenced both physical health and cognitive outcomes, despite adjustment for demographic covariates.

4.4.3 Future Directions

Despite its limitations, this study provides insights into a field with limited data, highlighting disparities in cognitive function between immigrants and non-immigrants amidst health challenges. Understanding these differences is pivotal for advancing research on cognitive function in diverse populations. Future studies should examine the mechanisms underlying these disparities, including the role of structural and social determinants such as healthcare access, socioeconomic status, and acculturation. Longitudinal research incorporating repeated biomarker assessments beyond CRP may offer deeper insights into the physiological pathways linking physical health conditions and cognition. Additionally, research should explore protective factors such as resilience, cognitive reserve, and multilingualism, as these may mitigate poorer cognitive outcomes among immigrants.

Investigating how these factors interact with health-related vulnerabilities may help inform strategies that support cognitive health across aging populations.

Given the heterogeneity within immigrant groups, such as refugees, asylum seekers, and economic migrants, future research should aim for more detailed classification of immigrant status and, where possible, conduct cognitive assessments in participants' native languages. This would improve the validity of cross-cultural comparisons and clarify the influence of language-related factors on cognitive performance.

4.4.4 Conclusion

These findings underscore the complex relationship between physical health stress, cognitive function, and immigrant status. Non-immigrants exhibited greater vulnerability to the cognitive effects of physical health conditions, while immigrants, particularly immigrant men, appeared more resilient. Although the “healthy immigrant effect” is often thought to diminish over time, these results suggest that factors such as resilience, cognitive reserve, and multilingualism may provide enduring cognitive benefits. Public health efforts should increase awareness of the cognitive consequences of chronic conditions and promote strategies to support cognitive health in aging populations, particularly among those at greater risk of poorer cognitive outcomes. These findings offer valuable insights into the intersection of health and cognition in aging Canadian immigrants and highlight the importance of considering both risk and protective factors in public health initiatives.

Chapter 5

Psychosocial Stress

Examining psychosocial stress, inflammation, and cognitive function in aging immigrants and non-immigrants: Findings from the CLSA

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5.1 Background

Understanding psychosocial stress, which stems from the combination of psychological and social factors that individuals perceive as threatening or demanding (Wheaton et al., 2013), can provide key insights into how everyday experience influences the aging process. Indeed, in response to psychosocial stress, cumulative changes throughout the body occur, leading to various health-related problems, including increased risk of disease (Hagström et al., 2018; Rosengren et al., 2004) and accelerated cognitive decline (Johansson et al., 2013; Rodriguez et al., 2023). Moreover, psychosocial stressors, such as social isolation (Evans et al., 2019; Lamar et al., 2021), financial strain (Koster et al., 2005; Wang et al., 2023), and housing concerns (Hamoudi & Dowd, 2014; Wu et al., 2015) have been clearly linked to cognitive impairment in later life. Further, an imbalance between everyday stressors and coping factors can be particularly challenging for older adults as they face increased vulnerability to illness, changes in social support networks, and potential loss of independence, all of which can heighten the emotional and psychological impact of stress.

Prolonged exposure to psychosocial stress elicits a cascade of physiological responses, including the activation of inflammatory pathways (Hänsel et al., 2010; Kiecolt-Glaser et al., 2003). Although inflammation is typically self-limiting, many individuals experiencing chronic psychosocial stress exhibit persistently elevated levels of circulating CRP, which is a common marker of inflammation (Bellingrath et al., 2009; Hintikka et al., 2009). For example, over 40 studies assessing socioeconomic position (e.g., education, income, employment status, social class) and CRP consistently showed that lower socioeconomic status (which is taken to reflect higher psychosocial stress) was linked to elevated CRP levels, often differing by approximately 1–2 mg/L between the highest and lowest socioeconomic status (SES) groups (Johnson et al., 2013; Nazmi & Victora, 2007). Notably, chronic inflammation, including elevated CRP, has been associated with neurodegeneration and cognitive decline, potentially serving as a mechanism through which psychosocial stress influences cognition (Walker et al., 2019).

Not surprisingly, inflammatory pathways are not the only link between psychosocial stress and cognition. For example, prolonged exposure to psychosocial stress can cause detrimental structural changes in brain regions essential for cognitive processes, such as

executive function and memory (Lupien et al., 2009; McEwen & Morrison, 2013). These changes can result in atrophy, hinder the generation of new neurons, and disrupt the brain's ability to adapt, ultimately impairing cognitive function (McEwen, 2007).

Notably, the effects of psychosocial stress on inflammation and cognition may not be uniform across populations (Myers et al., 2003). Individual differences, such as sex, influence stress-induced inflammatory responses which, in turn, depend on the type of psychosocial stressors encountered (Shimano et al., 2014, 2018). While both sexes experience inflammatory changes due to stress, the direction and magnitude of these changes differ, reflecting a complex interplay between sex and specific stressors (Shimano et al., 2014, 2018). For example, men and women exhibit different CRP responses when exposed to stressors such as lack of social support: 2.33 mg/L in men with high support compared to 2.81 mg/L in men with low support, and 2.88 mg/L in women with high support compared to 3.09 mg/L in women with low support (Ford et al., 2006) as well as 1.52 mg/L in those with high SES compared to 2.32 mg/L in those with low SES (Jousilahti et al., 2003). Given the role of inflammation in cognitive aging, these sex-based differences in stress responses may contribute to varying cognitive outcomes over time.

Sex differences in the stress response are particularly relevant for immigrant populations, as migration-related changes often lead to heightened and prolonged psychosocial stress (Garcia et al., 2022; Lupien et al., 2009). While few studies have explored psychosocial stress and inflammation in immigrants, multi-ethnic studies have shown that racial/ethnic minorities often exhibit higher CRP levels compared to non-minorities, even when socioeconomic disadvantages are similar (Nazmi & Victora, 2007), suggesting that additional factors, such as acculturative stress or social isolation, may contribute to inflammatory burden. The experience of adapting to a new culture, language, and social environment can be overwhelming and is often accompanied by a loss of social support networks (Berry & Hou, 2016; Novara et al., 2023; Yoo et al., 2009). Over time, the imprint of these stressors can accumulate, impacting the psychological well-being and cognitive health of older immigrants and increasing inflammation (Goreis et al., 2022; Muñoz et al., 2021), potentially in sex-specific ways.

By shifting the focus to Canada, this study builds on existing research from the U.S., which has primarily examined Latin American immigrants given their large representation in

the U.S. immigrant population (Black et al., 1999; Casanova & Aguila, 2020; Garcia et al., 2017, 2021, 2022; Hill, Angel, & Balistreri, 2012; Muñoz et al., 2021; Rote & Angel, 2021; Sheffield & Peek, 2009). Historically, most immigrants to Canada were of European origin, but since the mid-20th century, immigration has increasingly come from Asian countries, including India, China, and the Philippines (Statistics Canada, 2001). By 2021, India (18.6%), the Philippines (11.4%), China (8.9%), Syria (4.8%), and Nigeria (3.0%) were the top countries of origin for immigrants to Canada (Statistics Canada, 2022a). Studying this population offers insights that extend beyond Canada and may be relevant to other countries with similarly varied immigrant groups.

In this study we examined whether psychosocial stress was linked to poorer cognitive function in aging immigrants and non-immigrants in Canada, and whether a marker of systemic inflammation, CRP, mediated the association between psychosocial stress and cognitive health. We also explored the potential role of sex in these associations.

5.2 Methods

The details of the CLSA's study design and analytic sample, the dependent and mediation variables, and covariates are presented in the Methods section of Chapter 3 and duplicated below, with the exception of Sections 5.2.2.1 and 5.2.3.2.

5.2.1 Study Design and Population

This study analyzed data from the Comprehensive cohort of the CLSA (N = 30,093). The CLSA is a prospective, population-based panel study of non-institutionalized English and French-speaking Canadians aged 45 and 85 years at recruitment (Raina et al., 2019). Participant baseline (2011-2015) and follow-up (2015-2018) data were collected from both in-home interviews and clinical assessments at 11 Data Collection Sites across seven provinces. The immigrant subsample in this study represents a well-established population in Canada at the time of recruitment (mean years in Canada = 40.20 ± 16.28 SD).

At recruitment, CLSA excluded full-time members of the Canadian Armed Forces, First Nations Peoples living on federal reserves or other First Nations settlements, and residents of the three territories and some remote regions. Individuals with cognitive impairment were excluded if they were unable to provide informed consent, as determined by

trained interviewers at recruitment. Additional study details are available elsewhere (Canadian Longitudinal Study on Aging, 2020; Raina et al., 2019).

5.2.2 Measures

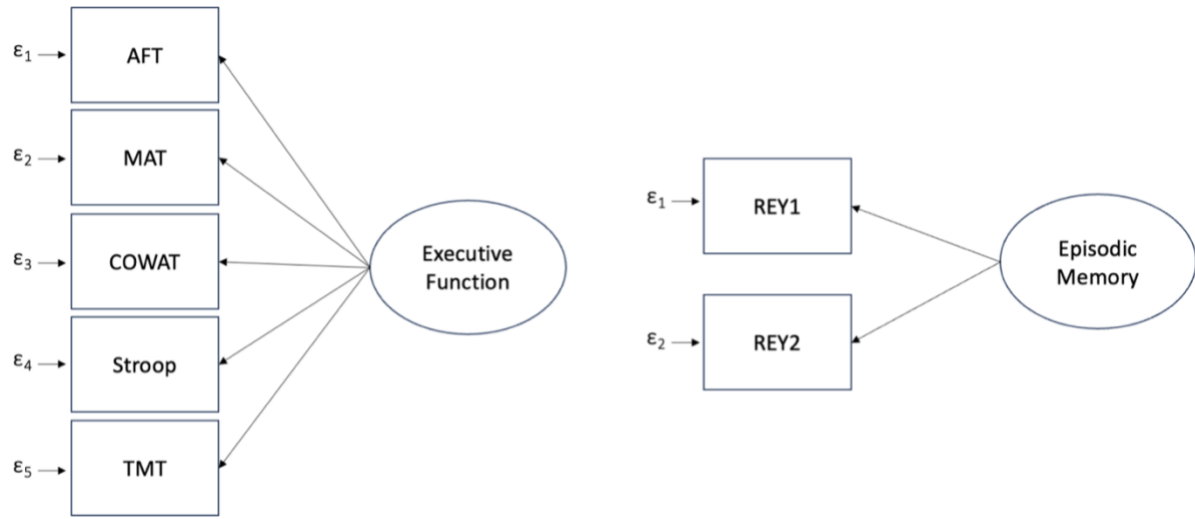
5.2.2.1 Independent Variable

This study assessed psychosocial stress using three indicators: barriers to social activities, financial need, and housing problems. Barriers to social activities were initially assessed with the question, “What prevented you from participating in more social, recreational or group activities?” (multiple response options allowed). While multiple reasons were reported (e.g., transportation, grief, health issues), CFA identified responses indicating “health condition/limitation” as the most relevant indicator, which was subsequently retained in the latent variable. Financial need was assessed by asking whether participants’ income met their needs (response options: very well, adequately, with some difficulty, not very well, or totally inadequately). Housing problems were assessed using two binary indicators—noise and heating issues—both coded as yes or no. These were combined into a single composite variable. Further details on the derivation of the psychosocial stress measure, including its latent variable construction, are provided in Section 5.2.3.2.

5.2.2.2 Dependent Variable

The dependent variables were baseline and follow-up executive function and episodic memory. Our analyses included the Animal Fluency Test (AFT; Goodglass & Kaplan, 1983; Read, 1987), Mental Alternation Test (MAT; Teng, 1995), Controlled Oral Word Association Test (COWAT; Benton & Hamsher, 1978), Victoria Stroop Neurological Screen Test (Stroop; Bayard et al., 2009, 2011; Moroni & Bayard, 2009; Troyer et al., 2006), and Time-based Prospective Memory Test (TMT; Lowenstein & Acevedo, 2001) for executive function (**Figure 7A**), and the Rey Auditory Verbal Learning Test (called REY in CLSA) 1 and 2 (immediate and delayed word recall, respectively) for episodic memory (**Figure 7B**; Rey, 1958). Tests were modified for use in the CLSA (Tuokko et al., 2017). For example, the lenient scoring of AFT, which gives points for each distinct animal, was used. In addition, the errors from the Stroop assessments and interference, and the learning trials from the REY, were not included in implementation of these tests in the CLSA. Scores for each test

were standardized using z-scores separately for English and French assessment to account for language-related differences and analyzed following established CLSA methods (Iacono et al., 2023; Oremus et al., 2019, 2020).



A.

B.

Figure 7. Path diagrams for displaying structural sub-models.

A. Executive function sub-model: Animal Fluency Test (AFT); Mental Alternation Test (MAT), Controlled Oral Word Association Test (COWAT), Victoria Stroop Neurological Screen Test (Stroop), and Time-based Prospective Memory Test (TMT).

B. Episodic memory sub-model: Rey Auditory Verbal Learning Test (REY)1 immediate word recall and REY2 delayed word recall.

5.2.2.3 Mediation Variable

Inflammation was measured using baseline serum CRP levels determined from venous blood samples collected at the Data Collection Sites (Canadian Longitudinal Study on Aging, 2015a, 2015b) and analyzed as a continuous variable.

5.2.2.4 Covariates

To assess immigrant status at baseline, participants were asked the open-ended question, “In what country were you born?”. The variable was then coded into a dichotomous variable: non-immigrant (born in Canada) and immigrant (born outside of Canada).

Baseline covariates included age (continuous), sex (at baseline, participants were asked “Are you male or female?”), education, and first language learned. First language learned was operationalized as the first official language(s) learned and still understood (“English or French; English and French; English and/or French and Other; Other”).

5.2.3 Data Analysis

5.2.3.1 Descriptives

Univariate analyses described means and standard deviations or medians with interquartile ranges for continuous variables, while frequencies and percentages were reported for categorical variables. Bivariate analyses used chi-square tests for categorical variables and Wald tests for group comparisons.

5.2.3.2 Measurement Models

The conceptual model is depicted in **Figure 8**. Standardized tests for executive function and episodic memory served as indicators for their respective latent variables (**Figure 7**). *Psychosocial stress* was modeled as a latent variable, with initial indicators tested for their relevance to the construct. Only those with adequate factor loadings were retained. Initial indicators included multiple jobs (two or more), caregiving, barriers to social activities, financial needs, and housing problems. However, multiple jobs and caregiving were subsequently excluded due to weak correlations with other indicators. The final *psychosocial stress* latent variable included barriers to social activities because of health reasons, financial needs, and housing problems.

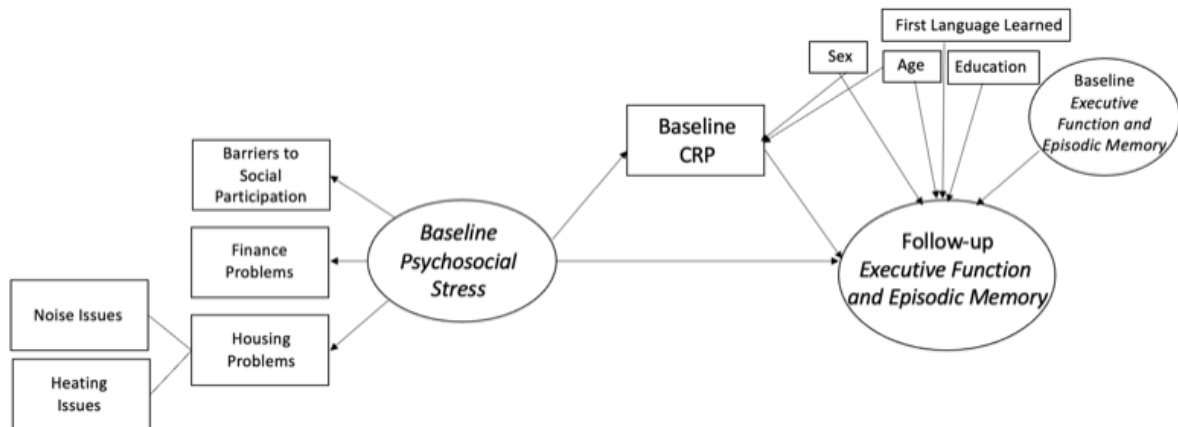


Figure 8. Path model for follow-up analysis illustrating the mediation model tested using a structural equation model.

The model includes latent variables for *psychosocial stress* (comprising barriers to social activities, finance problems, and housing problems which include noise and heat issues), *executive function* and *episodic memory*. Follow-up executive function and episodic memory models were run separately and were adjusted for their baseline counterparts (executive function or episodic memory).

Model fit was deemed acceptable when the Comparative Fit Index (CFI) exceeded 0.90 (Amorim et al., 2010; Bentler, 1990) and the Root Mean Square Error of Approximation (RMSEA) was below 0.08 (Barrett, 2007; Browne & Cudeck, 1993). While the chi-square test (X^2) is commonly used to assess model fit, it can be overly sensitive in larger samples (Alavi et al., 2020; Kline, 2023). Given our large sample size, we interpreted the X^2 results with caution, relying more on other fit indices to assess whether the model was adequate. Path coefficient significance was set at 0.05.

5.2.3.3 Structural Equation Models

SEM was used to explore the associations between the latent variable of *psychosocial stress* and the separate outcomes of *executive function* and *episodic memory*. Multiple group SEM first tested for structural invariance and examined group-specific effects between immigrant and non-immigrants, adjusting for age (continuous), sex, education, and first language(s) learned. While all four covariates were initially included on CRP, only age and sex were retained in the final models, as education and first language(s) learned were not statistically significant and their inclusion worsened model fit. To further investigate potential sex-specific effects, models stratified by both immigrant status and sex were estimated. The models assessing follow-up executive function and episodic memory performance were also adjusted for their respective baseline cognitive scores. CRP was natural log-transformed (ln-CRP) to address a positively skewed distribution and was included in all models as the mediator. For interpretation, a one-unit increase in the ln-CRP is associated with approximately a 100% increase in untransformed CRP.

Missing data affected 23.0% of executive function tests at follow-up and 21.0% of episodic memory tests at follow-up, which is within the range of missingness commonly observed in longitudinal studies of aging and cognition (Hernandez et al., 2024). Four participants did not respond to the immigrant status question and were excluded from the analysis. Full information maximum likelihood (FIML) was used to account for missing data (Enders & Bandalos, 2001) under the assumption that the data are Missing at Random (MAR). FIML does not impute missing values; instead, it estimates model parameters by maximizing the likelihood function for each individual based on the available observed data, thereby reducing bias associated with listwise deletion. Additional technical details regarding model specification, grouping strategy, and parameter constraints across studies are provided in Appendix B. Data were analyzed using Stata SE version 17 (StataCorp, 2021). Data access was approved by the Canadian Longitudinal Study on Aging (#2104054) and ethics approval was received for this project from the University of Waterloo Office of Research Ethics (#43403).

5.3 Results

5.3.1 Descriptive Analyses

At baseline, immigrants (mean age 64.70 ± 10.53 SD) were slightly older on average than non-immigrants (mean age 62.57 ± 10.15 SD; data not shown). A significant association was observed between immigrant status, sex, and stress ($\chi^2[3] = 40.25, p = 0.001$; **Figure 9**). Although the sex differences in prevalence were modest in magnitude (approximately 3.0–4.0%) they were statistically significant. **Figure 9** shows a consistent pattern whereby both immigrant and non-immigrant women (adjusted residuals = 3.96, $p < 0.001$ and 3.65, $p < 0.001$, respectively) were more likely to report at least one psychosocial stressor than immigrant and non-immigrant men. Overall, participants had relatively high levels of education (**Table 5**). On average, immigrant women (48.5%) and men (59.6%) were more likely than non-immigrant women (38.9%) and men (47.7%) to have at least a university degree.

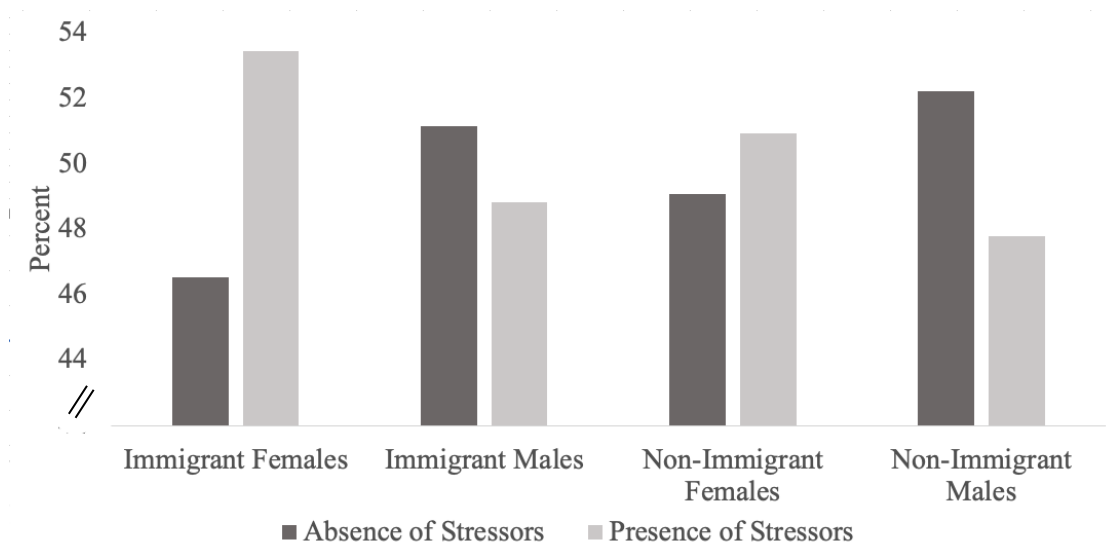


Figure 9. Percentage of absence or presence of stressors by immigrant status and sex. Values represent the proportion of participants reporting the absence or presence of stressor.

Non-immigrants generally showed better cognitive performance than immigrants (**Table 5**). When stratified by sex, both non-immigrant women and men outperformed immigrant women and men on tests of executive function at both baseline and follow-up, with all comparisons showing statistical significance ($\chi^2[3] = 33.38, p < 0.001$ and $\chi^2[3] =$

17.93, $p < 0.001$, respectively). On baseline and follow-up episodic memory tasks, immigrant and non-immigrant women performed better than their male counterparts, with all comparisons also significant ($X^2[3] = 1648.58$, $p < 0.001$ and $X^2[3] = 1580.26$, $p < 0.001$, respectively).

5.3.2 Measurement Models

The measurement model, which assesses the relationships between observed variables and their underlying latent constructs, included *psychosocial stress*, *executive function*, and *episodic memory* as latent variables. All measures significantly loaded onto psychosocial stress ($\beta = 0.24\text{--}0.68$ $p < 0.001$ for all, Appendix D, **Figure D1**), baseline and follow-up executive function ($\beta = 0.08\text{--}0.66$, $p < 0.001$ and $\beta = 0.10\text{--}0.65$, $p < 0.001$ for all, respectively, Appendix D, **Figure D2**) and baseline and follow-up episodic memory ($\beta = 0.70\text{--}0.98$, $p < 0.01$ for all and $\beta = 0.79\text{--}.98$, $p < 0.01$ for all, respectively, Appendix D, **Figure D3**), indicating that convergent validity was achieved. The measurement models demonstrated good fit indices for baseline and follow-up executive function (CFI = 0.91, RMSEA = 0.05, $X^2(60) = 3254.60$, $p < 0.001$ and CFI = 0.91, RMSEA = 0.05, $X^2(58) = 3818.09$, $p < 0.001$, respectively) and baseline and follow-up episodic memory (CFI = 0.98, RMSEA = 0.04, $X^2(60) = 483.92$, $p < 0.001$ and CFI = 0.98, RMSEA = 0.03, $X^2(24) = 499.42$, $p < 0.001$, respectively), which indicated that construct validity was achieved. However, X^2 indicated a lack of fit for all models. The data fit the hypothesized measurement model and all measures that represented the four latent variables were highly reliable. Baseline and follow-up executive function ($R^2 = .69$ and $R^2 = .95$, respectively) and baseline and follow-up episodic memory ($R^2 = .67$ and $R^2 = .79$) showed strong model fit, indicating that a substantial variance in cognitive outcomes was explained in all four main models.

Table 5. Descriptive characteristics by immigrant status and sex (N = 30,093).

Baseline Characteristics	Immigrants (n = 5,449)				Non-Immigrants (n = 24,644)			
	Females (n = 2,544)		Males (n = 2,905)		Females (n = 12,774)		Males (n = 11,870)	
	Md (IQR)	n (%)	Md (IQR)	n (%)	Md (IQR)	n (%)	Md (IQR)	n (%)
Age	65 (16)		65 (18)		61 (16)		62 (16)	
Education								
Up to High school/GED		519 (20.4)		442 (15.2)		3,184 (24.9)		2,595 (21.9)
Trade/College		792 (31.1)		731 (25.2)		4,620 (36.2)		3,615 (30.5)
University degree or higher		1,234 (48.5)		1,727 (59.6)		4,968 (38.9)		5,657 (47.7)
First language was English or French								
Yes		1,544 (60.7)		1,785 (61.5)		12,341 (96.6)		11,453 (96.5)
No		1,000 (39.3)		1,120 (38.6)		430 (3.4)		417 (3.5)
CRP (mg/L)	1.40 (2.30)		1.10 (1.70)		1.40 (2.50)		1.10 (1.90)	
Executive Function (T ₀)	-0.21 (4.73)		-0.14 (4.95)		0.11 (4.67)		0.35 (4.67)	
Executive Function (T ₁)	0.08 (4.58)		-0.16 (4.63)		0.23 (4.65)		0.41 (4.72)	
Episodic Memory (T ₀)	0.36 (2.41)		-0.64 (2.34)		0.46 (2.27)		-0.52 (2.02)	
Episodic Memory (T ₁)	0.27 (2.58)		-0.59 (2.51)		0.31 (2.35)		-0.59 (2.36)	

Note: CRP = C-reactive protein; IQR = interquartile range; M = mean; Md = median; mg/L = milligram per litre; n = subsample size; T₀ = baseline and T₁ = follow-up; Trade/College = Trade/community college/university certificate. Executive function and episodic memory scores are standardized z-scores based on CLSA procedures and are reported as medians and interquartile ranges. These reflect relative performance within the CLSA sample, with wider IQRs expected due to the composite nature of the scores (see Methods, Section 5.2.2.2).

5.3.3 Structural Equation Models: Examining Differences by Immigrant Status

SEMs, building on the measurement model by adding the structural component, make it possible to explore the direct and indirect relationships between latent variables. These SEMs revealed consistent significant negative associations of psychosocial stress with executive function and episodic memory at both baseline and follow-up for immigrants and non-immigrants (**Table 6**). However, the association between psychosocial stress and baseline executive function was significantly stronger for immigrants compared to non-immigrants ($\chi^2[1] = 10.21, p = 0.001$). This significant difference in the association between groups was not observed for executive function at follow-up (**Table 6**). While psychosocial stress was negatively associated with baseline episodic memory in both groups, no significant group difference was observed. For follow-up episodic memory, the difference in this association between immigrants and non-immigrants reached $p = 0.05$ ($\chi^2[1] = 3.77$).

Overall, ln-CRP showed limited mediation in the relationship between psychosocial stress and cognitive function, with effects that were minimal across both immigrant and non-immigrant groups (**Table 6**). Although some statistically significant partial mediation was observed, the small log-transformed coefficients (e.g., $b = -.05$) suggest negligible differences when interpreted on the original scale. Wald tests indicated that there were no statistical differences in mediation between immigrant and non-immigrant groups for baseline executive function or baseline episodic memory.

Table 6. Effect of baseline psychosocial stress on baseline and follow-up executive function and episodic memory by immigrant status, mediated by baseline ln-CRP.

	Models							
	Executive Function (T₀)		Executive Function (T₁)		Episodic Memory (T₀)		Episodic Memory (T₁)	
	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>
Baseline Characteristics	<i>Immigrants</i>							
Psychosocial Stress	-1.95*** (-2.53, -1.38)	-.21	-.51** (-.82, -.19)	-.06	-.76** (-1.21, -.30)	-.06	-.83*** (-1.25, -.42)	-.07
ln-CRP	-.04* (-.07, -.005)	-.004	-.01 (-.04, .01)	-.001	-.03* (-.07, -.004)	-.002	-.02 (-.04, .01)	-.001
	<i>Non-immigrants</i>							
Psychosocial Stress	-.98*** (-1.15, -.80)	-.13	-.38*** (-.50, -.26)	-.05	-.72*** (-.90, -.54)	-.06	-.39*** (-.55, -.23)	-.03
ln-CRP	-.05*** (-.07, -.03)	-.01	-.01* (-.02, -.003)	-.002	-.03** (-.04, -.01)	-.003	-.02* (-.03, -.000)	-.001

Note. *b* = unstandardized regression coefficient value; *B* = standardized regression coefficient value; CI= 95% confidence interval; Covariates: age, sex, education, and first language learned; ln-CRP = natural log-transformed C-reactive protein; T₀ = baseline and T₁ = follow-up. **Bold** indicates a significant relationship * *p* < 0.05; ** *p* < .01; *** *p* < .001

5.3.4 Structural Equation Models: Examining Sex Differences Within Immigrant Status

Further analyses examined sex differences in the associations between psychosocial stress and cognitive function among immigrants and non-immigrants (**Table 7**). Among non-immigrant women and men, the associations between psychosocial stress and cognition were similar across time points. In contrast, among immigrants, distinct patterns emerged.

Immigrant men exhibited the strongest and most persistent effects of psychosocial stress on cognition. The negative association between psychosocial stress and baseline executive function was significantly more pronounced for immigrant men compared to immigrant women ($\chi^2[1] = 5.26, p = 0.02$), non-immigrant women ($\chi^2[1] = 8.31, p = 0.004$), and non-immigrant men ($\chi^2[1] = 10.20, p = 0.001$). The association between psychosocial stress and baseline episodic memory was significantly stronger for immigrant men compared to immigrant women ($\chi^2[1] = 6.66, p = 0.01$). No further significant differences were observed between immigrant women and non-immigrant men or women for either cognitive domain.

In contrast, immigrant women showed variable associations. Psychosocial stress was negatively associated with executive function at baseline, but this association was not present at follow-up. Conversely, while there was no association between psychosocial stress and episodic memory at baseline, a significant negative association emerged at follow-up. As in the model stratified by immigrant status alone, ln-CRP showed negligible mediation between psychosocial stress and cognitive function after stratification by sex (**Table 7**). Among non-immigrant men, ln-CRP significantly partially mediated associations between psychosocial stress and baseline executive function, as well as baseline and follow-up episodic memory. For immigrant and non-immigrant women, partial mediation effects were less consistent. Ln-CRP significantly partially mediated the association between psychosocial stress and baseline episodic memory in immigrant women, while baseline executive function was significantly partially mediated in non-immigrant women. Wald tests indicated no significant differences in mediation by ln-CRP between immigrant women and non-immigrant women or men, suggesting similar partial mediation effects across groups. No mediation by ln-CRP was observed among immigrant men.

Table 7. Effect of baseline psychosocial stress on baseline and follow-up executive function and episodic memory by immigrant status and sex, mediated by baseline ln-CRP.

		Models							
		Executive Function (T ₀)		Executive Function (T ₁)		Episodic Memory (T ₀)		Episodic Memory (T ₁)	
		<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>
Baseline Characteristics		<i>Immigrants</i>							
Females									
Psychosocial Stress		-1.29***(-1.89, -.70)	-.16	-.36 (-.77, .05)	-.05	-.13 (-.69, .42)	-.02	-.74**(-1.27, -.21)	-.07
ln-CRP		-.06 (-.11, .001)	-.01	-.01 (-.05, .02)	-.001	-.07*(-.13, -.002)	-.01	-.02 (-.08, .03)	-.002
Males									
Psychosocial Stress		-2.89***(-4.12, -1.66)	-.27	-.65*(-1.20, -.09)	-.06	-1.28***(-1.96, -.61)	-.12	-.95**(-1.61, -.28)	-.08
ln-CRP		-.02 (-.05, .01)	-.002	-.01 (-.02, .01)	-.001	-.02 (-.04, .01)	-.001	-.01 (-.03, .01)	-.001
		<i>Non-immigrants</i>							
Females									
Psychosocial Stress		-1.05***(-1.28, -.83)	-.15	-.38***(-.53, -.23)	-.05	-.67***(-.89, -.44)	-.08	-.31**(-.52, -.09)	-.05
ln-CRP		-.04**(-.06, -.01)	-.004	-.02 (-.03, .001)	-.001	-.01 (-.04, .01)	-.000	-.002 (-.03, .02)	-.000
Males									
Psychosocial Stress		-.83***(-1.12, -.55)	-.10	-.39***(-.58, -.20)	-.04	-.27*(-.53, -.01)	-.05	-.52***(-.78, -.27)	-.05
ln-CRP		-.07***(-.09, -.04)	-.01	-.01(-.03, .003)	-.001	-.04**(-.06, -.02)	-.004	-.03**(-.05, -.01)	-.003

Note. *b* = unstandardized regression coefficient value; *B* = standardized regression coefficient value; CI= 95% confidence interval; Covariates: age, sex, education, and first language learned; ln-CRP = natural log-transformed C-reactive protein; T₀ = baseline and T₁ = follow-up. **Bold** indicates a significant relationship * *p* < 0.05; ** *p* < .01; *** *p* < .001

Sensitivity Analysis

To assess potential age-related variation in associations, models were stratified by age using multiple approaches: as a continuous variable (ages 45–85), two broad groups (45–64 and 65–85), and four narrower categories (45–54, 55–64, 65–74, and 75–85). Across all stratifications, no consistent or significant differences in the pattern or magnitude of associations were observed.

5.4 Discussion

This study examined cross-sectional and longitudinal associations of psychosocial stress with executive function and episodic memory in aging immigrant and non-immigrant Canadians while exploring whether CRP mediated these relationships. Higher levels of psychosocial stress were associated with poorer executive function and episodic memory among both immigrants and non-immigrants, with the associations being strongest among immigrants. Once stratified by sex, immigrant men showed the most pronounced effects, while non-immigrant women and men also demonstrated significant associations. Although immigrant women reported higher levels of psychosocial stressors, these psychosocial stressors were not consistently associated with poorer executive function and episodic memory. No meaningful mediation by CRP was observed.

Our findings suggest that psychosocial stress negatively affects cognitive functions, with some differences observed between immigrants and non-immigrants. Psychosocial stress has been associated with cognitive decline through chronic activation of the stress response system, leading to structural and functional brain changes (Lupien et al., 2009; Sandi, 2013). In this study, the influence of psychosocial stress on cognition was generally more pronounced among immigrants than non-immigrants. While cumulative exposure to psychosocial stressors, such as financial need and social barriers, could explain poorer cognitive outcomes, this was likely not the only relevant factor. That is, immigrant men reported similar levels of stressors as non-immigrant men, but had poorer cognitive performance, while immigrant women, despite reporting more stressors than immigrant men, performed cognitively better. This suggests that the measured stressors do not fully capture the broader range of factors influencing cognitive outcomes in immigrants. Immigrants may also experience distinct psychosocial factors including acculturation challenges, language barriers, and reduced access to culturally responsive mental health or community resources (de Almeida Vieira Monteiro & Serra, 2011; Lin, 2023). These unmeasured factors may contribute to heightened cognitive vulnerability even when levels of socioeconomic stressors appear similar to those of non-immigrants.

In this study, immigrant men exhibited greater changes in cognitive function than all other groups, diverging from findings in Latin American immigrant populations, where men

often experience more stable cognitive trajectories while women show greater vulnerability to cognitive decline (Garcia et al., 2022; Rote & Angel, 2021). While immigrant women may experience greater cognitive decline due to heightened psychosocial stress exposure (Casanova & Aguila, 2020; Lamar et al., 2021), our results did not follow this pattern. Instead, psychosocial stress was more strongly associated with executive function in immigrant men, suggesting that the effect of stress on cognition may be moderated by sex. These discrepancies likely stem from the focus on Latin American immigrants in the U.S., particularly Mexican immigrants. While this group is diverse, studies on predominantly Mexican-origin populations may not capture the full range of migration experiences, socioeconomic contexts, and cultural factors shaping cognitive aging in other immigrant groups. Importantly, our findings highlight that cognitive trajectories among immigrants in Canada differ from those of Latin American immigrants in the U.S., emphasizing the need to consider migration context in cognitive aging research and the importance of examining sex-based differences in cognitive resilience and vulnerability across diverse migration experiences.

Although immigrant women have historically reported greater psychosocial stress (Debesay et al., 2022; Islam & Gilmour, 2023; Momani et al., 2021), consistent with the higher prevalence of stressors we observed, this did not translate into greater cognitive vulnerability in our study. Despite reporting higher levels of stress, immigrant women did not exhibit the same pattern of change in cognitive function as other groups. Immigrant women may develop adaptive strategies that buffer against chronic stress and strengthen coping mechanisms that support cognitive resilience (Corley & Sabri, 2020; Kuo, 2014). Support networks within their cultural or religious communities may also provide emotional and practical support (Hynie et al., 2011), further buffering against stress-related cognitive decline.

While immigrant women appeared resilient, immigrant men exhibited the most pronounced changes to executive function and episodic memory, which may be linked to structural disadvantages, such as those seen in the labour market. For example, immigrant men often face lower job autonomy and skill underutilization than their non-immigrant counterparts, a disparity that persists over time (Loi et al., 2022; Reitz et al., 2014). While such disadvantages may be less pronounced in a well-established immigrant sample like the

CLSA, cumulative exposure earlier in the migration trajectory, combined with other persistent occupational and social stressors, could still exert lasting effects on cognitive outcomes. These challenges may include barriers such as retraining requirements and language proficiency, which may contribute to “brain waste” (the underutilization of migrants’ skills and qualifications) and limited career mobility (Chiswick & Miller, 2009; Reitz et al., 2014). Although more pronounced for recent immigrants, long-term immigrants may also experience career stagnation due to discrimination, weaker professional networks, and cultural differences (Farashah et al., 2023). Non-immigrant men, in contrast, often benefit from job stability and social capital that buffer work-related stress (Lancee, 2010), advantages that immigrant men may lack. As well, long hours, multiple jobs, or unstable employment may limit opportunities for social engagement and community integration (Ornek et al., 2022), which are important coping resources. Additionally, cultural norms may discourage men from seeking emotional support, a pattern observed more broadly among men than women (Courtenay, 2000) and intensified by migration-related isolation (Lu & Wong, 2013). Without strong social connections, stress may persist and become harder to manage, worsening cognitive vulnerability. How individuals perceive their ability to cope further influences the cognitive effects of psychosocial stress. That is, stress may be less harmful when individuals feel capable of managing it, but overwhelming stress can intensify its impact (Tsai et al., 2019). For immigrant men, occupational stress, limited social networks, and restricted access to support systems may make stress feel inescapable, worsening their cognitive vulnerability.

In this study, CRP did not meaningfully mediate the association between psychosocial stress and either cognitive domain, contrasting with many prior investigations (Johnson et al., 2013; Nazmi & Victora, 2007), but consistent with others. For example, two studies found no effect of psychosocial stress on CRP (Duchaine et al., 2021; Shirom et al., 2008). While Shirom et al. (2008) found no direct connection between psychosocial stressors (measured as job demands, control, and support) and CRP, they identified associations with other pro-inflammatory markers, such as white blood cell count and fibrinogen levels, suggesting that alternative upstream markers may better capture stress-related inflammation. While our study found a limited association between CRP and cognitive function, prior research has linked elevated CRP to grey matter volume atrophy (Janowitz et al., 2020), which may serve as an

early indicator of inflammation's role in neurodegenerative diseases, even in the absence of direct cognitive effects. In other words, CRP may not have mediated stress-related differences in cognitive function in our study, possibly because it does not reflect the more subtle inflammatory mechanisms linked to psychosocial stress. Alternative upstream inflammatory markers or mechanisms, not reflected by CRP levels, may better explain the complex pathways connecting psychosocial stress to cognitive outcomes.

5.4.1 Strengths

This study takes advantage of Canada's distinctive immigration landscape to address the largely overlooked issue of cognitive health among older immigrants. By utilizing the rich biopsychosocial data from the CLSA, including a large and demographically varied sample of aging adults, we examined cognitive change within and between immigrant groups across two timepoints, offering novel insights into these associations. The use of repeated cognitive assessments over three years strengthened our ability to assess how psychosocial stress relates to cognitive function over time, providing a more dynamic picture than cross-sectional studies.

By stratifying analyses by both immigrant status and sex, this study identified cognitive vulnerabilities that were not apparent when examining immigrant status alone, highlighting key disparities that warrant further investigation. The patterns observed suggest that stress-related cognitive changes do not occur uniformly across populations, emphasizing the importance of considering both social and biological factors when examining cognitive aging.

By modelling latent variables—psychosocial stress, executive function, and episodic memory—SEM provided a multidimensional assessment of these constructs, accounting for their measurement properties and reducing error. Unlike methods that sum indicators into a single variable, SEM weighted each indicator appropriately, leading to a more precise estimation of associations. Additionally, the use of maximum likelihood estimation addressed missing data efficiently, enhancing the robustness of our findings (Yaffe et al., 2003).

5.4.2 Limitations

Measuring psychosocial stress is inherently challenging due to its subjective nature and complexity. While the study included relevant stressors, the reliance on self-reported data introduces potential response bias, which may be particularly relevant for immigrants, especially men, who might underreport financial and social difficulties due to stigma (Ayón, 2018; Deding et al., 2008; Tam, 2019). Additional variables, such as caregiving and working multiple jobs, were considered in constructing the psychosocial stress factor, but were excluded due to weak correlations with other indicators. While the psychosocial stress model showed good fit, it did not capture all relevant stressors. Notably, racial and ethnic discrimination, which disproportionately affects immigrant populations, was not measured (Williams & Mohammed, 2009). The absence of such factors highlights the challenges of comprehensively assessing stress and its broader effects. While the models adjusted for multiple sociodemographic, health, and lifestyle factors, unmeasured or imprecisely measured factors, such as early-life socioeconomic conditions, occupational exposures, or the quality of social networks, may still influence the observed associations (Hajat et al., 2021). While this limitation is inherent to observational research (Munkholm et al., 2020), the use of a large, well-characterized sample and multiple covariates likely reduced, but did not eliminate, this source of bias.

The measurement of inflammatory markers also presents a key limitation. Our findings relied solely on baseline CRP, which showed a minimal effect, limiting our ability to assess its role in the association between psychosocial stress and cognitive decline. Although additional inflammatory markers, such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF- α), were available in the CLSA, they were collected only from a subsample and could not be included in the full analysis. This constraint, along with the absence of other relevant markers such as cortisol or IL-1 β , limited our ability to capture a more complete picture of the inflammatory pathways through which stress may affect cognition.

In addition, our measures of the immigrant experience were limited. Although age of arrival was initially considered, first language learned (English, or French versus another language) was found to be more informative, likely reflecting that our immigrant sample had become well established. Further, cognitive assessments administered in a non-first language may have affected accuracy; even with language adjustments, we may not have fully

accounted for some differences in cognitive performance. A more detailed classification of immigrant status, including distinctions among refugees and other groups as well as administering cognitive assessments in native languages, is needed to accurately capture the diverse stressors and health outcomes in this population. Future research should use more detailed immigrant classification and conduct cognitive assessments in participants' native languages to enhance accuracy and relevance.

Lastly, some cognitive assessments in this study were adapted by the CLSA to better suit the study's specific requirements. For example, the Rey assessment omitted interference and learning trials and the modified Victoria Stroop assessment did not measure errors. While these adaptations mean that our outcomes may not directly align with those of studies conducted outside the CLSA, they provide valuable insights into between-group cognitive outcomes.

5.4.3 Future Directions

Future research should continue to explore the complex pathways linking psychosocial stress to cognitive decline in aging populations. Longer follow-up periods may clarify the long-term cognitive effects of psychosocial stress. Examining biomarkers with immune-moderating properties, such as cortisol, could provide insight into biological mechanisms underlying cognitive decline. Additionally, assessing daily psychosocial stressors not captured in the CLSA, such as perceived lack of control, may help identify additional contributors to cognitive decline. Lastly, future studies should also consider how social and community engagement buffer stress-related cognitive health and how protective factors vary by culture, migration experience, and social context. These efforts could inform the development of more effective, targeted interventions supporting cognitive health in both immigrant and non-immigrant aging populations.

5.4.4 Conclusion

This study shows that psychosocial stress affects cognitive function over both the short and long-term, with immigrant men appearing particularly vulnerable. These findings contribute to a growing body of evidence on the intersection of migration, aging, and cognitive health, a topic of increasing global relevance as aging immigrant populations

expand worldwide. While much of the literature on immigrant cognitive function focuses on Latin American populations in the U.S., our study, based on a well-established immigrant sample in Canada, highlights how migration-related stressors may contribute to cognitive aging in a different policy and social context. Even among long-term immigrants, cognitive outcomes were generally poorer than those of non-immigrants, highlighting the need for targeted public health strategies. Efforts should focus on reducing stress exposure, enhancing coping resources, and strengthening informal and community-based social supports.

Chapter 6

Mental Health Stress

Psychological distress, inflammation, and cognitive function in aging immigrant and non-immigrant Canadians: Findings from the CLSA

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6.1 Background

Mental health, including conditions such as anxiety and depression, is a significant public health challenge worldwide. In Canada, one in five individuals live with clinically diagnosed mental health disorders, while many others experience symptoms, such as fatigue and negative affect, that do not meet diagnostic thresholds but which can still significantly affect daily functioning and well-being (Kessler et al., 2002; Smetanin et al., 2011). These subclinical symptoms have been consistently linked to poorer cognitive outcomes in older adults and an increased risk of dementia (Freire et al., 2017; Johansson et al., 2012). Subclinical symptoms of anxiety and depression are often assessed using scales of psychological distress, which measure their frequency and severity in the general population. Psychological distress has been shown to impair cognitive functions such as executive function and episodic memory, which are critical for everyday tasks and overall quality of life (Eysenck et al., 2007; Joorman et al., 2006).

In older adults, psychological distress can impair executive function and episodic memory—key cognitive domains critical for maintaining independence and quality of life. Executive function skills, such as concentrating and adapting to new information, are particularly vulnerable, leading to difficulties in decision-making, multitasking, and cognitive flexibility (Joormann & Gotlib, 2008; Koster et al., 2017). Difficulties in cognitive flexibility may increase the tendency to dwell on negative thoughts, creating a cycle of distress and cognitive impairment (Koster et al., 2017; Lindert et al., 2021). Episodic memory, the ability to recall specific past experiences, may also be affected, leading to subjective memory gaps or distortions (Henry & Crawford, 2005; Lindert et al., 2021). These disruptions may amplify age-related cognitive decline, further reducing overall quality of life (Maillet & Rajah, 2014).

Psychological distress has also been linked to systemic inflammation (Goldsmith et al., 2016), which may mediate the association between distress and cognition. This inflammation, often clinically assessed by measuring elevated CRP levels, has been associated with cognitive decline through various pathways (Howren et al., 2009; Mac Giollabhui et al., 2021). While CRP itself does not cross the blood-brain barrier, it is a marker of elevated levels of pro-inflammatory cytokines, which are proteins that drive inflammation and that can enter the brain. Once these cytokines penetrate the brain, they may cause neuroinflammation, disrupting cognitive functions such as memory and attention (Felger et al., 2020). Chronic inflammation can also weaken the blood-brain barrier, allowing more pro-inflammatory cytokines to enter and exacerbate cognitive

deficits (Yang et al., 2022). Although CRP is a helpful tool to investigate these mechanisms, it remains unclear whether inflammation causes cognitive decline, is a result of it, or is simply a related factor in individuals experiencing psychological distress.

Certain populations, such as aging immigrant Canadians, may be particularly vulnerable to the combined effects of psychological distress and systemic inflammation. Unique stressors, including language barriers, cultural adjustment, discrimination, and social isolation, can exacerbate psychological distress in immigrants (Choy et al., 2021; Pumariega et al., 2005; Yoo et al., 2009). Immigrants are also less likely to access mental health services, often due to systemic barriers and a lack of culturally sensitive care (Straiton et al., 2014; Subedi & Rosenberg, 2014). These disparities may contribute to higher levels of anxiety and depression among immigrants compared to non-immigrants. Furthermore, immigrant populations may have distinct inflammatory profiles influenced by factors such as acculturation stress and health behaviours, which could affect their levels of CRP and other inflammatory markers (Scholaske et al., 2021).

Sex differences influence the experience and expression of psychological distress, though these patterns are often further shaped by gendered social roles and expectations. Women tend to report higher levels of psychological distress, often alongside symptoms of anxiety and depression, while men are more likely to exhibit behavioural symptoms such as substance misuse and antisocial tendencies (Cheon et al., 2020; Eaton et al., 2012; Matud et al., 2015). Both women and men experience common stressors, such as low social support, but may differ in the way they respond to these stressors. Women tend to internalize distress, which may amplify feelings of sadness or worry, while men may be more likely to externalize their stress, exhibiting behaviours like frustration or disengagement (Matud et al., 2015). Among older men, the risk of psychological distress increases as social support diminishes due to bereavement and retirement (Cheon et al., 2020). Understanding these sex-based differences in psychological distress is essential for examining disparities in mental health outcomes and their broader implications.

Although psychological distress is known to impact cognitive health, its role in driving disparities between immigrant and non-immigrant populations remains unclear. This study examined psychological distress to better understand its contribution to cognitive health disparities and assessed whether these associations varied by immigrant status and sex.

Additionally, systemic inflammation, measured by CRP, was explored as a potential mediator to provide insight into the biological mechanisms linking mental health and cognitive function.

6.2 Methods

The details of the CLSA's study design and analytic sample, the dependent and mediation variables, and covariates are presented in the Methods section of Chapter 3 and duplicated below, with the exception of Sections 6.2.1.1 and 6.2.3.2.

6.2.1 Study Design and Population

This study analyzed data from the Comprehensive cohort of the CLSA (N = 30,093). The CLSA is a prospective, population-based panel study of non-institutionalized English and French-speaking Canadians aged 45 and 85 years at recruitment (Raina et al., 2019). Participant baseline (2011-2015) and follow-up (2015-2018) data were collected from both in-home interviews and clinical assessments at 11 Data Collection Sites across seven provinces. The immigrant subsample in this study represents a well-established population in Canada at the time of recruitment (mean years in Canada = 40.20 ± 16.28 SD).

At recruitment, CLSA excluded full-time members of the Canadian Armed Forces, First Nations Peoples living on federal reserves or other First Nations settlements, and residents of the three territories and some remote regions. Individuals with cognitive impairment were excluded if they were unable to provide informed consent, as determined by trained interviewers at recruitment. Additional study details are available elsewhere (Canadian Longitudinal Study on Aging, 2020; Raina et al., 2019).

6.2.2 Measures

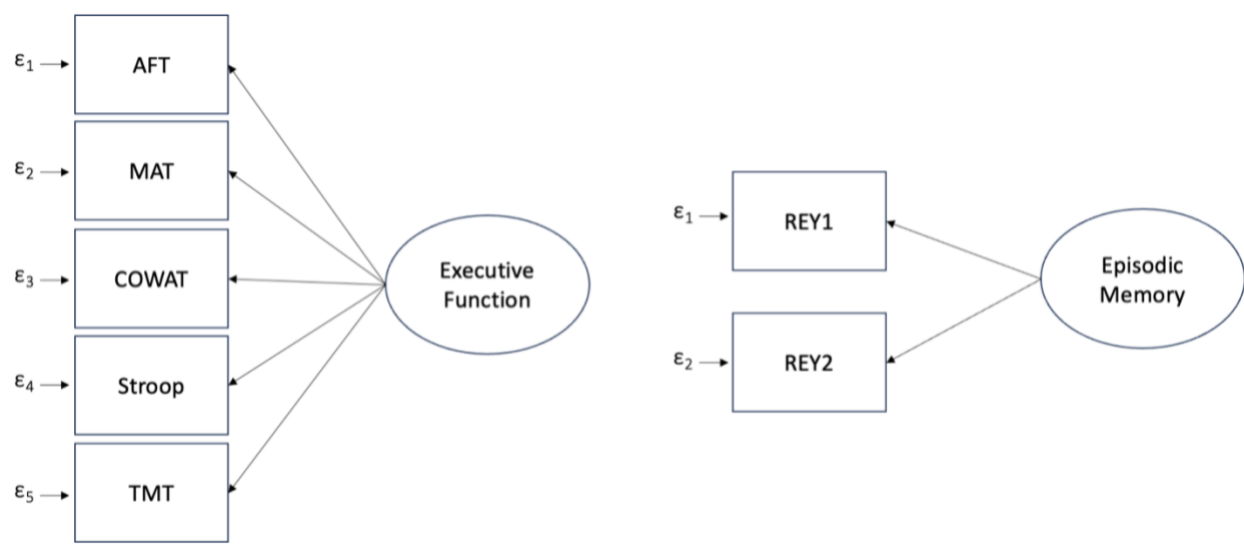
6.2.2.1 Independent Variable

The Kessler Psychological Distress Scale (K10) was used to measure subclinical symptoms of mental health conditions (Kessler et al., 2003). The K10 is a 10-item measure of global non-specific psychological distress based on questions regarding anxiety and depression symptoms and scored from 10-50, with 10 indicating no psychological distress and 50 indicating severe psychological distress (Appendix E, **Figure E1**) The K10 is a validated screening tool for identifying individuals who may be experiencing psychological distress and has been shown to

correlate with the severity of symptom associated with common psychiatric conditions such as of depression and anxiety (Kessler et al., 2003). Given many Canadian adults perceive a stigma associated with mental illness (28 Ipsos, 2019), utilizing the K10, an indicator of general mental health, could help identify a broader range of individuals than those captured by clinical diagnoses alone. The K10 has been shown to be psychometrically valid and appropriate for use in immigrant and general aging populations (Davison et al., 2019; Tong et al., 2020).

6.2.2.2 Dependent Variable

The dependent variables were baseline and follow-up executive function and episodic memory. Our analyses included the Animal Fluency Test (AFT; Goodglass & Kaplan, 1983; Read, 1987), Mental Alternation Test (MAT; Teng, 1995), Controlled Oral Word Association Test (COWAT; Benton & Hamsher, 1978), Victoria Stroop Neurological Screen Test (Stroop; Bayard et al., 2009, 2011; Moroni & Bayard, 2009; Troyer et al., 2006), and Time-based Prospective Memory Test (TMT; Lowenstein & Acevedo, 2001) for executive function (**Figure 10A**), and the Rey Auditory Verbal Learning Test (called REY in CLSA) 1 and 2 (immediate and delayed word recall, respectively) for episodic memory (**Figure 10B**; Rey, 1958). Tests were modified for use in the CLSA (Tuokko et al., 2017). For example, the lenient scoring of AFT, which gives points for each distinct animal, was used. In addition, the errors from the Stroop assessments and interference, and the learning trials from the REY, were not included in implementation of these tests in the CLSA. Scores for each test were standardized using z-scores and calculated separately for each cognitive domain in English and in French. These were then combined following published methods (Iacono et al., 2023; Oremus et al., 2019, 2020).



A.

B.

Figure 10. Path diagrams for displaying structural sub-models.

A. Executive function sub-model: Animal Fluency Test (AFT); Mental Alternation Test (MAT), Controlled Oral Word Association Test (COWAT), Victoria Stroop Neurological Screen Test (Stroop), and Time-based Prospective Memory Test (TMT).

B. Episodic memory sub-model: Rey Auditory Verbal Learning Test (REY)1 immediate word recall and REY2 delayed word recall.

6.2.1.1 Mediation Variable

Inflammation was measured using baseline serum CRP levels determined from venous blood samples collected at the Data Collection Sites (Canadian Longitudinal Study on Aging, 2015a, 2015b) and analyzed as a continuous variable.

6.2.1.2 Covariates

To assess immigrant status at baseline, participants were asked the open-ended question, “In what country were you born?”. The variable was then coded into a dichotomous variable: non-immigrant (born in Canada) and immigrant (born outside of Canada).

Baseline covariates included age (continuous), sex (at baseline, participants were asked “Are you male or female?”), education, and first language learned. First language learned was operationalized as the first official language(s) learned and still understood (“English or French; English and French; English and/or French and Other; Other”).

6.2.3 Data Analysis

6.2.3.1 Descriptives

Univariate analyses described medians with interquartile ranges for continuous variables, while frequencies and percentages were reported for categorical variables. Bivariate analyses used chi-square tests for categorical variables and Wald tests for group comparisons between immigrant and non-immigrant groups. However, formal group comparisons using Wald tests were only conducted when both groups showed statistically significant associations with the cognitive outcomes. Comparisons were not conducted when effects were non-significant or directionally inconsistent, as these did not represent meaningful or interpretable differences.

6.2.3.2 Measurement Models

The conceptual model is depicted in **Figure 11**. Standardized tests for executive function and episodic memory served as indicators for their respective latent variables (**Figure 10**). The K10 10-item measures were factors for the *psychological distress* latent variable.

Model fit was deemed acceptable when the Comparative Fit Index (CFI) exceeded 0.90 (Amorim et al., 2010; Bentler, 1990) and the Root Mean Square Error of Approximation (RMSEA) was below 0.08 (Barrett, 2007; Browne & Cudeck, 1993). While the chi-square test (χ^2) is commonly used to assess model fit, it can be overly sensitive in larger samples (Alavi et al., 2020; Kline, 2023). Given our large sample size, we interpreted the χ^2 results with caution, relying more on other fit indices to assess whether the model was adequate. Path coefficient significance was set at 0.05.

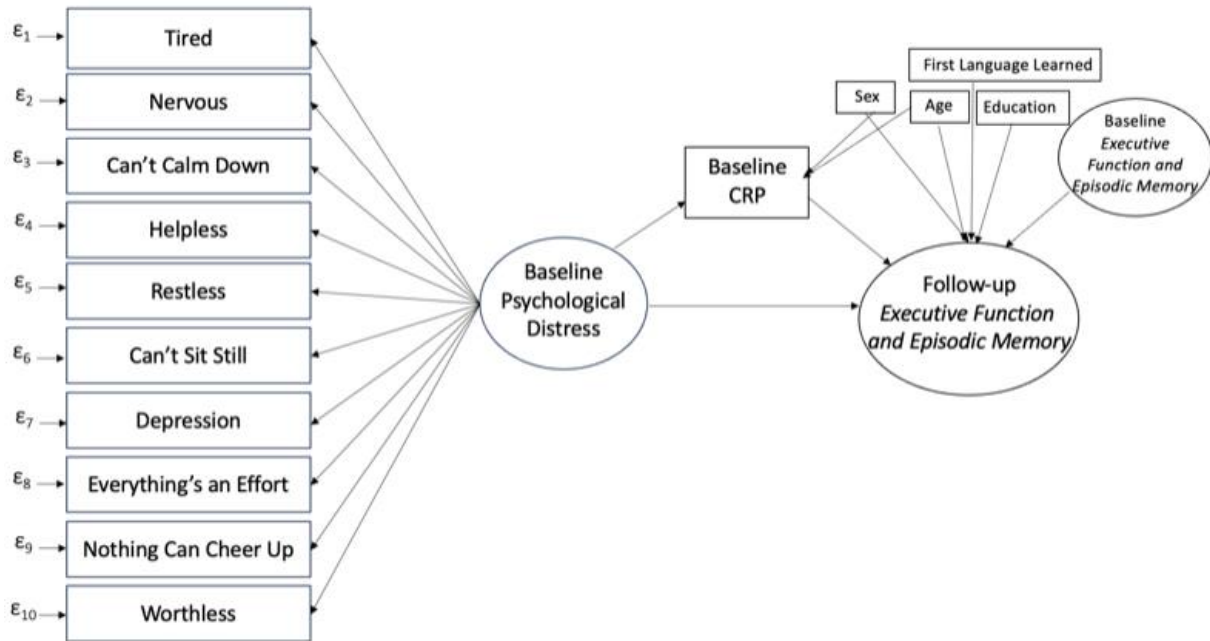


Figure 11. Path model for follow-up analysis illustrating the mediation model tested using a structural equation model.

The model includes latent variables for *psychological distress* (consisting of items from the Kessler Psychological Distress Scale; K10), *executive function* and *episodic memory*. Follow-up executive function and episodic memory models were run separately and were adjusted for their baseline counterparts (executive function or episodic memory).

6.2.3.3 Structural Equation Models

SEM was used to explore the associations between the latent variable of *psychological distress* and the separate outcomes of *executive function* and *episodic memory*. Multiple group SEM first tested for structural invariance and examined group-specific effects between immigrants and non-immigrants, adjusting for age (continuous), sex, education, and first language(s) learned. While all four covariates were initially included on CRP, only age and sex were retained in the final models, as education and first language(s) learned were not statistically significant and their inclusion worsened model fit. To further investigate potential sex-specific

effects, models stratified by both immigrant status and sex were estimated. The models assessing follow-up executive function and episodic memory performance were also adjusted for their respective baseline cognitive scores. CRP was natural log-transformed (ln-CRP) to address a positively skewed distribution and was included in all models as the mediator. For interpretation, a one-unit increase in the ln-CRP is associated with approximately a 100% increase in untransformed CRP.

Missing data affected 23.0% of executive function tests at follow-up and 21.0% of episodic memory tests at follow-up, which is within the range of missingness commonly observed in longitudinal studies of aging and cognition (Hernandez et al., 2024). Four participants did not respond to the immigrant status question and were excluded from the analysis. FIML was used to account for missing data (Enders & Bandalos, 2001) under the assumption that the data are MAR. FIML does not impute missing values; instead, it estimates model parameters by maximizing the likelihood function for each individual based on the available observed data, thereby reducing bias associated with listwise deletion. Additional technical details regarding model specification, grouping strategy, and parameter constraints across studies are provided in Appendix B. Data were analyzed using Stata SE version 17 (StataCorp, 2021). Data access was approved by the Canadian Longitudinal Study on Aging (#2104054) and ethics approval was received for this project from the University of Waterloo Office of Research Ethics (#43403).

6.3 Results

6.3.1 Descriptive Analyses

At baseline, immigrants (median age 65 ± 17 IQR) were slightly older on average than non-immigrants (median age 62 ± 16 IQR; data not shown). In general, immigrants were more educated than non-immigrants (**Table 8**): on average, immigrant women (48.5%) and men (59.6%) were more likely than non-immigrant women (38.9%) and men (47.7%) to have at least a university degree. Immigrants were more likely than non-immigrants to speak a language other than English or French as a first language (**Table 8**). Across immigrant and non-immigrant groups, women were more likely to have higher median levels of CRP than men (**Table 8**).

Non-immigrant men were significantly less likely to experience psychological distress compared to non-immigrant women, immigrant women, and immigrant men ($\chi^2[3] = 232.21, p <$

0.001; **Table 8**). However, median K10 scores were low across all groups and differences were small in absolute terms, suggesting limited practical significance despite statistical significance. Immigrants had poorer median executive function scores compared to non-immigrants (**Table 8**). When stratified by sex, both non-immigrant women and men outperformed immigrant women and men on tests of executive function at both baseline and follow-up, with statistically significant difference observed across the four groups ($\chi^2[3] = 33.38, p < 0.001$ and $\chi^2[3] = 17.93, p < 0.001$, respectively). On baseline and follow-up episodic memory tasks, immigrant and non-immigrant women performed better than their male counterparts, with all comparisons also significant ($\chi^2[3] = 1648.58, p < 0.001$ and $\chi^2[3] = 1580.26, p < 0.001$, respectively).

6.3.2 Measurement Model

The measurement model included psychological distress, executive function, and episodic memory as latent variables. All measures significantly loaded onto psychological distress ($\beta = 0.42\text{--}0.75, p < 0.001$; Appendix E, **Figure E1**), baseline and follow-up executive function ($\beta = 0.08\text{--}0.67, p < 0.001$ and $\beta = 0.10\text{--}0.66, p < 0.001$ for all, respectively; Appendix E, **Figure E2**) and baseline and follow-up episodic memory ($\beta = 0.70\text{--}0.98, p < 0.01$ for all and $\beta = 0.79\text{--}0.98, p < 0.01$ for all, respectively; Appendix E, **Figure E3**), indicating convergent validity was achieved. The measurement models depicted good fit indices for baseline and follow-up executive function (CFI = 0.82, RMSEA = 0.07, $\chi^2(159) = 22298.23, p < 0.001$ and CFI = 0.84, RMSEA = 0.06, $\chi^2(174) = 22834.62, p < 0.001$, respectively) and baseline and follow-up episodic memory (CFI = 0.85, RMSEA = 0.07, $\chi^2(108) = 19196.78, p < 0.001$ and CFI = 0.85, RMSEA = 0.07, $\chi^2(120) = 19476.69, p < 0.001$, respectively), indicating construct validity was achieved. Models of baseline and follow up executive function ($R^2 = .91$ and $R^2 = .98$, respectively) and baseline and follow-up episodic memory ($R^2 = .91$ and $R^2 = .92$, respectively) had high predictive accuracy.

Table 8. Descriptive characteristics by immigrant status and sex (N = 30,093).

Baseline Characteristics	Immigrants (n = 5,449)				Non-Immigrants (n = 24,644)			
	Females (n = 2,544)		Males (n = 2,905)		Females (n = 12,774)		Males (n = 11,870)	
	Md (IQR)	n (%)	Md (IQR)	n (%)	Md (IQR)	n (%)	Md (IQR)	n (%)
Age	65 (16)		65 (18)		61 (16)		62 (16)	
Education								
Up to High school/GED		519 (20.4)		442 (15.2)		3,184 (24.9)		2,595 (21.9)
Trade/College		792 (31.1)		731 (25.2)		4,620 (36.2)		3,615 (30.5)
University degree or higher		1,234 (48.5)		1,727 (59.6)		4,968 (38.9)		5,657 (47.7)
First language was English or French								
Yes		1,544 (60.7)		1,785 (61.5)		12,341 (96.6)		11,453 (96.5)
No		1,000 (39.3)		1,120 (38.6)		430 (3.4)		417 (3.5)
Kessler Psychological Distress	13 (6)		13 (5)		13 (6)		12 (5)	
CRP (mg/L)	1.40 (2.30)		1.10 (1.70)		1.40 (2.50)		1.10 (1.90)	
Executive Function (T ₀)	-0.21 (4.73)		-0.14 (4.95)		0.11 (4.67)		0.35 (4.67)	
Executive Function (T ₁)	0.08 (4.58)		-0.16 (4.63)		0.23 (4.65)		0.41 (4.72)	
Episodic Memory (T ₀)	0.36 (2.41)		-0.64 (2.34)		0.46 (2.27)		-0.52 (2.02)	
Episodic Memory (T ₁)	0.27 (2.58)		-0.59 (2.51)		0.31 (2.35)		-0.59 (2.36)	

Note: CRP = C-reactive protein; IQR = interquartile range; M = mean; Md = median; mg/L = milligrams per litre; n = subsample size; pg/mL = picograms per millilitre; SD = standard deviation; T₀ = baseline and T₁ = follow-up; Trade/College = Trade/community college or university certificate. Executive function and episodic memory scores are standardized z-scores based on CLSA procedures and are reported as medians and interquartile ranges. These reflect relative performance within the CLSA sample, with wider IQRs expected due to the composite nature of the scores (see Methods, Section 6.2.2.2).

6.3.3 Structural Equation Models: Examining Differences by Immigrant Status

SEM was used to examine the association between psychological distress and cognitive function by immigrant status. Higher levels of psychological distress were consistently associated with poorer executive function and episodic memory at both baseline and follow-up for immigrant and non-immigrants (**Table 9**). At baseline, the association with executive function was significantly stronger among immigrants compared to non-immigrants ($\chi^2[1] = 15.05, p = 0.001$), while the strength of associations at follow-up did not significantly differ between groups. No significant group differences were observed for episodic memory at either time point.

The potential mediating role of ln-CRP in the association between psychological distress and cognitive outcomes was also examined. Although partial mediation effects were observed, they were small in magnitude and clinically negligible across all groups (**Table 9**). There was a small partial mediation by ln-CRP between psychological distress and baseline executive function for both immigrants and non-immigrants, with no significant difference between the groups. For follow-up executive function, partial mediation by ln-CRP was observed only among non-immigrants. For episodic memory, ln-CRP partially mediated the association with psychological distress only at baseline for both groups. However, as with executive function, no significant differences were found between immigrants and non-immigrants for these mediation effects.

Table 9. Effect of baseline psychological distress on baseline and follow-up executive function and episodic memory by immigrant status, mediated by baseline ln-CRP.

	Models							
	Executive Function (T₀)		Executive Function (T₁)		Episodic Memory (T₀)		Episodic Memory (T₁)	
	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>
Baseline Characteristics	<i>Immigrants</i>							
Psychological Distress	-.19***(-.24, -.14)	-.07	-.08***(-.12, -.05)	-.04	-.13***(-.18, -.07)	-.07	-.08***(-.11, -.05)	-.05
ln-CRP	-.005*(-.01, -.001)	-.001	-.002(-.004, .001)	-.000	-.004*(-.01, -.000)	-.001	-.002(-.004, .000)	-.000
	<i>Non-immigrants</i>							
Psychological Distress	-.09***(-.12, -.08)	-.04	-.06***(-.07, -.04)	-.03	-.10***(-.12, -.07)	-.05	-.05***(-.07, -.04)	-.04
ln-CRP	-.01***(-.01, -.001)	-.001	-.002**(-.003, -.001)	-.001	-.003***(-.005, -.001)	-.001	-.001**(-.002, -.001)	-.001

Note. *b* = unstandardized regression coefficient value; *B* = standardized regression coefficient value; CI= 95% confidence interval; Covariates: age, sex, education, and first language learned; ln-CRP = natural log-transformed C-reactive protein; T₀ = baseline and T₁ = follow-up. **Bold** indicates a significant relationship * *p* < 0.05; ** *p* < .01; *** *p* < .001

6.3.4 Structural Equation Models: Examining Sex Differences Within Immigrant Status

Further analyses examined sex differences in the associations between psychological distress and cognitive function among immigrants and non-immigrants (**Table 10**). Psychological distress had a consistent negative association with executive function and episodic memory at both baseline and follow-up across all immigrant and non-immigrant groups, with some variation in the strength of these associations by sex and immigrant status. Wald tests were conducted across the four immigrant/sex subgroups, and only significant group differences are reported here. The association between psychological distress and baseline executive function was significantly stronger for immigrant women ($X^2[1] = 6.46, p = 0.01$) and immigrant men ($X^2[1] = 9.35, p < 0.01$) compared to non-immigrant women. Similarly, significant differences were found for immigrant women ($X^2[1] = 5.85, p = 0.02$) and immigrant men ($X^2[1] = 8.60, p < 0.01$) compared to non-immigrant men.

The overall effect of psychological distress on executive function and episodic memory, as mediated by ln-CRP, was limited across most groups, with only a few noteworthy findings emerging (**Table 10**). Partial mediation by ln-CRP was generally small and inconsistent, and no statistically significant group difference was observed. At baseline, ln-CRP partially mediated the association between psychological distress and executive function among immigrant women, non-immigrant women, and non-immigrant men, while only non-immigrant women showed a partial mediation at follow-up. For episodic memory, partial mediation was observed only among non-immigrant men at both time points. Together, these findings suggest that while systemic inflammation may play a minor role in the relationship between psychological distress and cognition, it does not explain the group differences observed.

Sensitivity Analysis

To assess potential age-related variation in associations, models were stratified by age using multiple approaches: as a continuous variable (ages 45–85), two broad groups (45–64 and 65–85), and four narrower categories (45–54, 55–64, 65–74, and 75–85). Across all stratifications, no consistent or significant differences in the pattern or magnitude of associations were observed.

Table 10. Effect of baseline psychological distress on baseline and follow-up executive function and episodic memory by immigrant status and sex, mediated by baseline ln-CRP.

	Models							
	Executive Function (T ₀)		Executive Function (T ₁)		Episodic Memory (T ₀)		Episodic Memory (T ₁)	
	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>	<i>b</i> (95% CI)	<i>B</i>
Baseline Characteristics	<i>Immigrants</i>							
Females								
Psychological Distress	-.17*** (-.24, -.11)	-.13	-.07** (-.12, -.03)	-.05	-.10** (-.17, -.03)	-.06	-.08*** (-.12, -.05)	-.10
ln-CRP	-.01* (-.01, -.001)	-.01	-.002(-.01, .001)	-.001	-.01(-.01, .000)	-.004	-.003(-.01, .001)	-.003
Males								
Psychological Distress	-.21*** (-.28, -.13)	-.13	-.09** (-.15, -.04)	-.06	-.16*** (-.23, -.09)	-.09	-.07*** (-.11, -.03)	-.08
ln-CRP	-.002(-.01, .002)	-.001	-.001(-.003, .001)	-.001	-.002(-.005, .001)	-.001	-.001(-.002, .001)	-.001
	<i>Non-immigrants</i>							
Females								
Psychological Distress	-.10*** (-.12, -.07)	-.07	-.06*** (-.08, -.04)	-.05	-.08*** (-.12, -.05)	-.05	-.07*** (-.11, -.03)	-.05
ln-CRP	-.005*** (-.01, -.002)	-.004	-.002* (-.003, -.000)	-.001	-.002(-.005, .000)	-.001	-.001(-.002, .000)	-.001
Males								
Psychological Distress	-.10*** (-.13, -.06)	-.06	-.05*** (-.08, -.02)	-.03	-.12*** (-.16, -.08)	-.07	-.07*** (-.11, -.03)	-.07
ln-CRP	-.01*** (-.01, -.003)	-.004	-.001(-.002, .000)	-.001	-.004** (-.01, -.001)	-.002	-.002** (-.003, -.001)	-.002

Note. *b* = unstandardized regression coefficient value; *B* = standardized regression coefficient value; CI= 95% confidence interval; Covariates: age, sex, education, and first language learned; ln-CRP = natural log-transformed C-reactive protein; T₀ = baseline and T₁ = follow-up. **Bold** indicates a significant relationship * *p* < 0.05; ** *p* < .01; *** *p* < .001

6.4 Discussion

This study examined cross-sectional and longitudinal associations of psychological distress with executive function and episodic memory in aging immigrant and non-immigrant Canadians while exploring whether CRP mediated these associations. Higher levels of psychological distress were associated with poorer executive function and episodic memory across both immigrant and non-immigrant groups, with the associations being strongest among immigrants. Once stratified by sex, immigrant women and men demonstrated greater vulnerability to the effects of psychological distress on baseline executive function than their non-immigrant counterparts. Immigrant men exhibited the most pronounced acute effects of psychological distress on executive function and episodic memory compared to immigrant women and non-immigrant women and men. There was no meaningful mediation by CRP.

Our findings suggest that psychological distress significantly impacts cognitive function, with slight differences observed between immigrants and non-immigrants. The consistent association across groups points to potential shared mechanisms, particularly the cognitive effects of symptoms commonly associated with psychological distress, including anxiety and depression. Mild anxiety and depression are well documented as contributors to poor cognitive performance, particularly in executive function and episodic memory (Beaudreau & O'Hara, 2009; Geiger et al., 2019; Petkus et al., 2017). Beaudreau & O'Hara (2009) found that the co-occurrence of anxiety and depression was more strongly associated with deficits in executive function and episodic memory than either condition alone. Overlapping symptoms, such as persistent worry and negative thinking, may place a continuous demand on cognitive resources, interfering with tasks of executive function and episodic memory. Additionally, certain symptoms, such as worry and sadness, can serve as bridges linking anxiety and depression, reinforcing each other and keeping both conditions active (Beard et al., 2016). This ongoing interaction likely increases cognitive burden, which may explain why individuals experiencing both anxiety and depression show greater difficulties in cognitive performance than those experiencing only one of the two conditions.

Overall, participants in this study showed greater cognitive vulnerability to psychological distress at baseline compared to follow-up. This pattern suggests that acute mental stress may have a more immediate impact on cognitive resources, particularly in tasks requiring executive function, compared to cognitive effects observed over time. Executive function, which relies on processes such as problem-solving, cognitive flexibility, and decision-making, may be especially sensitive to the heightened mental demands associated with acute stress (Shields et al., 2016). Episodic memory, which depends on retrieving past experiences, may be less immediately affected by acute stress than executive function, but remains susceptible to impairment under prolonged psychological distress (Shields et al., 2017). Although both immigrant and non-immigrant subgroups were affected, the heightened cognitive sensitivity to distress was most evident in immigrant men, who exhibited the most pronounced deficits at baseline in both executive function and episodic memory. Despite median K10 scores being low across all immigrant and sex groups, significant associations with both cognitive domains were observed at each time point. This suggests that even modest variations in psychological distress can affect cognition, consistent with evidence linking subclinical distress to poorer cognitive trajectories (James et al., 2020).

This pattern in immigrant men may reflect the cumulative effect of stressors uniquely experienced by this group. The stronger association between psychological distress and executive function among immigrants compared to non-immigrants may reflect the added burden of sociocultural stressors and cognitive load—the mental effort required to manage information and navigate daily life in an unfamiliar environment. For many immigrants, early-life adversity such as interrupted education, displacement, or exposure to conflict may shape long-term stress reactivity, compounding vulnerability to distress and its cognitive effects in adulthood (Hazer & Gredebäck, 2023; Kirmayer et al., 2011). Immigrants who feel excluded from the dominant culture or pressured to assimilate to the point of losing their own cultural identity are more likely to experience poor mental health (Choy et al., 2021). These challenges likely increase psychological distress, placing even greater strain on cognitive resources.

For immigrant men specifically, stressors such as economic instability, workplace discrimination, and limited career advancement—due to barriers such as credential recognition or employer prejudice—may further elevate distress (Abdikadir et al., 2024;

Anita, 2022; Kirmayer et al., 2011). These challenges are compounded by limited access to mental health services that addresses cultural and systemic factors (Abdikadir et al., 2024; Forray et al., 2024). Cultural expectations to be financial providers can also heighten distress. While lower income is often associated with increased stress due to financial strain, even men with higher income may experience pressure to sustain that role, contributing to psychological distress (Cheon et al., 2020). Immigrant women, on the other hand, may face different but equally taxing challenges, such as caregiving responsibilities and fewer opportunities to engage in restorative activities, which can intensify distress (Matud et al., 2015) and impact cognitive function. Taken together, these systemic and sociocultural stressors help explain why immigrant men and women are particularly vulnerable to the cognitive effects of psychological distress, with immigrant men potentially facing added strain due to employment-related pressures, social expectations, and reduced access to culturally responsive care.

Several factors may explain CRP's limited association with psychological distress and cognition in this study, including the influence of covariates, the non-clinical nature of the psychological symptoms assessed, and the lack of association with long-term cognitive outcomes. Other studies have shown that adjusting for demographic variables, such as age and ethnicity, significantly reduces the association between psychological distress and CRP, particularly in women (Sewpaul et al., 2019). Similarly, associations between CRP and anxiety or stress-related disorders often disappear after accounting for physical health conditions, such as BMI and metabolic syndrome, as well as more severe psychological symptoms, such as depressive disorders (Kennedy & Niedzwiedz, 2022; Puustinen et al., 2011). This pattern may reflect that the psychological distress measured in our study represents a broader range of symptom severity without requiring a clinical diagnosis, whereas stronger associations between CRP and inflammation have been observed in individuals with more severe psychological conditions, such as major depressive disorder (Penninx et al., 2003). Furthermore, one study found that while CRP was linked to baseline memory and verbal fluency, it did not predict cognitive decline over a 12-year follow-up (Arce Rentería et al., 2020). Although our follow-up period was shorter, the absence of an association at follow-up similarly suggests a limited role for CRP in long-term cognitive outcomes. These findings align with ongoing questions regarding the extent to which

inflammation, particularly low-grade inflammation as measured by CRP, contributes to cognitive outcomes. CRP levels observed in this study would typically be considered within the normal to mildly elevated range (e.g., 1–3 mg/L). Even if these levels are interpreted as slightly elevated, they may fall below the threshold required to produce measurable effects on cognitive outcomes, which are shaped by multiple and complex biological and social processes. Additionally, median CRP values and ranges did not differ substantially across groups, further limiting the likelihood of detecting group-specific effects. Taken together, these findings suggest that CRP may play only a limited role in linking psychological distress and cognition, at least within relatively healthy populations and over shorter follow-up periods such as in this study.

6.4.1 Strengths

This study takes advantage of Canada’s distinctive immigration landscape to address the largely overlooked issue of cognitive health among older immigrants. By utilizing the rich biopsychosocial data from the CLSA, including a large, varied sample of aging adults, we examined cognitive change within and between immigrant groups across two timepoints, offering novel insights into these associations. The use of repeated cognitive assessments over three years strengthened our ability to assess how psychosocial distress relates to cognitive function over time, providing a more dynamic picture than cross-sectional studies.

By stratifying analyses by both immigrant status and sex, this study identified cognitive vulnerabilities that were not apparent when examining immigrant status alone, highlighting key disparities that warrant further investigation. The patterns observed suggest that stress-related cognitive changes do not occur uniformly across populations, emphasizing the importance of considering both social and biological factors when examining cognitive aging.

By modelling latent variables—psychological distress, executive function, and episodic memory—SEM provided a multidimensional assessment of these constructs, accounting for their measurement properties and reducing error. Unlike methods that sum indicators into a single variable, SEM weighted each indicator appropriately, leading to a more precise estimation of associations. Additionally, the use of maximum likelihood

estimation addressed missing data efficiently, enhancing the robustness of our findings (Yaffe et al., 2003).

6.4.2 Limitations

Despite these strengths, certain methodological limitations should be noted, particularly in relation to model fit and the interpretation of complex associations. The SEM demonstrated mixed goodness of fit. While RMSEA indicated a good fit, CFI values ranged from 0.82 to 0.85, which are below the conventional threshold of 0.90. However, in the context of complex models with multiple latent variables and numerous observed indicators, some researchers consider CFIs in the mid-0.80s to be within an acceptable range, particularly when other fit indices, such as RMSEA, support model adequacy (Kline, 2023). Nonetheless, the models demonstrated high predictive accuracy, reinforcing the robustness of the finding.

While CRP was assessed as a potential mediator, its limited effect underscores the need for further exploration of alternative biomarkers such as cortisol an upstream marker of the HPA axis, which may better capture the subtle impacts of psychological distress on cognition, particularly in healthy populations (Stalder et al., 2016). The measurement of inflammatory markers also presents a key limitation. Our findings relied solely on baseline CRP, which showed a minimal effect, limiting our ability to assess its role in the association between psychosocial stress and cognitive decline. Although inflammatory markers, such as IL-6 and TNF- α , were available in the CLSA, they were measured only in a subsample and could not be included in the full analysis. This constraint, along with the absence of other relevant markers such as cortisol or IL-1 β , limited our ability to capture a more complete picture of the inflammatory pathways through which stress may affect cognition.

Additionally, reliance on self-reported measures of psychological distress, such as the K10, may introduce bias. This is particularly true in populations where cultural stigma around mental health could affect reporting or where individuals may be less attuned to their emotional states (Mirowsky & Ross, 2003). Although the models adjusted for age, sex, education, and first language learned, residual confounding from unmeasured factors, such as access to mental health care (Reynolds et al., 2022) and early-life adversity (Brown et al., 2022), is possible and reflects a limitation inherent to observational research (Munkholm et

al., 2020). The study focused on a generally healthy population, which limits generalizability to more vulnerable groups, the findings remain valuable for understanding aging among relatively healthy older adults, a demographic that is growing due to increased life expectancy and the rising number of people reaching older age in good health (Tam, 2020; World Health Organization, 2015).

Lastly, our measures of the immigrant experience were limited. Although age of arrival was initially considered in analyses, first language learned (English, or French versus another language) was found to be a more useful indicator of language-related cognitive demands and societal integration. This likely reflects that most immigrants in our sample were well established in Canada, having lived in the country for many years. Additionally, completing cognitive assessments in a non-first language may have affected accuracy; even with language adjustments, some differences in performance may not have been fully captured.

6.4.3 Future Directions

Future research should continue to explore the mechanisms linking psychological distress and cognitive function, especially in aging and immigrant populations. While this study identified sex-based differences, additional work is needed to examine how other intersecting factors, such as socioeconomic status, influence these associations. Longitudinal studies with more frequent follow-up assessments could clarify how psychological distress affects cognition over time. Accounting for early-life adversity or cumulative exposure to stress may also help explain variation in outcomes, as such experiences can shape long-term vulnerability to psychological distress and its cognitive effects. Incorporating a broader range of biomarkers may also improve our understanding of these pathways. Integrating biomarker research into public health strategies could enhance early detection and intervention efforts, particularly for older adults experiencing subclinical distress. As populations age and mental health needs grow, these strategies may support more equitable and proactive approaches to preserving cognitive function. Expanding mental health support beyond clinical diagnoses to address subclinical distress, particularly among older adults, may help reduce cognitive impacts of unaddressed psychological symptoms. Early identification and access to mental health services is especially important for individuals facing barriers related to cost, stigma,

or limited culturally appropriate services. For immigrant populations, more equitable outcomes could be supported through culturally tailored, language-inclusive services, and targeted supports that address migration-related stressors.

Cortisol may offer greater sensitivity than CRP in detecting the cognitive impacts of psychological distress (Chida & Steptoe, 2009). Unlike CRP, which reflects general inflammation and is often confounded by physical health conditions, cortisol is more directly linked to stress physiology and mental health (Stalder et al., 2017). Its responsiveness to both acute and chronic stress suggests it may better capture early cognitive changes, particularly in healthy populations. Research would also benefit from greater sample diversity. Examining these associations across different immigration contexts, such as refugee or economic migrants, and across countries with varying settlement policies could offer broader insights into how psychological distress interacts with sociocultural conditions to affect cognition. Using more detailed classifications of immigrant status, including distinctions among refugees, asylum seekers, and other groups, and administering cognitive assessments in participants' native languages may improve both the accuracy and relevance of findings in immigrant health research.

6.4.4 Conclusion

This study shows that psychological distress is associated with poorer cognitive function in both immigrants and non-immigrants, with immigrant men appearing particularly vulnerable. These findings contribute to a growing body of evidence on the intersection of migration, mental health, and cognitive function, a topic of increasing global relevance as immigrant populations continue to age. While much of the literature on immigrant mental health focuses on clinical diagnoses, this study highlights how preclinical symptoms may also contribute to cognitive outcomes. Even among well-established immigrants, psychological distress showed stronger associations with cognitive function than in non-immigrants, underscoring the importance of considering both psychological and sociocultural factors when examining cognitive aging across populations.

Chapter 7

Conclusion

7.1 Summary of Findings

Understanding how different forms of stress affect cognitive performance in later life is an important but understudied area, particularly within Canadian immigrant populations. This research responds to that gap by using a consistent analytic approach to examine associations between biopsychosocial stressors and cognitive outcomes in older immigrant and non-immigrant adults. Each of the three studies followed the same model structure and differed only in its primary independent variable: physical health, psychosocial, or mental health stress. SEM was used to assess baseline and follow-up executive function and episodic memory, and to test whether CRP mediated these associations.

In the first study, physical health stress was associated with poorer cognitive performance primarily among non-immigrants. Among this group, significant associations were observed across all cognitive domains and timepoints: baseline and follow-up executive function and baseline and follow-up episodic memory. Among immigrants, the pattern

differed by sex. Immigrant women showed negative associations of physical health stress with baseline executive function and follow-up episodic memory, whereas immigrant men only showed a negative association with baseline episodic memory. CRP did not meaningfully mediate these associations.

In the second study, psychosocial stress was significantly associated with poorer cognitive performance in both immigrant and non-immigrant groups, although patterns varied by sex. Immigrant men showed significant negative associations across all cognitive domains—executive function and episodic memory at both baseline and follow-up—and these associations were stronger and more consistent than those observed in immigrant women or in non-immigrant women and men. Immigrant women also demonstrated a significant negative association of psychosocial stress with baseline executive function and follow-up episodic memory, but no significant associations were observed for follow-up executive function or baseline episodic memory. Among non-immigrants, psychosocial stress was significantly associated with poorer cognitive outcomes across all domains and time

points; however, no significant sex differences were observed. Again, CRP did not meaningfully mediate these effects.

In the third study, mental health stress, measured by psychological distress, was significantly associated with poorer executive function and episodic memory among both immigrant and non-immigrant adults. Immigrant women and men showed more pronounced negative associations between psychological distress and baseline executive function compared to non-immigrant women and men. Immigrant men also demonstrated a strong negative association with baseline episodic memory, which was greater than that observed in other groups. While there were statistically significant mediations by CRP, they were clinically negligible.

Across the three studies, the pattern of associations varied by stressor type, subgroup, and timepoint (**Figure 12**). Physical health stress was most strongly associated with poorer cognitive performance among non-immigrants, with consistent associations across both cognitive domains and timepoints. Among immigrants, associations with physical health stress were limited and varied by sex. In contrast, psychosocial stress showed the strongest overall effects on cognition compared to the other stressor types, with immigrant men demonstrating significant associations across all domains and timepoints. Immigrant women showed fewer and more variable associations. Psychological distress was consistently associated with poorer cognitive outcomes in all subgroups, with particularly pronounced associations among immigrant men and women at baseline. Overall, Studies 2 and 3, which examined psychosocial stress and mental health stress (measured by psychological distress), focused on stressors with shared links to mental health burden and therefore show conceptual overlap; however, Study 1 examined physical health stress, measured through chronic physical health conditions, was conceptually distinct (**Figure 13**). While CRP was assessed as a potential mediator, it did not meaningfully explain any of the associations in any of the three studies.

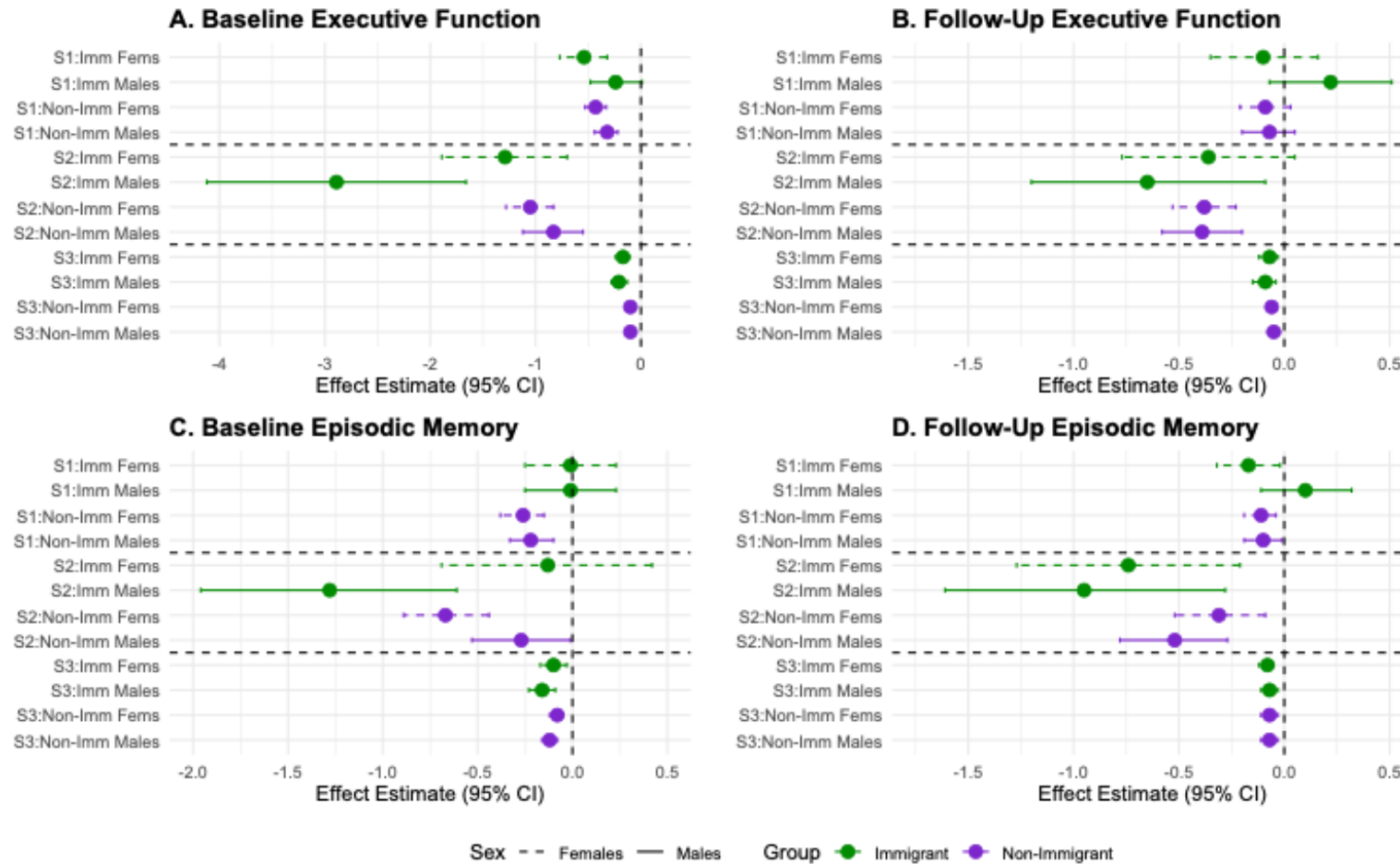


Figure 12. Associations between stress measures and cognitive outcomes across three studies, stratified by immigrant status and sex. Note: S1 = Study 1; imm = immigrants; fems = females; non-imm= non-immigrants. Vertical dashed line indicates the null value (no association). Horizontal dashed lines separate study groups.

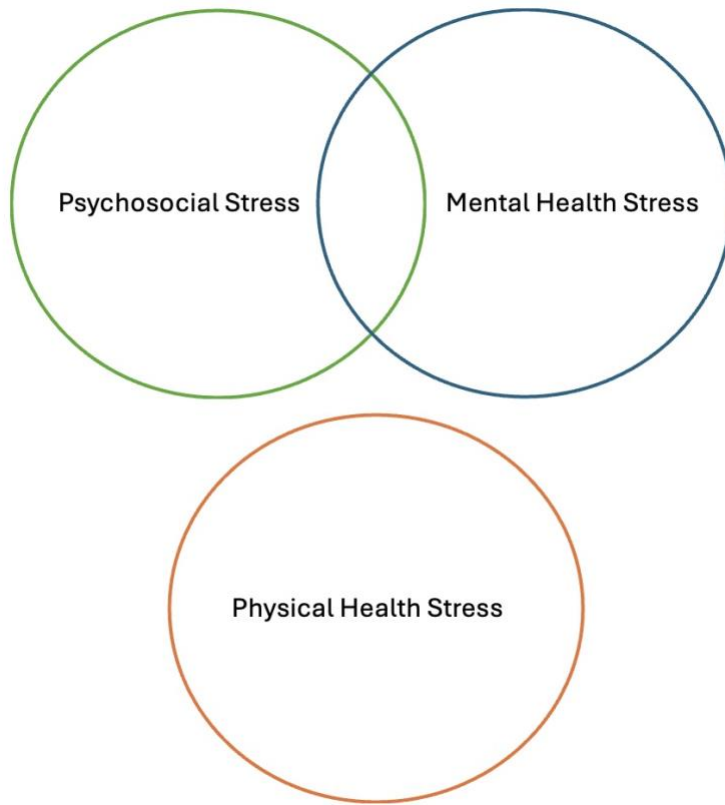


Figure 13. Conceptual overlap across the three studies among immigrants.

7.2 Consistencies and Inconsistencies with Literature

This research was guided by the premise that chronic exposure to stress—whether arising from physical illness, psychosocial adversity, or mental health–related symptoms—can disrupt biological systems involved in stress regulation and contribute to cognitive decline in later life. To investigate this, the three studies examined distinct pathways through which health and social experiences may influence cognitive performance among adults aged 45 and older. These stressors were selected to reflect variation in how closely they are tied to biological or social processes. The analyses assessed whether each stressor was associated with executive function and episodic memory in immigrant and non-immigrant groups, whether these associations varied by sex, and whether the associations were mediated by systemic inflammation. While many of the findings aligned with the study hypotheses and prior research, several diverged from expectations and revealed more complex patterns of association across subgroups than initially anticipated.

The first study focused on physical health stress and its associations with cognitive performance. Chronic physical illness has been consistently linked with cognitive decline in aging populations, particularly when comorbidities are present (Grande et al., 2021; Mayeda et al., 2013; Vassilaki et al., 2015). These effects are thought to occur through several biological pathways, including vascular damage, reduced cerebral blood flow, neurodegenerative changes, and elevated systemic inflammation (Gottesman et al., 2017; Iadecola, Yaffe, Biller, Bratzke, Faraci, Gorelick, Gulati, Kamel, Knopman, Launer, Saczynski, Seshadri, Zeki Al Hazzouri, et al., 2016; Ogoh, 2017). These biological pathways are particularly relevant in populations at risk of experiencing multiple health burdens. Immigrants have historically tended to arrive in better physical health than non-immigrants—a pattern often referred to as the healthy immigrant effect—but these advantages diminish over time (Blair & Schneeberg, 2014; Fennelly, 2008; Matlin et al., 2018; Vang et al., 2017). Given the long-term residency of immigrants in this sample, it was hypothesized that physical health stress and cognitive outcomes would be similar across immigrant and non-immigrant groups. However, the findings showed that non-immigrants experienced stronger associations between physical health stress and cognitive performance, despite similar rates of conditions across groups. This raises the possibility that immigrants may retain some protection against the cognitive effects of physical illness from an initial healthy immigrant effect, even after their overall health burden converges with that of non-immigrants. Although systemic inflammation was expected to mediate these associations (Glaser & Kiecolt-Glaser, 2005; Kyrou & Tsigos, 2009), CRP did not meaningfully explain the observed effects: while some statistically significant mediation was detected, the effects were clinically negligible.

In addition, sex differences in the association between physical health stress and cognition were anticipated based on evidence that immune responses and inflammation-related disease risk often differ by sex. In general, women tend to exhibit stronger immune reactivity, which may offer some protection against infections but can increase susceptibility to inflammatory and autoimmune disorders (Klein & Flanagan, 2016; Márquez et al., 2020). Men, in contrast, are more likely to develop cardiometabolic diseases—such as hypertension, diabetes, and heart disease—that are closely linked to systemic inflammation and associated with cognitive decline (Taylor et al., 2018). Based on these patterns, stronger negative

associations between physical health stress and cognitive outcomes were expected among men. However, the finding that immigrant men showed the weakest associations was not consistent with these expectations and is explored later in this chapter (Section 7.3.3).

The second study examined associations between psychosocial stress and cognitive performance, and results were also not fully consistent with expectations based on prior literature. Psychosocial stress has been shown to interfere with executive function and memory, with financial strain, social isolation, and other chronic stressors contributing to reduced cognitive performance (James et al., 2020; Muñoz et al., 2021; Pevalin et al., 2008). These stressors may also promote immune dysregulation through repeated activation of the body's stress response systems, particularly the HPA axis, resulting in elevated inflammation over time (Glaser & Kiecolt-Glaser, 2005; Hänsel et al., 2010; Ong & Williams, 2019). These expectations were supported by the observed results, with psychosocial stress showing associations with cognitive performance across immigrant and non-immigrant groups. However, although women are generally more likely to report higher levels of stress (Taylor et al., 2018), it is not well established whether this results in greater cognitive vulnerability and few studies have examined how these effects differ by sex within immigrant populations. The finding that immigrant men showed the strongest and most consistent associations across executive function and episodic memory was not anticipated, particularly given that immigrant women were expected to be more affected due to their disproportionate exposure to many of the stressors measured (Alemi & Stempel, 2018; Toselli et al., 2014). CRP was tested as a mediator given its known role in inflammation, but while statistically significant effects were observed, they were clinically negligible (Scholaske et al., 2021; Steffen et al., 2016).

The third study examined associations between mental health stress and cognitive performance. Consistent with prior work, psychological distress was associated with poorer cognition across both immigrants and non-immigrants (Paradise et al., 2011). Among immigrants, cognitive outcomes may be shaped by cumulative exposure to stressors such as social adversity and reduced access to protective resources (Drapeau et al., 2011; Li & Anderson, 2016). However, in the current study, non-immigrant women and men were also affected, and a notable sex difference emerged among immigrants. In several instances, immigrant men demonstrated stronger associations than immigrant women and non-

immigrant women and men. Although immigrant women are more likely to report psychological distress, particularly in the context of social isolation following migration (Ryan et al., 2008), the findings from the current research did not indicate greater cognitive vulnerability in this group. These results raise important questions about how sex and migration-related stress interact to shape cognitive performance, including through differences in exposure to discrimination, healthcare engagement, or perceived control. As in the other two studies, CRP showed statistically significant mediation effects, but these were clinically negligible. This aligns with previous research showing that inflammation, as measured by CRP, does not meaningfully mediate the relationship between stress and cognition (Scholaske et al., 2021).

7.3 Interpretation of Findings

Thus, several findings diverged from initial expectations, and this section explores possible explanations for those patterns. Three key considerations are examined: 1) the more consistent associations observed with cognition at baseline compared to at follow-up, 2) the limited role of systemic inflammation as a mediation pathway, and 3) the greater cognitive vulnerability to mental health-related stress observed among immigrant men.

7.3.1 Acute versus Longer-Term Effects of Stress on Cognition

Across all three studies, associations between stress and cognitive performance were more consistently observed at baseline than at follow-up. This pattern was not anticipated, as it was expected that stress exposures would exert lasting effects on cognition over time. Prior longitudinal research has linked higher levels of perceived and social stress with both prevalent and incident cognitive impairment, supporting the role of chronic stress in longer-term cognitive decline (Lindert et al., 2022; Liu et al., 2025). However, the current findings suggest that stress may have a more immediate impact on cognitive processes such as attention and working memory, functions that map onto executive function and to a lesser extent, episodic memory, which can also be affected in the short term depending on type, intensity, and duration of stress exposure (Lupien et al., 2009; McEwen & Morrison, 2013; Shields et al., 2016, 2017). It is also possible that the three-year interval between baseline and follow-up was too short to detect meaningful change in a relatively healthy sample

(Salthouse, 2019), such that differences fell within the range of normal variation, or that acute stress from the testing context itself may have influenced performance and inflated baseline associations relative to follow-up (Shields et al., 2016, 2017).

In contrast, more sustained or severe stressors than those measured here may be required to detect long-term changes in cognitive functioning, particularly in a sample with relatively high baseline cognitive performance. These findings also suggest that subtle cognitive decline may be more difficult to detect over time using population-based measures in a relatively healthy sample. Indeed, participants in longitudinal aging cohorts tend to be healthier, better educated, and more cognitively intact at baseline than the general population (Raina et al., 2019; Wu et al., 2020). These characteristics may buffer against the long-term effects of chronic stress, making it harder to observe meaningful cognitive decline over shorter periods. It is also possible that fluctuations in stress, coping, or life circumstances between the two waves of data collection attenuated follow-up associations, particularly in a diverse aging sample where life course factors—such as caregiving roles, social support dynamics, or cumulative disadvantage—may interact to shape both stress experiences and cognitive resilience. The absence of strong associations with cognition at follow-up in this study does not rule out chronic stress as a relevant factor in cognitive aging. Rather, the findings highlight the importance of considering the timing and persistence of stress, as well as the measurement approaches used, when evaluating stress-related cognitive outcomes.

7.3.2 Limited Evidence for CRPs as a Mediator of Cognitive Associations

CRP showed limited evidence of mediation between stress and cognitive outcomes in this research. This was unexpected, as prior research has identified inflammation as a plausible biological mechanism linking stress to cognition (Grande et al., 2021; Marsland et al., 2015; Yaffe et al., 2003). CRP, an acute-phase protein, is commonly used as a marker of systemic inflammation and has been associated with both stress exposure and cognitive decline in prior work, making it a reasonable candidate for mediation analysis (Janowitz et al., 2020). A small mediating effect was observed between physical health stress and cognition among immigrants, but these findings were inconsistent across all group or stressor types, and the effects were not clinically meaningful. Prior studies have similarly found that associations between stress and CRP diminish after adjusting for demographic or health-

related factors (Kennedy & Niedzwiedz, 2022; Sewpaul et al., 2019) or are absent altogether depending on the type of stressor measured (Duchaine et al., 2021; Shirom et al., 2008). These mixed findings suggest that CRP may not be the most appropriate marker for capturing the physiological effects of psychosocial stress or psychological distress, particularly in relatively healthy, mid- to late-life populations. Considering this, alternative biomarkers may offer greater sensitivity. For example, biomarkers such as cortisol, while subject to short-term fluctuations including time of day and recent exposure, are more closely linked to the HPA axis and stress reactivity and may be better suited to detecting the effects of mental or psychosocial stress on cognition (Chida & Steptoe, 2009; Stalder et al., 2017).

While CRP showed limited explanatory power in this study, this does not rule out the possibility that other biological or social mechanisms underlie the associations between stress and cognitive performance. Although inflammation is often proposed as a mechanism linking chronic stress to cognitive decline (Johnson et al., 2013; Nazmi & Victora, 2007), the limited mediation by CRP across all three stressor types suggests that other mechanisms may be involved. Behavioural, social, and structural factors, such as long-term economic strain, social isolation, and inconsistent access to care, can place a sustained burden on individuals that is not adequately captured by CRP. These stressors have been shown to influence cognition through chronic activation of stress response systems, limited opportunities for cognitive stimulation, and challenges in maintaining health-promoting behaviours (Evans et al., 2019; Hostinar et al., 2015). A study using the Canadian Community Health Survey similarly found that racial disparities in later-life cognitive functioning were partially explained by differences in income, education, and wealth (Haq & Penning, 2020). Together, these findings are consistent with prior research suggesting that cognitive vulnerability may result from exposure to long-standing social disadvantage. These pathways may involve inflammatory processes not detectable through CRP, such as those involving cytokines like TNF- α or immune cell signalling (Glaser & Kiecolt-Glaser, 2005), or may operate through entirely non-inflammatory mechanisms, including neuroendocrine dysregulation, oxidative stress, and cerebrovascular dysfunction (Prenderville et al., 2015).

7.3.3 An Overlooked Pattern? Mental Health–Related Cognitive Vulnerability in Immigrant Men

Immigrant men consistently showed greater cognitive vulnerability to psychosocial stress and psychological distress than other subgroups, with stronger and more persistent associations across cognitive domains. These forms of stress, while distinct, both involve factors that can undermine mental health, such as barriers to social participation, financial strain, and symptoms of anxiety or depression. In contrast, physical health conditions were less predictive of later cognitive outcomes among immigrant men, particularly at follow-up. This pattern may reflect an early cognitive advantage in our sample consistent with the ‘healthy immigrant effect’, where historically, individuals who migrate were often healthier and more educated than the general population (reflecting both government selection and self-selection into migration). This early advantage may offer a form of cognitive reserve that buffers against the cognitive effects of chronic physical health conditions in later life (Stern, 2009). In this cohort, higher rates of occupational engagement among immigrant men relative to immigrant women may have contributed to differences in the accumulation of cognitive reserve, as sustained participation in cognitively and socially demanding work is known to strengthen cognitive resilience over time. For those benefiting from the healthy immigrant effect, this occupational engagement may have further reinforced early advantages in health and education, supporting cognitive function well into later life.

However, this reserve may not extend to stressors that are psychological or social in nature, especially when they go unrecognized or unsupported. The cognitive effects of psychosocial stress and psychological distress appeared more pronounced and less effectively buffered in immigrant men than other subgroups, suggesting that these stressors may be more salient in shaping later-life cognitive outcomes in this group. In contrast, immigrant women appeared more resilient in certain cognitive domains, despite being expected to show greater vulnerability due to higher exposure to social and economic stressors (Toselli et al., 2014) and more frequent reporting of psychological distress (Ryan et al., 2008). These findings suggest a need to revisit assumptions about which groups are most affected by mental health–related stress and to consider how these stressors are experienced, recognized, and addressed among immigrant men. While social and structural factors likely explain much of the pattern, biological differences, such as the role of sex hormones in shaping stress reactivity and mood

regulation, may also help explain why cognitive vulnerability differs between men and women (Rubinow & Schmidt, 2019).

Immigrant men's greater cognitive vulnerability may reflect not only differences in the type or intensity of stressors experienced but also in how those stressors are recognized and addressed. Immigrant women in Canada often assume caregiving responsibilities within their families, which brings them into more regular contact with the healthcare system (Wray, 2024). These interactions may provide informal opportunities for emotional wellbeing to be noticed or addressed, even without direct help-seeking. In clinical settings, providers are more likely to raise mental health concerns with women, even when these issues are not explicitly disclosed (Bertakis, 2009). In contrast, immigrant men have fewer healthcare encounters and are less likely to report emotional concerns during visits. They are also significantly less likely than immigrant women to access mental health services, even after accounting for symptom severity (Mohammadifirouzeh et al., 2023). Additionally, some immigrant men describe experiences of isolation, disrupted sense of identity, language barriers, and a lack of belonging as ongoing challenges that shape how they manage emotional wellbeing (Islamic Family and Community Services, 2023). While these experiences may not be universal, they underscore the importance of recognizing the diversity of migration histories, cultural backgrounds, and resettlement contexts that shape emotional wellbeing. These challenges are compounded by stigma and cultural expectations—particularly for men—to cope privately, which discourage help-seeking and reduce engagement with available supports (AMSSA, 2019). Collectively, these patterns may limit early recognition of distress in immigrant men, allowing psychological strain to accumulate and ultimately affect cognitive function.

Cultural norms around masculinity, emotional expression, and mental health stigma may further contribute to the cognitive vulnerability observed in immigrant men. In many cultural contexts, men are expected to cope with stress privately and to avoid disclosing emotional difficulties (Mostoller & Mickelson, 2024; Seidler et al., 2016). This can discourage help-seeking and limit conversations about mental wellbeing, both in social settings and within healthcare encounters. Beyond external barriers, some men may also struggle to recognize their symptoms as mental health issues, often describing their emotional strain as “stress” even when their symptoms meet criteria for depression,

suggesting a disconnect between experience and mental health labeling (Cornish et al., 2017). As a result, psychological distress may go unrecognized and unaddressed, allowing symptoms to accumulate over time. While the stressors examined in this research were not necessarily more common among immigrant men, they appeared to have a stronger association with cognitive outcomes in this group. This pattern may not reflect greater symptom severity but rather a lack of recognition and support, suggesting that psychological strain can affect cognition even in the absence of formal diagnosis or intervention. Taken together, these cultural and perceptual barriers underscore the need for greater attention to how mental health challenges are experienced across intersecting lines of gender, migration, and aging, and how these experiences shape cognitive health in later life.

7.4 Strengths and Limitations

This research provides one of the first comparative examinations of how multiple types of stressors, including physical health, psychosocial, and mental health stress, are associated with cognitive performance in aging immigrant and non-immigrant populations. By focusing on older immigrants in Canada, this work addresses a significant gap in cognitive aging research, which has largely centered on non-immigrant populations or on immigrant groups in the United States. The inclusion of immigrants from a range of countries provides broader insight into cognitive aging across cultural and policy contexts, improving relevance and potential generalizability of findings (Brewster et al., 2019; Meyer et al., 2023).

One of the key strengths of this research is its use of the CLSA, a large, population-based dataset that captures a wide range of biopsychosocial factors. The CLSA included measures of cognitive function at two time points, which enabled an examination of changes over time, while also providing a large, diverse sample of immigrants—a feature often missing in aging research. In addition, the methodological comparability across the three studies strengthened the overall design. Each used a consistent SEM approach, varying only in the independent variable of interest, which allowed for clearer comparison of how different stressors are associated with executive function and episodic memory. SEM also enabled the modelling of latent variables, adjustment for measurement error, and handling of missing data through maximum likelihood estimation. Together, these features strengthened

the overall consistency of the study design and improved the validity of comparisons across the three analyses.

This research also has several methodological limitations, including the use of baseline-only CRP data, minor omissions in cognitive test components, and potential selection bias associated with the relatively healthy CLSA sample. These issues may have affected measurement precision or limited generalizability to populations with poorer health or with less access to resources. While relevant methodological limitations were discussed in more detail within each individual study, they are briefly reviewed here. In Study 1, reliance on self-reported physical health conditions and a single inflammatory marker (CRP) may have reduced the precision of physiological stress measurement. In Study 2, psychosocial stress was operationalized using available CLSA variables, which may not fully capture relevant stressors such as occupational exposures or the quality of social networks. Study 3 included fewer covariates, increasing susceptibility to residual confounding from factors such as access to mental health care or life-course experiences. Although these issues were specific to each study, several limitations have broader relevance for interpreting the overall findings.

Although follow-up cognitive assessments were conducted three years after baseline, the exposure–outcome relationships in all three studies were assessed over a relatively short time frame. This limits the ability to capture longer-term trajectories or to make strong causal inferences about the direction of associations. While SEM helped account for missing data and supported the modelling of latent constructs, model fit indices were not always optimal, and some models explained only modest proportions of variance in cognitive outcomes. Still, R^2 values often showed that the predictors accounted for a meaningful proportion of variance in cognitive outcomes, suggesting that the stressors examined, though complex and not always easily measured, were nonetheless relevant for understanding differences in cognitive performance across groups.

One limitation of this study concerns the assumption that data were MAR, which underlies the use of FIML. The plausibility of MAR was supported by analyses showing that missingness in cognitive outcomes was related to observed variables, such as age, sex, immigrant status, and physical health conditions. Under the MAR framework, when variables that predict missingness are included in the model, the bias from missing data is reduced.

Therefore, incorporating these predictors into the SEM helped to address potential bias due to missingness, although the assumption itself cannot be empirically tested. Recent literature highlights that in large-scale, multi-wave longitudinal studies, such as the CLSA, it may be challenging to fully assess or justify MAR, particularly when missingness occurs across multiple variables (outcomes, exposures, covariates) and not all relevant predictors are observed (Mainzer et al. 2024). In this study, the inclusion of relevant predictors and the consistency of results between FIML and a sensitivity analysis utilizing listwise deletion suggests that any resulting bias is likely to be minimal, though the possibility of non-ignorable missingness cannot be fully excluded.

When interpreting cognitive performance differences between immigrants and non-immigrants, it is important to consider that test scores may be influenced by factors beyond cognitive ability. Immigrants scored lower on language-based tasks such as word generation, but these differences may reflect challenges related to language of administration rather than true impairment. Many immigrants in this sample were multilingual and may have been assessed in a second or third language, which can influence performance on verbally mediated tasks (Boone et al., 2007; Kisser et al., 2012). Additionally, cultural familiarity with test content and expectations may shape how individuals engage with cognitive assessments, further complicating cross-cultural comparisons (Antoniou, 2019). Taken together, these factors underscore the importance of interpreting group differences with caution, as cognitive test results may reflect a mix of linguistic, cultural, and contextual influences.

Some stressors relevant to immigrant populations were also not directly captured. While the CLSA provides rich biopsychosocial measures, it lacks indicators of acculturative stress, discrimination, and varying immigration status. These factors may influence access to care and shape cognitive outcomes, particularly in immigrant populations. Additionally, the operationalization of stress relied on available indicators within the dataset and may not fully reflect the complexity or chronicity of individual stress experiences. As with all observational research, residual confounding is also possible, as unmeasured factors such as early-life adversity (Brown et al., 2022), neighbourhood context (Hajat et al., 2021), or access to mental health care (Reynolds et al., 2022) may also influence the observed associations. While this limitation is inherent to observational research (Munkholm et al., 2020), the use of

a large, well-characterized sample and multiple covariates likely reduced, but did not eliminate, this source of bias.

In this research, each study focused on one stress domain—physical health stress in Study 1, psychosocial stress in Study 2, and mental health stress in Study 3—rather than adjusting for the other stress domains. Although these domains are conceptually distinct, they are also empirically correlated, and including them simultaneously could introduce multicollinearity, which can distort parameter estimates and reduce interpretability in SEM (Kyriazos & Poga, 2023). The approach taken in these three studies allowed each stress domain to be evaluated independently in relation to cognitive outcomes, but also means that potential interactive or cumulative effects of multiple stressors were not assessed.

While this study examined differences by sex, gender identity was not captured at baseline in the CLSA and could not be separately assessed. This reflects a broader limitation in population-based research, where sex and gender are often conflated or inconsistently measured (Bauer, 2023), limiting the ability to fully disentangle biological and sociocultural influences on both stress exposures and cognitive outcomes. Although the CLSA began collecting gender identity at follow-up, sex was used at baseline. Sex and gender at follow-up indicated over 99% agreement (Chamberlain et al., 2022), which precluded separate assessment of their independent effects in this study. These measurement gaps are part of a wider set of unmeasured variables in the CLSA that may influence findings. Among long-term immigrants, unmeasured stressors and protective factors may continue to shape cognitive outcomes. Although acculturative stress and discrimination may be less salient in a sample with long-term residence in Canada, sustained exposure to structural inequities or barriers to care may remain. Protective factors such as social cohesion or extended family support, which may help explain some of the resilience observed among immigrant women (Guruge et al., 2024), were also not directly measured.

7.5 Future Directions

This research provides evidence on how physical health, psychosocial, and mental health stressors relate to cognitive outcomes across aging immigrant and non-immigrant populations. By using a consistent analytic framework across three studies, it demonstrated how these stressors may relate to cognition in varying ways across different subgroups. The

findings point to several underexplored areas, including the limited explanatory power of CRP as a marker of inflammation and the need to understand how stress is experienced across immigrant and non-immigrant populations. Future research should also prioritize more nuanced measurement of both sex and gender, allowing for clearer distinction between biological and sociocultural factors in shaping stress exposure and cognitive health. Improved data collection on gender identity, in addition to sex, would enhance the interpretability and relevance of findings, particularly when examining intersecting health inequities. While the majority of Canadians have a gender identity that aligns with their sex (Statistics Canada, 2022b), distinguishing between the two can support more inclusive research practices and ensure that emerging differences in health experiences are better understood and addressed. Although this project focused on cognition, the observed patterns may also inform understanding of how stress affects overall health in later life. Taken together, the results underscore the need for more inclusive research on aging and health equity in migrant populations, which remain underrepresented in population health studies.

Building on these findings will require both expanded measurement of stress and refined methodological approaches. Incorporating biomarkers more closely tied to stress physiology, such as cortisol, may offer greater sensitivity than CRP, particularly when measured over multiple time points. In parallel, the use of mixed-methods designs or community-engaged research could provide a deeper understanding of how stress is experienced in diverse populations, especially where traditional indicators fall short. For example, qualitative work could help identify culturally relevant stressors or coping mechanisms that are not captured by standard survey tools. Additional longitudinal research with more time points or trajectory-based modeling would also help capture how stressors accumulate and shape health outcomes over the life course. Finally, addressing within-group heterogeneity, such as variation by country of origin, immigration pathway (e.g., refugee, economic migrant, etc.) and time since arrival, will be essential to ensure findings reflect diverse experiences that influence aging and cognitive health in immigrant communities. This type of work is essential for informing health strategies that are not only culturally appropriate but also responsive to the diverse realities faced by aging immigrant and non-immigrant communities.

7.6 Implications

This thesis contributes to a more inclusive understanding of cognitive aging by examining how different types of stressors, including physical health, psychosocial, and mental health stress, affect cognitive performance in both immigrant and non-immigrant older adults. The findings highlight that those most affected by stress are not always those most often assumed to be vulnerable. While immigrant women are frequently centred in research on social disadvantage and aging, this work draws attention to the cognitive effects of mental health–related stress among immigrant men, a group whose needs are often overlooked in both research and policy. These results challenge assumptions about uniform vulnerability and suggest that the relationship between stress and cognition must be understood in more specific, population-informed ways.

At the same time, the findings underscore the need for public health strategies that reflect the full range of stress exposures shaping later-life cognitive health. The results point to the consequences of unaddressed psychological distress and psychosocial stress, particularly for individuals who may not access mental health support or regularly interface with the healthcare system. Supporting the cognitive health of older adults will require efforts that are not only culturally appropriate but also attentive to social isolation, stigma, and patterns of care-seeking. Programs such as *Lighten UP!*, which integrate support into primary care and community settings, have shown success in improving well-being among older adults (Friedman et al., 2017, 2019). Similar approaches could be adapted to meet the needs of diverse older adults, particularly immigrant men who may face barriers to formal support but would benefit from accessible mental health and wellness interventions. Given that the effects of psychosocial stress may accumulate over time, these efforts may be more effective if implemented earlier in adulthood and sustained across the life course.

Beyond its contributions to Canadian research, this work also holds relevance for global efforts to promote healthy aging across diverse populations. As countries around the world grapple with aging demographics and increasing migration, understanding how social and health-related stressors shape cognitive outcomes will be essential for building equitable public health responses. By centring the experiences of immigrant subgroups and highlighting variation across sex and stressor type, this research contributes to a more expansive framework for cognitive aging that recognizes diversity in both exposure and

resilience. In doing so, it offers not only insight but also direction for more responsive, evidence-informed approaches to population aging.

7.7 Conclusion

Taken together, the findings across all three studies demonstrate that stress—whether physical health, psychosocial, or mental health—is associated with poorer cognitive performance, although the strength and pattern of associations vary by stressor type, immigration status, and sex. Non-immigrants were more affected by physical health stress, while psychosocial and mental health stressors showed more pronounced associations with cognition among immigrant men. Patterns among immigrant women were more variable across stressor types and outcomes. Across all analyses, CRP showed limited evidence of mediation with effects that, although statistically significant, were small and not clinically meaningful. These findings reinforce the need for cognitive aging research that better reflects population diversity and the complex ways that different forms of stress affect later-life health. Addressing these gaps will require improved measurement of stress, greater attention to social context, and more inclusive approaches to data collection and intervention design. Future research should also consider a broader range of inflammatory markers beyond CRP to better capture the biological pathways linking stress and cognition. By advancing a more differentiated understanding of stress and cognition, this research supports the development of more responsive and equitable strategies to promote healthy aging.

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Appendix A: Supplementary Material for Chapter 3 Methodology

Table A1. Summary of variables used in analyses and measurement source in the CLSA.

Variables	Question(s) Asked
Covariates	
Immigrant Status sdc_fimm_com	Variable created from: “In what country were you born?” If answer is not Canada, then immigrant.
Age age_nmbr_com	So your age is [insert age as calculated based on date of birth]? Is that correct? Yes/No
Sex sex_ask_com	Are you male or female? Yes/No
First Language Learned sdc_dfl1_com	What is the language that you first learned at home in childhood and can still understand?
Education ed_high_com	What is the highest degree, certificate, or diploma you have obtained? 1) No post-secondary degree, certificate, or diploma; 2) Trade certificate or diploma from a vocational school or apprenticeship training; 3) Non-university certificate or diploma from a community college, CEGEP, school of nursing, etc.; 4) University certificate below bachelor’s level; 5) Bachelor’s degree; 6) University degree or certificate above bachelor’s degree; 7) Other (please specify: _____)
CRP bld_hscrp_com	N/A
Chronic Conditions	
Heart Disease ccc_heart_com	Has a doctor ever told you that you have heart disease (including congestive heart failure, or CHF)? Yes/No
PVD ccc_pvd_com	Has a doctor ever told you that you have peripheral vascular disease or poor circulation in your limbs? Yes/No
Ulcer ccc_ulcr_com	Has a doctor ever told you that you have intestinal or stomach ulcers? Yes/No
IBS ccc_ibdibs_com	Has a doctor ever told you that you have a bowel disorder such as Crohn’s Disease, ulcerative colitis, or Irritable Bowel Syndrome? Yes/No
Allergy ccc_allrg_com	Has a doctor ever told you that you have allergies? Yes/No

Diabetes dia_diab_com	Has a doctor ever told you that you have diabetes, borderline diabetes or that your blood sugar is high? Yes/No
CVA ccc_cva_com	Has a doctor ever told you that you have experienced a Stroke or CVA? Yes/No
TIA ccc_tia_com	Has a doctor ever told you that you have experienced a ministroke or TIA (Transient Ischemic Attack)? Yes/No
Hypothyroidism ccc_uthyr_com	Has a doctor ever told you that you have an UNDER-active thyroid gland (sometimes called hypothyroidism or myxedema)? Yes/No
Hyperthyroidism ccc_othyr_com	Has a doctor ever told you that you have an OVER-active thyroid gland (sometimes called hyperthyroidism or Graves' disease)? Yes/No
Hypertension ccc_hbp_com	Has a doctor ever told you that you have high blood pressure or hypertension? Yes/No
Angina ccc_angi_com	Has a doctor ever told you that you have angina (or chest pain due to heart disease)? Yes/No
Heart Attack ccc_ami_com	Has a doctor ever told you that you have had a heart attack or myocardial infarction? Yes/No
Asthma ccc_asthm_com	Has a doctor ever told you that you have asthma? Yes/No
COPD ccc_copd_com	Has a doctor told you that you have/had any of the following: emphysema, chronic bronchitis, chronic obstructive pulmonary disease (COPD), or chronic changes in lungs due to smoking? Yes/No
Osteoarthritis: Hand ccc_oahand_com	Has a doctor ever told you that you have osteoarthritis in one or both hands? Yes/No
Osteoarthritis: Hip ccc_oahip_com	Has a doctor ever told you that you have osteoarthritis in one or both hip? Yes/No
Osteoarthritis: Knee ccc_oaknee_com	Has a doctor ever told you that you have osteoarthritis in the knee? Yes/No
Rheumatoid Arthritis ccc_ra_com	Has a doctor ever told you that you have rheumatoid arthritis? Yes/No
Arthritis ccc_artot_com	Has a doctor ever told you that you have any other type of arthritis? Yes/No
Psychosocial Stress	
Barriers to Social Participation: Health spa_prevac_hc_com	What prevented you from participating in more social, recreational or group activities? 6) Health condition/limitation

Home Problems: Noise env_hmprb_noi_mcq	Current home has problems with noise? Yes/No
Home Problems: Heat env_hmprb_heat_mcq	Current home has problems with heating? Yes/No
Income Meeting Needs wea_incneeds_mcq	Income satisfies basic needs: 1) Very well, 2) Adequately, 3) With some difficulty 4) Not very well, 5) Totally inadequately

K10 Psychological Distress

Tired k10_tired_mcq	About how often during the past 30 days did you feel tired out for no good reason — would you say all of the time, most of the time, some of the time, a little of the time, or none of the time? (repeat the response options for all the questions below)
Nervous k10_nrvs_mcq	During the past 30 days, about how often did you feel nervous?
Nervous, Can't Calm k10_nrvsclmd_mcq	How often did you feel so nervous that nothing could calm you down?
Hopeless k10_hpls_mcq	During the past 30 days, about how often did you feel hopeless?
Restless k10_rstls_mcq	During the past 30 days, about how often did you feel restless or fidgety?
Restless, Can't Sit Still k10_rstlsstl_mcq	How often did you feel so restless that you could not sit still?
Depressed k10_dep_mcq	During the past 30 days, about how often did you feel depressed?
Everything an Effort k10_effrt_mcq	During the past 30 days, about how often did you feel that everything was an effort?
No Cheer-up k10_nochrup_mcq	During the past 30 days, how often did you feel so depressed that nothing could cheer you up?
Worthless k10_wrthlss_mcq	During the past 30 days, about how often did you feel worthless?

Note: CRP (bld_hscrp_com) was measured as a biomarker in CLSA's laboratory assessment and was not captured via questionnaire. (Canadian Longitudinal Study of Aging, 2014; Canadian Longitudinal Study of Aging, 2018c)

Table A2. Summary of cognitive variables used in analyses.

Executive Function	
Baseline	Follow-Up
AFT	AFT
cog_aft_score_2_com	cog_aft_score_2_cofl
MAT	MAT
cog_mat_score_com	cog_mat_score_cofl
COWAT	COWAT:
fas_f_score_com	fas_f_score_cofl
fas_a_score_com	fas_a_score_cofl
fas_s_score_com	fas_s_score_cofl
Stroop	Stroop:
stp_dotime_ss_com	stp_dotime_ss_cofl
stp_coltime_ss_com	stp_coltime_ss_cofl
TMT	TMT
tmt_acc_com	tmt_acc_cofl
Episodic Memory	
Baseline	Follow-Up
REYI	REYI
cog_reyi_score_com	cog_reyi_score_cofl
REY2	REY2
cog_reyii_score_com	cog_reyii_score_cofl

Note: Executive Function: Animal Fluency Test (AFT); Mental Alternation Test (MAT), Controlled Oral Word Association Test (COWAT), Victoria Stroop Neurological Screen Test (Stroop), and Time-based Prospective Memory Test (TMT). Episodic memory: Rey Auditory Verbal Learning Test immediate word recall (REY1) and delayed word recall (REY2). (Canadian Longitudinal Study of Aging, 2014; Canadian Longitudinal Study of Aging, 2018a; Canadian Longitudinal Study of Aging, 2018b; Canadian Longitudinal Study of Aging, 2018c)

Appendix B: SEM Specification Across All Studies

SEMs were estimated using a consistent multi-group framework to examine associations between stress, systemic inflammation, and cognitive performance across six subgroups: immigrants, non-immigrants, immigrant women, immigrant men, non-immigrant women, and non-immigrant men. Models were estimated in Stata using FIML, under the assumption that data were MAR. In each study, the primary stressor variable varied: physical health stress (Study 1), psychosocial stress (Study 2), and mental health stress (Study 3). These were modeled as latent constructs using observed indicators appropriate to each conceptualization. Systemic inflammation was modeled using log-transformed baseline CRP, and covariates included age, sex, education, and first language learned.

Two latent cognitive outcomes (executive function and episodic memory) were modeled, with each assessed at both baseline and follow-up. Executive function was defined using five tests: AFT, MAT, COWAT, Stroop, and TMT. Episodic memory was defined using two indicators: REY1 and REY2. For both constructs, baseline and follow-up latent variables were estimated separately, with one indicator loading fixed to 1 for scaling. Structural paths from the stressor, baseline CRP, and covariates to the cognitive outcomes were estimated at baseline, with follow-up cognition modelled as a downstream outcome. Baseline CRP was included as a potential mediator between the stressor and baseline cognitive function.

All models were estimated using the `group()` option in Stata to compare subgroups defined by immigrant status and by immigrant status and sex. No measurement invariance constraints were imposed beyond the scaling of one indicator per latent variable; factor loadings, intercepts, variances, and structural paths were otherwise estimated freely across groups. Covariances among covariates (age, sex, education) were included, and residual covariances among the physical health indicators were specified at both baseline and follow-up to account for shared clinical variance where applicable.

Appendix C: Supplementary Material for Study 1 Physical Health Stress

Table C1. Chronic health conditions included in the construction of latent variables physical health conditions.

Variables included in initial models	
Variables	Chronic Health conditions
<i>Physical Health conditions</i>	
<i>Inflammatory</i>	Bowel disorders (e.g., ulcerative colitis), asthma, chronic obstructive pulmonary disease (COPD), ulcers, rheumatoid arthritis, osteoarthritis, and allergies
<i>Cardiometabolic</i>	Heart disease and congestive heart failure, angina, myocardial infarct, diabetes, and hypertension
<i>Vascular</i>	Peripheral vascular disease, transient ischemic attack (TIA), and stroke
<i>Endocrine</i>	Hypothyroidism, hyperthyroidism, osteoporosis
<i>Neurological</i>	Memory impairment, dementia, multiple sclerosis, Parkinson's disease, epilepsy, and migraines
Other Variables	Back pain, kidney disease, and cancers
Variables included in final models	
Variables	Chronic Health conditions
<i>Physical Health conditions</i>	
<i>Inflammatory</i>	Bowel disorders (e.g., ulcerative colitis), asthma, chronic obstructive pulmonary disease (COPD), ulcers, rheumatoid arthritis, osteoarthritis, and allergies
<i>Cardiometabolic</i>	Heart disease and congestive heart failure, angina, myocardial infarct, diabetes, and hypertension
<i>Vascular</i>	Peripheral vascular disease, transient ischemic attack (TIA), and stroke

Note: *Italicized* variables are latent.

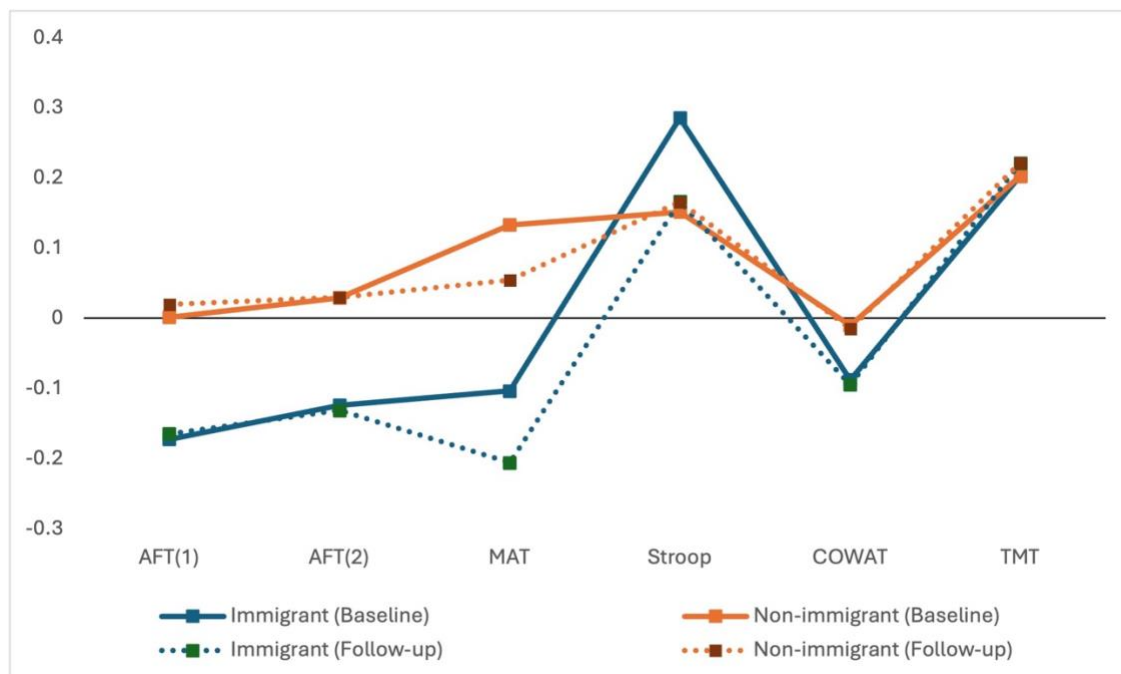


Figure C1. Median baseline and follow-up executive function tasks by immigrant status. The Animal Fluency Tests (AFT1 and AFT2), Mental Alternation Test (MAT), Controlled Oral Word Association Test (COWAT), Victoria Stroop Neurological Screen Test (Stroop), and Time-based Prospective Memory Test (TMT).

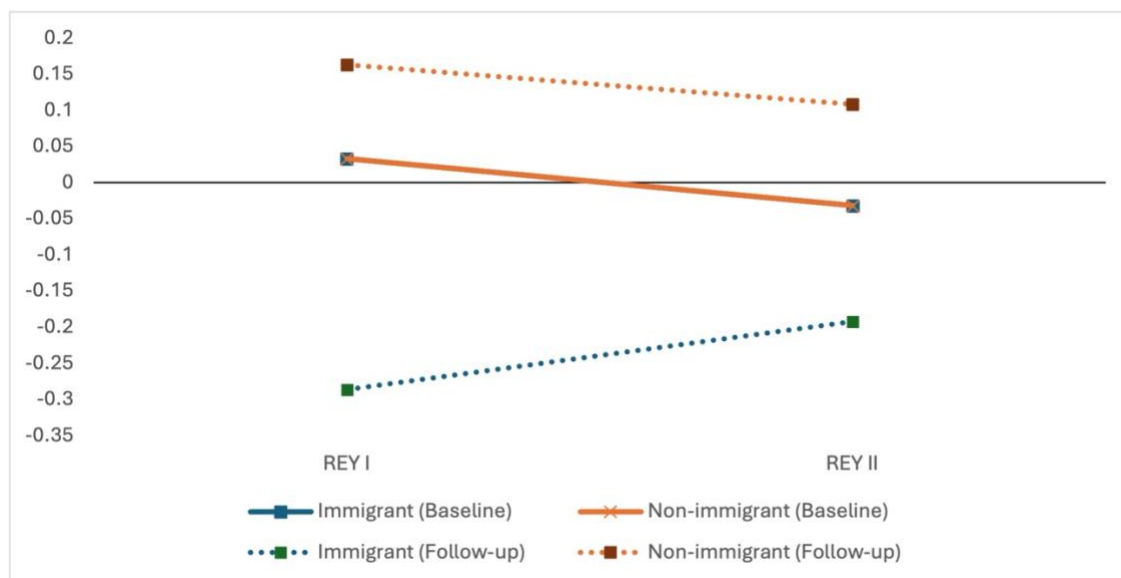


Figure C2. Median baseline and follow-up episodic memory tasks by immigrant status. The Rey Auditory Verbal Learning Test: immediate word recall (REY I) and delayed word recall (REY II). *Note:* values were identical for immigrant and non-immigrant median baseline REY I and REY II scores.

Section C1. First Language and Age at Arrival as Predictors of Cognition

Given that age but not exact birth dates are released by the CLSA, age at arrival to Canada was determined by subtracting approximate year of birth (subtracting age from first year of recruitment [2011]) from year of arrival in Canada. Results from our study suggest that the first language(s) learned were stronger predictors of cognitive performance among immigrants than the age at arrival to Canada. Surprisingly, age at arrival in our study populations proved to be a poor indicator, contrary to findings in other studies (Boone et al., 2007; Garcia et al., 2017; Meyer et al., 2023; Razani et al., 2007). These studies indicate a positive association between immigrant cognitive performance, measured in English, and the number of years residing in the United States. One potential explanation for this disparity may lie in the differing immigration policies of Canada and the United States. Canada's points-based system favours younger, highly educated individuals proficient in English or French (Bhuyan et al., 2017), while the United States prioritizes family reunification and employment-based preferences, such as having a valid job offer (Gubernskaya & Dreby, 2017). In the United States, where language proficiency isn't a primary concern in immigration policy, the timing of arrival becomes critical for language acquisition. In contrast, immigrants to Canada often arrive already proficient in English or French, diminishing the significance of the age at arrival.

Table C2. Association of first language learned and age at arrival in Canada with cognition (executive function and episodic memory) among immigrants.

Baseline Characteristics	Executive Function (T ₀)	Executive Function (T ₁)	Episodic Memory (T ₀)	Episodic Memory (T ₁)
	<i>b</i> (95% CI)			
First Language Learned (Ref: English/French)	-.58*** (-.63, -.53)	-.19*** (-.24, -.14)	-.30*** (-.35, -.25)	-.09*** (-.14, -.06)
Age of Arrival in Canada	-.01*** (-.01, -.01)	-.01*** (-.01, -.004)	-.003** (-.004, -.001)	.001 (-.001, .002)

Note. *b* = unstandardized regression coefficient value; CI= 95% confidence interval; models also included physical health conditions, C-reactive protein, and covariates (age, sex, and education); T₀ = baseline and T₁ = follow-up.

* *p* < 0.05; ** *p* < .01; *** *p* < .001

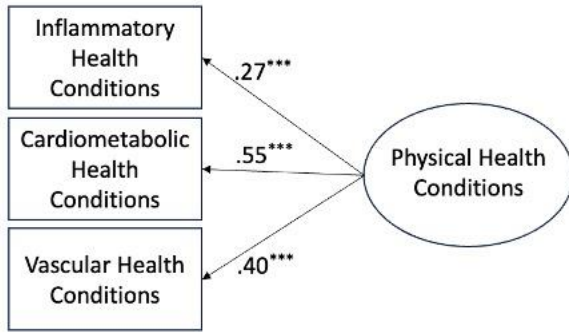


Figure C3. Factor loading for physical health conditions.
Note. Standardized regression coefficients, *** $p < .001$.

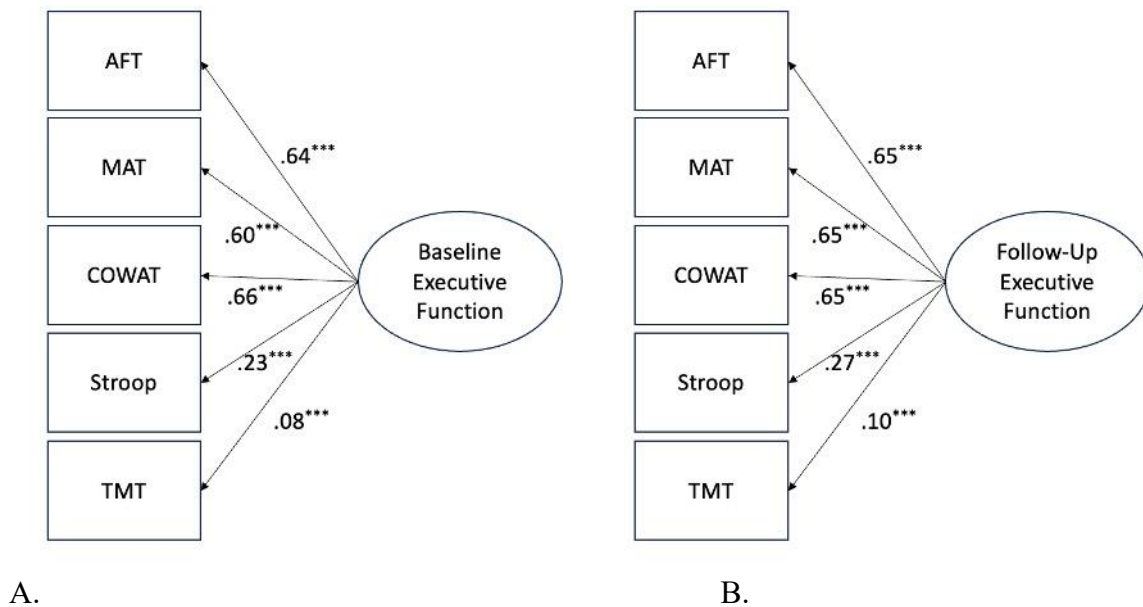
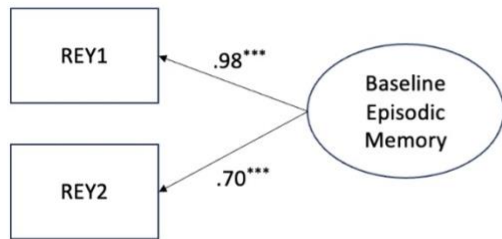
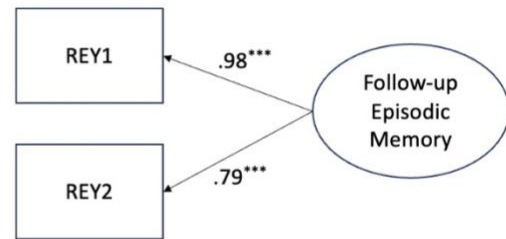


Figure C4. Factor loading for A. baseline and B. follow-up executive function in Study 1.
Note. Animal Fluency Test (AFT); Mental Alternation Test (MAT), Controlled Oral Word Association Test (COWAT), Victoria Stroop Neurological Screen Test (Stroop), and Time-based Prospective Memory Test (TMT), standardized regression coefficients, *** $p < .001$.



A.



B.

Figure C5. Factor loading for A. baseline and B. follow-up episodic memory in Study 1.

Note: Rey Auditory Verbal Learning Test (REY)1 immediate word recall and REY2 delayed word recall, standardized regression coefficients, *** $p < .001$

Appendix D: Supplementary Material for Study 2 Psychosocial Stress

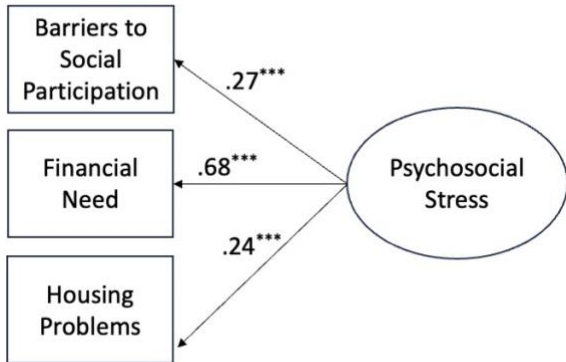


Figure D1. Factor loading for psychosocial stress.
Note. Standardized regression coefficients, *** $p < .001$.

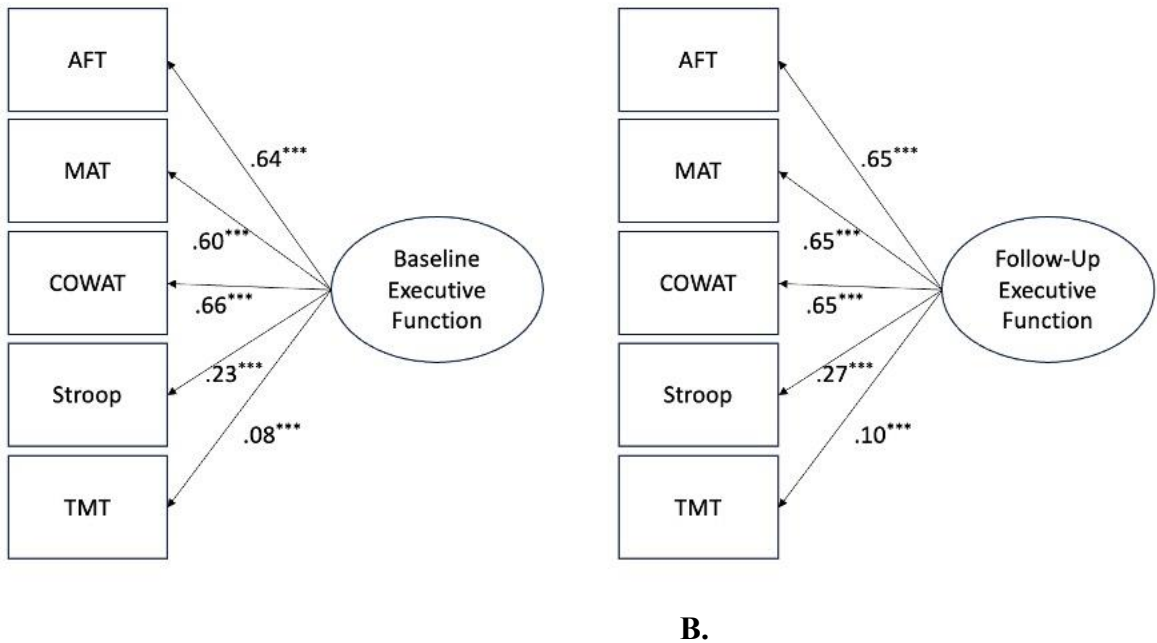
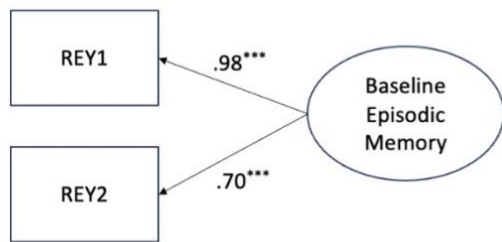
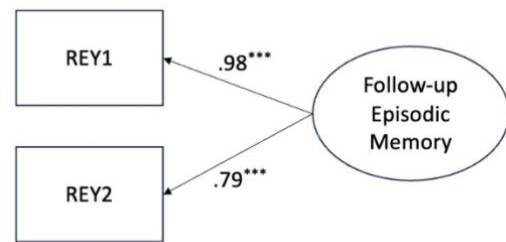


Figure D2. Factor loading for A. baseline and B. follow-up executive function in Study 2.
Note. Animal Fluency Test (AFT); Mental Alternation Test (MAT), Controlled Oral Word Association Test (COWAT), Victoria Stroop Neurological Screen Test (Stroop), and Time-based Prospective Memory Test (TMT), unstandardized regression coefficients, *** $p < .001$.



A.



B.

Figure D3. Factor loading for A. baseline and B. follow-up episodic memory in Study 2.
Note: Rey Auditory Verbal Learning Test (REY)1 immediate word recall and REY2 delayed word recall, standardized regression coefficients, ***p < .001

Appendix E: Supplementary Material for Study 3 Mental Health Stress

Table E1. Kessler Psychological Distress Scale (K10)

	All of the time (Score 5)	Most of the time (Score 4)	Some of the time (Score 3)	A little of the time (Score 2)	None of the time (Score 1)
1. In the past 4 weeks, how often did you feel tired for no reason?					
2. In the past 4 weeks, how often did you feel nervous?					
3. In the past 4 weeks, how often did you feel so nervous nothing could calm you down?					
4. In the past 4 weeks, how often did you feel hopeless?					
5. In the past 4 weeks, how often did you feel restless or fidgety?					
6. In the past 4 weeks, how often did you feel so restless you could not sit still?					
7. In the past 4 weeks, how often did you feel depressed?					
8. In the past 4 weeks, how often did you feel that everything was an effort?					
9. In the past 4 weeks, how often did you feel so sad that nothing could cheer you up?					
10. In the past 4 weeks, how often did you feel worthless?					

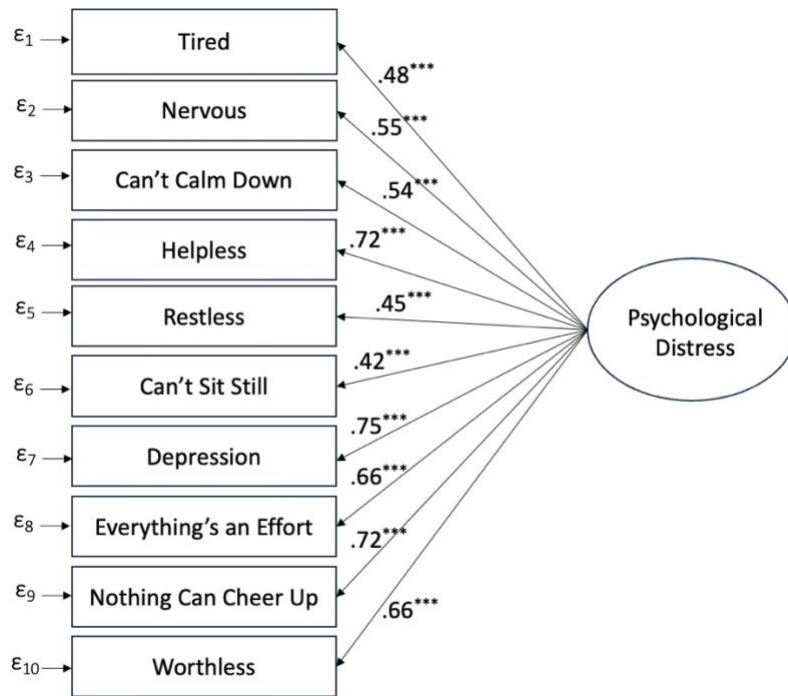
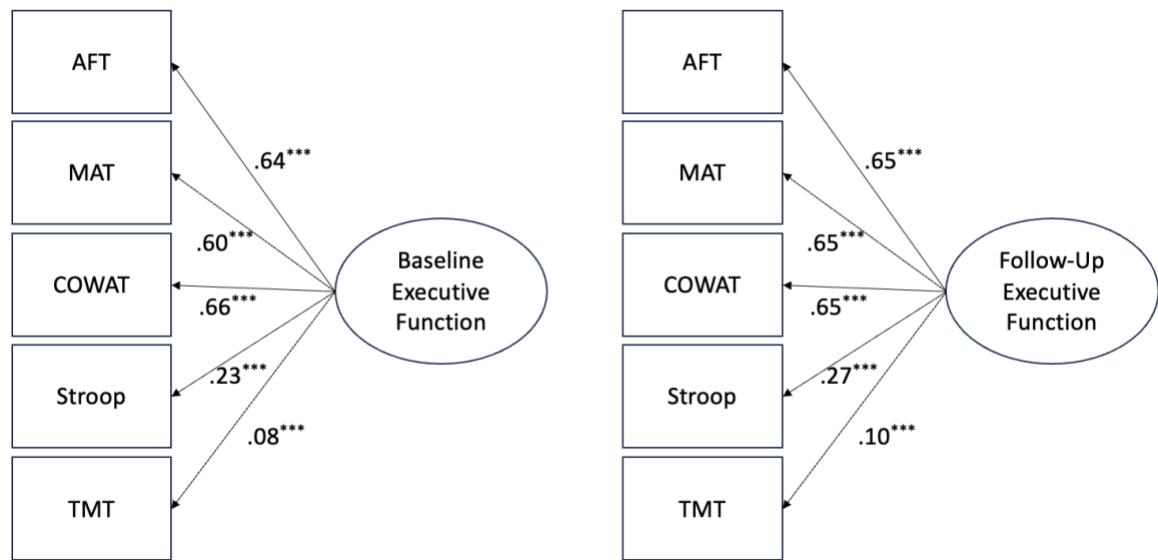


Figure E1. Factor loading for psychological distress.

Note: Standardized regression coefficients, *** $p < .001$.

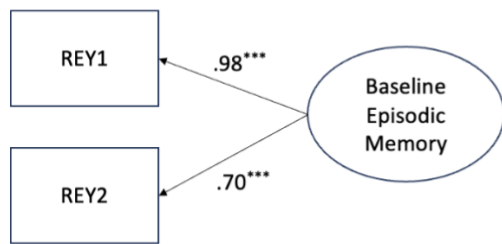


A.

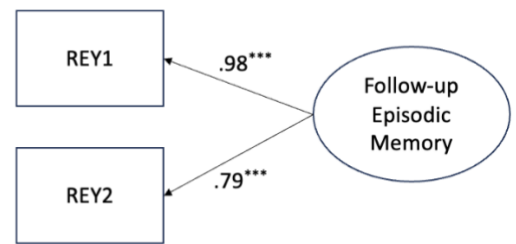
B.

Figure E2. Factor loading for A. baseline and B. follow-up executive function in Study 3.

Note: Animal Fluency Test (AFT); Mental Alternation Test (MAT), Controlled Oral Word Association Test (COWAT), Victoria Stroop Neurological Screen Test (Stroop), and Time-based Prospective Memory Test (TMT), unstandardized regression coefficients, *** $p < .001$.



A.



B.

Figure E3. Factor loading for A. baseline and B. follow-up episodic memory in Study 3.
Note: Rey Auditory Verbal Learning Test (REY)1 immediate word recall and REY2 delayed word recall, standardized regression coefficients, ***p < .001