THE BIOLOGICAL IMPACTS OF RESIDENTIAL SCHOOLING ON THE DEVELOPMENT OF INTERGENERATIONAL TRAUMA AMONG INDIGENOUS PEOPLE

KATHRINA CHIEF MOON-RILEY
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Dr. C. Currie Co-Supervisor	Associate Professor	Ph.D.
Dr. G. Metz Co-Supervisor	Professor	Ph.D.
Dr. J. Copeland Thesis Examination Committee Member	Associate Professor	Ph.D.
Dr. D. Christensen Thesis Examination Committee Member	Assistant Professor	Ph.D.

DEDICATION

I would like to dedicate my thesis to my late grandma, Mildred Chief Moon, my father John Chief Moon, and my mother Gloria Chief Moon. They always taught me the importance of our Blackfoot traditions, and instilled in me the importance of education. Their continuous love and support has molded me into the person I am today, and I am tremendously thankful for that. I am forever grateful for their love, kind words, and encouragement, which helped me throughout this process.

ABSTRACT

Objective: Examine associations between residential school experiences, adverse childhood experiences, and allostatic load scores among Indigenous students (n = 90) at the University of Lethbridge.

Methods: Data for this cross-sectional study were collected through in-person surveys and physical measurements.

Results: Participants who had a mother attend residential school evidenced higher allostatic load scores. Having a mother attend residential school was significantly associated with higher adverse childhood experiences. There was no association between feeling the way they were parented was influenced by residential school and higher allostatic load scores. There were also no association between adverse childhood experiences and allostatic load scores.

Conclusion: Participants who had a mother attend residential school were significantly more likely to have an allostatic load score in the mid-range rather than a low-range, compared to individuals who did not have a mother attend. Results provide biological evidence for the multigenerational transmission of trauma.

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LIST OF ABBREVIATIONS

ACEs	Adverse Childhood Experiences
AL	Allostatic Load
BMI	Body Mass Index
CAR	Cortisol Awakening Response
CIHR	Canadian Institute of Health Research
CRP	C – Reactive Protein
DHEA-S	Dehydroepiandrosterone Sulfate

CHAPTER 1: INTRODUCTION

The Indigenous people are a young, rapidly growing population. In 2011, 1.4 million Canadians identified as Indigenous, suggesting a growth rate of 20% since the 2006 census.[1,2] The average age of the Indigenous population in 2011 was 27.7 years compared to the non-Indigenous Canadian population average of 40.6 years.[3] The term Indigenous in Canada encompasses First Nation, Métis, and Inuit people.[4] This population has diverse cultural, linguistic, social, and environmental experiences across Canada.[5] Yet, there is a common thread of social and health disparities across populations.[6] A statistical profile focused on the health of First Nations showed that the leading causes of mortality are injury and poisoning, circulatory disease, cancer, and respiratory disease.[7–10] In terms of morbidity, Indigenous Canadians experience disproportionate rates of chronic diseases, most significantly diabetes, as well as infectious diseases, including pertussis, chlamydia, hepatitis A, and tuberculosis.[11–14] The incidences of HIV and AIDS are also on the rise in this population. In 2011, Indigenous Canadians accounted for 12.2% of new cases of HIV and 18.8% of reported AIDS cases.[10,15] The goal of this thesis was to shed light on the potential role of residential schools on the disproportionate health burdens of this population.

Residential Schools

A historical issue of particular concern among Indigenous Canadians is residential schools. Many Indigenous have been directly or indirectly affected by the legacy of residential schools. Beginning in 1879, the Canadian government mandated church-run residential schools to provide education for Indigenous children.[16] Residential schools were implemented with explicit policies aimed at cultural suppression and forced assimilation.[4,17] Indigenous children were not allowed to speak their language, engage in

their spiritual traditions, or maintain their cultural practices.[18] Residential schools used parenting models based on punishment, abuse, bullying, and control.[17] In the 1980s, the widespread sexual abuse of Indigenous children in residential schools became publically known.[19] The Government of Canada issued a formal apology for the residential school system in 2008. This acknowledgment led to the Truth and Reconciliation Commission (TRC), which has further exposed that widespread neglect, starvation, and harsh physical, emotional, and sexual abuse were common in these schools.[4,20] The final TRC report was recently released and acknowledged that the relationship between Indigenous Peoples and the government is deteriorating and needs to be repaired.[21] The TRC also acknowledged that the effects of residential schooling had adverse effects on the Indigenous population, specifically on parenting skills and, ultimately, the success of many Indigenous families.[21]

Considering and investigating the biological impacts of residential schooling and, more generally, the social and cultural implications of Indigenous people post-contact allowed for more holistic and culturally sensitive healing approaches. As a result, this thesis recognizes the importance of understanding how intergenerational trauma and residential schooling may contribute to disease prevalence in the Indigenous population.

Thesis Overview

For this thesis, two sets of hypotheses were proposed. First, it was hypothesized that an important pathway through which the residential school experience impacts the health of their adult children is the development and passing on of an abnormal stress response (to be operationalized by allostatic load score). A second hypothesized pathway was the passing on of adverse childhood experiences. Much research has shown that children who experience neglect and abuse are significantly more likely to parent in the same way.[22–24] Thus, I hypothesize that allostatic load scores among the adult children of

residential school survivors would be partially explained (i.e., mediated) by high adverse childhood experience scores. A mediator is a variable that functions as the passage through which causal effects operate.[25]

This thesis used a traditional-based format. This thesis will include an introduction, literature review, methods, results, and discussion to be submitted for publication. **Chapter 1** provides an overview of my thesis and meet the requirements for a thesis as outlined in the *Master of Science Policies & Guidelines* (p20) for the University of Lethbridge School of Graduate Studies. **Chapter 2** involves a literature review on the impacts of residential school on intergenerational trauma among Indigenous peoples, the impacts of stress on allostatic load, and the impacts of adverse childhood experiences on stress. **Chapter 3** discusses my methods, and **Chapter 4** examines my research questions. **Chapter 5** discusses and reflects on these findings.

Proposed Methods

Data were derived from the Canadian Institute Health Research-funded study led by researchers at the University of Lethbridge. This cross-sectional study is entitled *What Social Determinants Contribute to High Allostatic Load among Aboriginal Adults*. The sample population consisted of individuals who self-identified as First Nations, Métis, or Inuit. The study also assembled an Aboriginal Advisory Committee comprised of key members of the Indigenous community to provide input into this project as it unfolded. The committee was consulted with the findings of this thesis to ensure they were presented in culturally sensitive manner.

Measures

In order to investigate the research questions, three variables were measured. The fist variable is residential school experience, which is the exposure variable. The outcome

variable is allostatic load scores. The third variable is ACEs, which has been hypothesized as a mediator variable between the exposure and outcome variables. A mediation model was utilized to determine the relationship between the three variables. Each variable will be explained and how they were measured.

Exposure Variables: Residential School Experience

Parental residential school experiences were assessed via: parental residential school attendance, and adult offspring feeling the way they were parented or cared for was influenced by residential school. To examine the impacts of residential school on the offspring of survivors, participants were asked "Did you have any family members attend residential school (check all that apply)." Participants could select mother, father, 1 or both grandmothers, 1 or both grandfathers, no relatives attended. The second variable was assessed using one question, which asked participants "Do you feel the way you were parented and cared for as a child was influenced by residential school experiences in your family?" Participants could answer with the following options: 0 = No, 1 = Yes.

Outcome Variable – Allostatic Load

Allostasis is the concept explaining that the body has several levels of stress-responsive regulatory systems: the hypothalamic-pituitary-adrenal (HPA-axis), the autonomic system, the metabolic system, and the immune system, which respond to the body state (for example, sleeping, waking, walking) as well as the external environment that stimulates adaptation to activities such as locomotion and to adverse stimuli, such as noise and crowding, hostility, and fatigue.[26] Allostatic load refers to the wear and tear of the body due to repeated cycles of stress.[27] Furthermore, allostatic load refers to an imbalance of these systems, resulting in improper coping and adaptation due to exposure of repeat or chronic stress.[28]

The outcome measure, allostatic load score, was based on seven biomarkers. These biomarkers included neuroendocrine (i.e., cortisol, DHEA-S), immune (i.e., C-reactive protein), cardiovascular system functioning (i.e., systolic and diastolic blood pressure), and anthropometric (i.e., body mass index, waist circumference) measures.

Third Variable: Adverse Childhood Experiences

The formal term for the maltreatment experienced by residential school survivors is called adverse childhood experiences (ACEs), which includes child maltreatment.[29] ACE experience studies have investigated, retrospectively and prospectively, the long-term impacts of abuse, neglect, and household dysfunction on children over their life course.[29] These studies have prospectively documented that ACEs are associated with increased physical and mental health problems in adulthood.[29,30] In addition, research has suggested that ACEs have been linked to alterations in the biological systems responsible for maintaining physiological stability through environmental changes—or allostasis.[26,31] However, little research has specifically linked ACEs to residential schooling.

The third variable, ACE scores among adult children of residential school survivors, were measured using questions modified from the original study.[29] The original study adapted questions from published surveys to create an ACE questionnaire, including questions from the Conflicts Tactics Scale, the National Health Interview Survey[32], and the Behavioral Risk Factors Survey.[29,33]

Analysis Strategy

For my data analysis, the allostatic load scores were analyzed using a multinomial logistic regression method to determine if there is an association with the exposure variables: residential school attendance and adult offspring feeling the way they were parented or cared for was influenced by residential school. Similarly, ACEs were

analyzed using a multinomial logistic regression to determine an association with the exposure variable as well. The hypothesized mediating role of ACEs between parental residential school experience and adult child allostatic load was then examined using a simple mediation model developed by Preacher and Hayes (Figure 1-1).[25,34] Please note that figures and tables are at the end of chapters. Given the smaller anticipated sample size (N = 90), this simple mediation model utilized a bootstrapping procedure.[25,35]

Results and Significance of Research

Indigenous populations experience a disproportionate burden of health inequities. My thesis research was intended to improve the understanding of the ways in which intergenerational trauma may contribute to disease at a biological level. This is an important and unexplored field of study in Indigenous health. I hope through this thesis to contribute to the literature by reporting novel findings and generating hypotheses that will benefit future research and intervention strategies. These results may be used to develop optimal interventions designed to improve Indigenous health.

Chapter 1 Figures

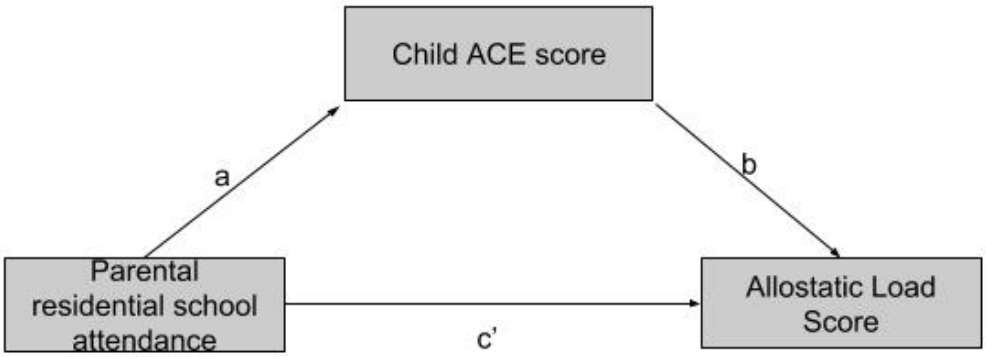

Figure 1-1. Proposed mediation model.

CHAPTER 2: LITERATURE REVIEW

Residential schools were part of a process that brought together European states and Christian churches in a complex and powerful manner.[21] These schools were utilized by the Canadian government and religious groups to assimilate Indigenous people into the dominant society.[36] Residential schools denied Indigenous children their culture, language, and basically their identity as Indigenous people.[21] Research has acknowledged the devastating effects of residential schools on the Indigenous population and has provided evidence that trauma has been passed along generations.[35]

The burden of health and social disparities borne by Indigenous Canadians are believed to be rooted fundamentally in colonialism, which has manifested a long history of oppression, systematic racism, and discrimination.[37–39] The *Final Truth and Reconciliation Report*, published in 2015, has asked governments and organizations to acknowledge that the current state of Indigenous health in Canada is a direct result of previous Canadian government policies and the residential school process.[21] Many other scholars and stakeholders have similarly argued that colonization, and specifically the impacts of residential schools on individuals, families, and communities, has had long-lasting health impacts.[10,35,40] The last residential school closed in 1996, ending more than a century of widespread child abuse and neglect across several generations of Indigenous families.[20]

Thesis Purpose

Most research to date has examined the impacts of residential schooling on psychological health. Little research has investigated the biological impacts of residential school. Yet, it is well documented that the impacts of abuse and neglect in childhood extend far beyond the psychological and affect neuro endocrine function, immune system

function, and behaviour among survivors and, potentially, among their offspring.[41–44] The overriding objective of this thesis was to examine the biological impacts of residential school on the offspring of residential school survivors.

Indigenous Health Profile

The focus of public health is to ensure the health of whole communities and populations. It emphasizes on protection, prevention of disease, and promotion of well-being.[45] In the beginning, public health policy only recognized individuals' genetics and lifestyle choices as the primary influences of health.[10,46] The idea of determinants of health existing outside the health care system influencing an individual's health was first hypothesized after Marmot et al. studied the health of British civil servants.[46] Marmot et al. illustrated that the social environment plays an important role in the health of individuals. Researchers and educators have since increasingly demonstrated that social factors have a great impact on health.[45,47,48] As a result, public health policy has incorporated four categories to consider when dealing with population health. These four elements include biology, environment, individual, and social conditions, which are known as the social determinants of health.[49,50] These factors will be discussed in terms of the Indigenous populations and how they play a role in their current health status.

Global Indigenous Populations

In spite of the progressive conceptual development in the field of public health at a global level, Indigenous populations continue to experience higher rates of poor health, poverty, poor diet, inadequate housing, and other social and health issues relative to non-Indigenous populations.[10,39,40] Health inequities are defined as avoidable differences in health among groups of people who have varying levels of social and economic advantage.[51] Health inequities are a major public health and social justice concern. Mitrou

et al.'s cohort study conducted from 1981 to 2006 investigated the current health state of Indigenous populations in Australia, Canada, and New Zealand.[40] They found that these nations, which each share a British colonial past, continue to show considerable health disparities in the Indigenous populations compared to the non-Indigenous populations.[40] Research has continued to show that despite the distinct differences that exist between Indigenous populations, such as geographic location, culture, and relative size of the Indigenous and settler populations, the impacts of colonization, conquest, and attempted assimilation into the dominant society endured by all Indigenous populations has resulted in similar patterns of health disparities.[17,40]

Canadian Indigenous Population

In Canada, the Indigenous population continues to show significant health inequities compared to the non-Indigenous population. The troubling patterns of health include high rates of chronic and infectious diseases paired with severely insufficient approaches for addressing the social determinants of Indigenous health.[10] A statistical profile focused on the health of First Nations showed that the leading causes of mortality are injury and poisoning, circulatory disease, cancer, and respiratory disease.[7–10] In terms of morbidity, Indigenous Canadians experience disproportionate rates of chronic diseases, most significantly diabetes, as well as infectious diseases, including pertussis, chlamydia, hepatitis A, and tuberculosis.[11–14]

National survey data have demonstrated that the prevalence of diabetes is 3 to 5 times higher in First Nation communities than in the general population.[52] Further, the age of onset for diabetes is also younger for First Nations.[13,52] Indigenous populations also experience higher rates of cardiovascular disease (18.5% to 7.5%) compared to non-Indigenous population.[53] Incidences of HIV and AIDS are also on the rise in this

population. In 2011, Indigenous Canadians accounted for 12.2% of new cases of HIV and 18.8% of reported AIDS cases.[10,15] In Canada, the only active national-level legislation specific to the First Nations population is the Indian Act.[10] The effects of the Indian Act are prevalent in all modern health, social, economic, and political indicates of Indigenous well-being.[9,10,40]

The Indigenous population experiences a disproportionate burden of inequality related to the workforce participation, low income, education, and sub-standard living conditions.[10,39,54] In 2005, the average annual income for the entire First Nation's population (including on and off reserve), aged 25 to 54, was $22,366, which is significantly lower than the identified non-Indigenous population income of $33,394.[55] The income disparity was far worse for on-reserve First Nation peoples, who had a median income of $14,000.[10,55] This is alarming, as research has shown that individuals in the lowest income category in Canada are five times more likely to experience fair or poor health compared to the highest income category.[39] In terms of education, Indigenous people continue to lag behind their non-Indigenous counterparts in obtaining a high school diploma.[54,55] Inadequate and insufficient housing continues to remain a critical issue for Indigenous people across Canada.[10] Such stark realities faced by the Indigenous population result in a disproportionate experience, with socioeconomic inequities that are rooted in unique and complex socio-historical contexts.[56]

Colonial legislation and policies continue to dictate the health of Indigenous Canadians, especially on First Nation reserves, which have unique jurisdictional complexities, result in disparities of service access and ongoing dislocation of traditional lands.[6,56] Not only has the Indian Act created the precedent for the current state of Indigenous health, it has shaped the Canadian public's perception of Indigenous people

and perpetuates racism and gender discrimination, which are important determinants of health as well.[10,57,58] Research looking at the relationship between stress and health has confirmed that individuals experience greater stress when exposed to systematic disadvantage, when they face barriers to possess control over their lives, and when they experience demoralizing treatment.[59]

Research has collectively demonstrated the health disparities experienced by the Indigenous Canadian population is entrenched in the history of relations between Indigenous people and the government. It has been demonstrated that the Canadian Indigenous population continues to be disadvantaged in key areas such as education, income, and other factors known as social determinants of health. Two theories will now be discussed, the life-course perspective and psychosocial model, to provide further detail on how disadvantages in these certain areas can impact an individual's health.

The Impacts of Stress and Socioeconomic Disadvantage over a Lifespan

The life-course perspective pathway has been chosen to describe how a history of disadvantaging events or stress can impact health later in life. A life-long trajectory of health starts during gestation, which dominates early child development, where circumstances of the physical and emotional environment impact not only a child's current state of health, but as well set the foundation for the child's future vulnerabilities and resiliencies.[9] The life-course perspective is a theoretical framework aimed at incorporating psychological, cognitive, and biological research on developmental processes from conception to death.[60] This framework is valuable in displaying how socioeconomic determinants of health throughout life independently, cumulatively, and interactively influence the onset of diseases.[60,61]

It is also appealing that the life-course perspective looks at life not in disconnected stages, but as an integrated continuum.[61,62] Specifically, this pathway is appropriate for the Indigenous population due to the fact that it is complementary to the importance of intergenerational relationships, community well-being, and holistic understandings of health in Indigenous communities.[61] In terms of stressors, it has been shown that Indigenous people are greatly impacted by their history: specifically, colonization and residential schools. With that in mind, individuals are collectively linked and intertwined with the lives of those around them, and social ties and relationships with family, friends, or acquaintances have the potential to alter one's life course trajectory in a positive or negative manner.[63] Hence, not only are the individuals who underwent traumatic experiences first hand (i.e., attending residential school) affected, but their family members can also be impacted by it. The life-course perspective illustrates how, longitudinally, disadvantaged events will lead to similar events later in life—or in future generations. This longitudinal description and its results can be further explained with the psychosocial model.

The Psychosocial Pathway

The psychosocial model is a theory that explains how stress or trauma can change the body and how the person responds to these occurrences. That is, this model shows the relationship between the biological responses of individuals to the social environment acting upon them.[48] In addition, this model shows how material circumstances, early life experiences, and cultural and genetic factors exert influence on health later in life. The human body has two major stress systems that are activated during times of stress: (1) the sympathetic nervous system (SNS) and (2) the hypothalamic-pituitary-adrenal axis (HPA axis).[64] The SNS, specifically the sympathetic-adrenal-medulla (SAM) axis, which is

active in the flight-or-fight response in humans, functions in releasing specific catecholamines, such as adrenaline (i.e., epinephrine) and noradrenaline (i.e., norepinephrine), to aid the body in times of stress or distress via the adrenal medulla and acts primarily on the cardiovascular system.[65] The HPA axis, on the other hand, serves as a neuroendocrine response system to stress.[65]

When an individual becomes stressed, the SNS stimulates the adrenal medulla, which, in turn, leads to the secretion of adrenaline and noradrenaline, which results in several stress-related changes in the body, including changes in blood pressure and heart rate.[64] Following the activation of the SNS, the HPA axis is activated; the hypothalamus releases the corticotropin-releasing factor, which stimulates the pituitary gland to secrete the adrenocorticotropic hormone, which then stimulates the adrenal cortex to release glucocorticoids (i.e., cortisol).[64,66] Cortisol is not only responsible for long-lasting effects, including mobilization of energy stores, heightened vigilance, and learning and memory, this hormone also exerts negative feedback control on the HPA axis to terminate when appropriate.[66,67] This timely activation and deactivation prompt of the HPA axis allows an individual to properly manage stress and subsequently return to normal function.

Adrenal glucocorticoids typically have adaptive effects in the short run, but promote pathophysiology when there is either repeated stress or dysregulation of the HPA axis. Furthermore, chronic over activation of SAM- and HPA-axis products results in a *domino effect* on interrelated biological systems that overcompensate and eventually fail themselves, leaving the individual susceptible to stress-related diseases.[68–70] This dysregulation due to the damaging actions of glucocorticoids is allostatic load, which illustrates how normal homeostatic functioning is shifted towards abnormal ranges via

prolonged secretion of stress hormones, which can result in the subsequent mal-adaptions this strain exerts on interdependent systems.[70]

The critical point these models illustrate is that acute stress can be adaptive, but if this stress response is activated too often and for too long, this can lead to multiple health risks.[48] They also explain how health problems can be linked to a constant or cluster of disadvantage throughout life. In addition, the psychosocial model begins to explain how exposure to stress can impact an individual's body. Allostasis and allostatic load build on the psychosocial model by demonstrating in greater detail what can happen to the body after repeated or chronic stress. These concepts are now introduced and how they can potentially explain the biological impacts of residential schooling on the Indigenous population.

Introducing the Dependent Variable: Allostatic Load

While it is evident that the Indian Act and current health legislations and supports in place for Indigenous Canadians are not sufficient in addressing their health inequities, it is also unclear what underlying biological mechanisms are causing these disparities. Beyond a few seminal reports, little is known about the distinct influence of social determinants of health on the physical health of the Indigenous populations.[9] Currently, research focuses more on downstream approaches aimed at treating previously diagnosed individuals. The iceberg concept of epidemiology is a notion that explains disease using an iceberg as an analogy.[71] The floating tip of the iceberg represents those who have visible symptoms of the disease and are recognized as cases. On the other hand, the vast submerged portion of the iceberg represents the unsuspected portion of the disease that is comprised of latent/pre-symptomatic cases and carriers in the community.[72] This idea illustrates that the symptomatic portion of disease is just a small portion. Instead, if

individuals could be assisted in the pre-symptomatic phase, this could greatly reduce health inequities experienced by not only the general population, but also the Indigenous population. Allostatic load is used by researchers as a pre-clinical marker of disease risk and an example of an upstream approach.[72]

Allostasis and Allostatic Load

Daily life can sometimes be challenging and stressful. Stress can arise from a variety of factors, including an individual's work, home life, neighbourhood, and major life events such as the loss of a loved one, trauma, or abuse.[73] The human body has several systems that respond to stress in order to maintain homeostasis, including the HPA axis, the autonomic nervous system, the metabolic systems, and the immune system.[27,64] More specifically, actual or interpreted threats to homeostasis initiate the SAM axis to release catecholamines and the HPA-axis secretion of glucocorticoids that mobilize energy necessary for fight-or-flight responses.[70] These body systems respond to the body state and to the external environment and promote adaptation to potential stressors or threats.[27,28] However, these systems can become dysfunctional if stress becomes frequent or prolonged, and it can have detrimental effects on the body. In order to avoid the negative impacts of stress, the physiological responses of these stress systems coordinate appropriately to protect and adapt the individual to the challenge.[27,28,64] The method through which the body deals with stress is referred to as *allostasis*.

Allostasis was first proposed by Sterling and Eyer[74] and has been further explored extensively by McEwen[27,28,73], among other researchers, to explain how the body handles stress. Allostasis refers to the process of adaptation to acute stress, which involves the release of stress hormones to aid in restoring homeostasis.[28] Allostasis allows the body to achieve stability through predictable and unpredictable changes by activating different

physiological regulation systems, including the cardiovascular, endocrine, nervous, and digestive systems. [27,75] Unlike the majority of homeostasis systems that work to maintain stability over a narrow range, allostasis maintains stability over a broader range of change.[73] However, if allostasis is activated too often or too extensively, it can have detrimental effects on the body.[27,28,75] This imbalance can lead to harmful long-term consequences, referred to as allostatic load.[27,75]

Allostatic load (AL) is the wear and tear on the body, which is the result of being forced to adapt to adverse psychosocial or physical situations.[28,76] It represents the chronic over-activity or inactivity of physiological systems that are normally involved in adaptation to environmental challenge, which can result in chronic disease.[27] The perception of threat and initialization of these allostatic mechanisms are fundamentally influenced by individual differences in constitutional (e.g., genetics, development, experience), behavioural (e.g., coping and health habits), and historical (e.g., trauma, abuse, stressful environment) factors that ultimately determine one's resiliency to stress.[27,70] Assessment of AL would ideally include information on both the resting or normal levels of allostatic mediators for individuals as well as assessments of system dynamics and information for parameters of the physiological regulatory systems.[28] AL was first measured by researchers of the MacArthur studies, who studied allostatic load among older Caucasian adults using the 10 original biomarkers (Table 2-1).[77]

The MacArthur studies allowed researchers to conclude a causal relationship between AL at baseline and functional decline over the follow-up period.[76] The participants' allostatic load scores were determined by summing across indices of subject's status with respect to these 10 components of AL.[28,77] For each of the 10

indicators, participants were categorized into quartiles based on the distribution of scores in the high-function cohort.[28,77] Since then, AL has been measured alternatively. For example, one method is based on averaging *z*-scores for each of the parameters, in which analyses produce essentially the same results as the quartile criteria, with this method showing stronger effects.[28] Both animal and human studies have subsequently provided additional knowledge on AL and exposure to chronic stress.[78,79] Petrovic et al. demonstrated how genetic and environmental factors can influence physiologic dysregulation, operationalized via AL scores.[78] This study found factors such education, occupation, and to a lesser extent genetic factors impacted individual's AL scores. In particular, it was found that education was inversely associated with AL in both females and males.[78] This thesis examined AL via quartiles, using a combination of seven variables (Table 2-2). Each biomarker and its significance will now be explained.

Allostatic Load Variables

Allostatic load is a composite measure of the wear and tear on the body due to stress. The goal of an allostatic load score is to represent the interplay of different systems that respond to environmental exposure.[80] Biomarkers should be selected with the aim of achieving a complete representation of the allostasis systems. Generally, metabolic and cardiovascular systems are stronger predictors of future health outcomes than inflammatory and neuroendocrine, and this should be taken into consideration by researchers.[80] A poor composite score would then consist of using biomarkers that are not relevant to the physiological dysregulation or failing to include biomarkers that are relevant.[80,81] Biomarkers selected for this thesis, and why each biomarker was important

to include, are presented in this section. These biomarkers include body mass index, waist circumference, blood pressure (systolic & diastolic), cortisol awakening response (CAR), C-reactive protein (CRP), and dehydroepiandrosterone sulfate (DHEA-S).

Body mass index (BMI)

BMI is one of the most commonly used anthropometric measures to diagnose obesity. Obesity has become one of the most significant threats to human health worldwide.[82] Research has shown the associations between obesity with diseases such diabetes, hypertension, coronary artery disease, cancer, and sleep apnea.[82] The World Health Organization (WHO) has agreed on an international standard for identifying individuals as overweight and obese using BMI, which is calculated as the ratio of weight to height squared (kg/m^2).[83] A normal range for BMI, as suggested by the WHO is 18.5–24.9; the overweight range is 25.0–29.9; and the obesity range is 30–39.9.[84] The use of BMI in predicting health risk has also been recognized by the United States National Heart, Lung, and Blood Institute of National Institute of Health and Health Canada.[85,86]

BMI has also been classified as a measure of the metabolic system and has been included in the construction of the allostatic load score. In addition, BMI has been used extensively in epidemiological studies and incorporated in clinical practice due to its simplicity.[82] However, research has also acknowledged increased cardiovascular disease existing in individuals with excess fat in the abdominal region[87,88], and at the present, there is no standard measure of abdominal obesity that is widely accepted.[83] This was taken into consideration with this thesis, and waist circumference was selected as a second anthropometric measure.

Waist circumference

Waist circumference has been defined as a good marker of the metabolic system. From a clinical perspective, visceral adipose tissue is known to lead to diabetes[89] and, thus, is more informative than total fat, which BMI is usually used to measure.[90] Waist circumference and waist-hip-ratio have both been used as measures of central obesity, where visceral adipose tissue is stored.[90] However, previous studies have shown that waist circumference is a better measure than waist-hip- ratio of central obesity due to several factors, including being easily measured and interpreted.[90] Research has shown the association of diabetes with central obesity rather than with general fat and, hence, indicates the importance of waist circumference as a measure of the metabolic system and its inclusion in the allostatic load systems.

Blood pressure (systolic & diastolic)

For the cardiovascular system, systolic and diastolic blood pressures were employed. Systolic blood pressure represents the flow of blood throughout the body while the heart beats; diastolic blood pressure reflects when the heart relaxes.[91] Blood pressure is created by the flow of blood pushing against the walls of the blood vessels as the heart pumps it. Normal blood pressure is defined as a systolic blood pressure value of 120 mmHg and a diastolic blood pressure value of 80 mmHg.[92] The WHO has defined high blood pressure when systolic is 140 mmHg or higher and/or a diastolic of 90 mmHg or higher.[91] An elevated systolic and/or diastolic level is referred to as hypertension.

Hypertension is a condition characterized by blood vessels that have persistent raised pressure, putting them under increased stress.[91] Hypertension is a common precursor for cardiovascular disease and other major health outcomes such as heart attacks and strokes.[93] Thus, blood pressure is an important measurement to include in

allostatic load scores. It is a good indication of an individual's current cardiovascular state.

Cortisol awakening response (CAR)

The HPA axis is an important pathway in the regulation of the stress response. Dysregulation of the HPA axis has been linked to several health outcomes, including psychiatric illnesses, cancer, and cognitive decline.[46,94–96] Several neuroendocrine biomarkers have been shown to be good measures for this dysregulation, including cortisol.[96,97]

The use of salivary cortisol as a biomarker of stress and HPA-axis function has been a well-established approach in research for the last 20 years.[96,98] For this thesis, cortisol was chosen as a measurement of the neuroendocrine system. Cortisol is a steroid hormone (glucocorticoid) produced by the adrenal gland.[28,99] Due to its marked diurnal rhythm, several approaches have been employed to collect and analyze cortisol. Common approaches include using standardized acute stressor and measuring unstimulated HPA-axis function.[96]

Increasingly, there has been a shift toward measuring the circadian rhythm of the diurnal pattern of cortisol, instead of focusing on absolute cortisol concentration.[96,97] This diurnal rhythm is characterized by high levels upon wakening, a substantial increase (50-60%) in cortisol levels 30 to 45 mins after wakening, and a subsequent decline over the remainder of the day.[97] This increase in cortisol upon awakening is referred to cortisol awakening response (CAR), which has become a popular measure used by researchers studying stress. In general, an abnormal cortisol awakening response, whether it is abnormally large or flattened, resulting in an atypical diurnal cortisol slope appears to be linked to HPA-axis dysregulation.[96]

Cortisol is normally released in response to events such as waking up, exercising, and acute stress.[98,99] During stressful periods, cortisol functions to prepare the body, alongside epinephrine, for the "flight-or-fight" response.[100–102] Specifically, cortisol's role is to organize the body's stress response by supplying glucose for immediate and temporary source of energy.[103] By doing this, cortisol simultaneously inhibits insulin production to prevent glucose from being stored when experiencing stress.[103] Further, cortisol also narrows the arteries while epinephrine increases heart rate, ultimately forcing blood to pump harder and faster.[104]

Short term these responses are advantageous, however, if stress becomes chronic, this can lead to detrimental impacts on the body. For instance, cortisol increases the amount of glucose in the body, and as a result elevated cortisol long term can result in high blood sugar levels leading to diabetes.[103] Since cortisol is active alongside the SNS, the parasympathetic nervous system (PNS) is suppressed as both systems cannot be simultaneously activated. The PNS is active during stagnant activities such as eating and digestion, and as a result cortisol subsequently reduces digestion when activated.[105,106] More generally, long-term elevated levels of cortisol have been linked to insomnia, thyroid disorders, and depression.[107–109] Hence, including the measurement of cortisol in the construction of an AL score is important as it provides crucial information about the stress response and how it benefits the body short term and can become detrimental over longer terms.

C-reactive protein (CRP)

Research has shown that inflammation is a key mechanism through which life adversity influences the development of physical health problems.[29,110] Circulating CRP

levels have been employed as an indicator of general inflammation as well as a marker of cardiovascular disease.[111,112]

CRP is a plasma protein produced by the liver, with circulation levels increasing dramatically in response to local and overall inflammation. Highly elevated levels of circulating CRP (> 10 mg/L) are an indication of acute infections or inflammatory disease[113], whereas intermediate levels of CRP are associated with chronic inflammation and increased risk of cardiovascular disease.[114,115]

For the construction of allostatic load scores, CRP is an important component. It is often included as a measure for the immune response, which is an important secondary outcome of allostasis.[80] Specifically, when a stressor is experienced, CRP is released as part of an innate immune response that acts as a surveillance molecule looking for altered pathogens activating an adaptive immune response.[116] It is also an indicative measure for diseases such as cardiovascular and atherosclerosis.

Dehydroepiandrosterone sulfate (DHEA-S)

Dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEA-S) are steroids synthesized by the adrenal cortex.[117,118] Levels of DHEA and DHEA-S decline following birth until age five, and then increase a few years prior to sexual maturation.[119,120] Moreover, the levels peak between the ages of 20 and 30, and subsequently decline over the remaining course of life.[120,121] Research has suggested that DHEA and DHEA-S are synthesized in the brain, indicating a role in brain function and development. Specifically, DHEA-S is a weak androgen and precursor to stronger steroid hormones, such as testosterone.[120] However, their exact physiological significance, mechanism of action, and possible role in disease is limited and not well understood.[117]

Despite little knowledge in their exact role, research has established several features about DHEA and DHEA-S. For one, there is an age-related decrease in DHEA and DHEA-S.[117,118,122] A distinct sex difference has also been established, with adult men having higher DHEA-S concentrations than women.[123,124] In addition, DHEA-S has been positively associated with mood, energy, and well-being, with lower levels of DHEA-S being linked to rheumatic disease, cardiovascular disease, immune disorders, and oesteoporosis.[104,121]

As mentioned previously, cortisol is a biomarker of the HPA-axis activity, and DHEA and DHEA-S are believed to counter regulate cortisol.[117,125] Thus, DHEA and DHEA-S form an important biomarker in terms of regulation of the neuroendocrine system indicating whether the system is functioning normally or abnormally. Low levels of DHEA-S are considered high risk, which is the opposite for the other biomarkers, where high values are typically considered high risk.[126] For this thesis, DHEA-S was included in the allostatic load score as a neuroendocrine marker.

In summary, seven variables were selected to create an allostatic load score that represented a comprehensive representation of the allostatic load systems. Each variable was selected based on previous research and how it can measure the functionality of these body systems. With the potential an allostatic load score can provide, it is important to apply this knowledge to populations that experience higher rates of health issues. An increasing amount of research has focused on marginalized populations. This is important in addressing and determining the causes of the health disparities that can exist in these populations.

Marginalized Populations

Allostasis and allostatic load have been shown to be important concepts in bridging the association between stress and disease. In addition, allostasis and allostatic load provide a framework for studying both the protective factors of stress mediators during acute stress encounters and the detrimental effects of chronic and/or repeated stress exposure.[76,127]

Allostatic load has been predicted by several factors, including socioeconomic disadvantage, household overcrowding, and childhood trauma, which are important factors influencing Indigenous peoples' health.[128] Increased allostatic load is also more prevalent in impoverished and marginalized populations.[129] Given this evidence, along with allostatic load being strongly associated with low economic status, it can be viewed as an important factor in health disparities.[128]

Social adversity, including poverty, unemployment, and disempowerment, have been recognized as risk factors for adverse health issues in different populations globally.[130] Epidemiological data have provided evidence to an increased risk for a wide range of psychiatric disorders in ethnic minority and disadvantaged populations.[130]

In 2016, Tomfohr and Dimsdale compared allostatic load scores among African Americans and Caucasians in the United States.[129] They recognized that African Americans often experience higher rates of social adversity, and they sought to determine whether this would impact their allostatic load scores. The results indicated that on average, African Americans had higher allostatic load scores compared to Caucasians. The study concluded that discrimination was an important mediator through which these racial differences in allostatic load occurred. Their results illustrated how social adversity, which many minority ethnic groups experience, is impacting their health.

In 2016, Sarnyai et al. published that the Australian Indigenous population had a mortality rate much higher compared to the non-Indigenous population.[128] For Indigenous populations, males had a lower life expectancy of 10.6 years and 9.5 years for females compared to the non-Indigenous population.[128] Researchers have recognized the link between low socioeconomic status and other social factors throughout the life cycle impacting the Indigenous population, including discrimination, racism, and intergenerational trauma, which could be underlying these observed health inequities.[128] However, research is only beginning to investigate health inequities and allostatic load in the Indigenous populations.

Building on these findings, Schmitt et al. found that both cortisol and adrenaline secretion was significantly higher in the Australian Indigenous population when compared to a United Kingdom sample, which itself was high by world standards.[128,131] Based on the research focused on marginalized populations, a clear link has been established between social adversity and health disparities, which can be operationalized via allostatic load. Hence, as argued in this paper, allostasis and allostatic load can begin to explain the health disparities observed in the Canadian Indigenous population.

In summary, an expanding area of research is focused on allostasis and allostatic load. This field of research has shown that allostatic load is a pre-clinical marker that if not dealt with, can lead to health problems in the future. Researchers have increasingly noted that allostatic load brings together a set of biomarkers that collectively characterise a multisystem approach to detect subclinical disorders.[130] The appealing nature of the allostatic load model is in its ability to demonstrate that the sum of a list of pre-selected biomarkers can predict health outcomes significantly better than a single biomarker would. That is, many of these biomarkers are commonly used in daily clinical practice;

however, cluster analysis of the allostatic load score is a stronger predictive value for health outcomes.[128,130] Research has also shown allostatic load is especially high in disadvantaged populations and is strongly associated with low economic status. Therefore, it can be argued that allostatic load may be an important factor in health inequities.[130,132]

Introducing Exposure Variable: Residential Schools

Residential schools were one of the most prominent historical events of colonization in Canada.[133] The first schools were opened in the late 1800s, with the last one closing in 1996.[21,133] Indigenous families typically had a traumatizing experience when the day came to send their children to residential school. Even though parents anticipated this day, one could not prepare for it. Often, children were torn from their parents, who only surrendered them due to threat of prosecution; children were then hurled into a strange and frightening place.[20,21] For the children, the arrival at the schools was even more traumatizing than the departure. One Elder described the ritual of children entering residential school:

> At the mission, the truck backed-up and off we went. Right away, boys were separated from girls. We were lined up, sat on chairs, and had our long, beautiful braided hair chopped off. We were thrown into the shower, then had DDT sprinkled hair and all over. It stunk. They gave me a number 79. My name was gone. I was only a number now. We all had the same little bundle of clothing, pinafores, black clothes, socks. You couldn't tell one kid from the other; they transformed individuals into a group. I don't understand how my Shuswap language was turned into English in just one day.[134(p.58)]

The schools were severely underfunded from the beginning, resulting in unsanitary conditions.[21,135] For instance, in 1937, Indian Affairs was paying, on average, $180 a year per Indigenous student. This was far less than a third of the per capita at that time for the Manitoba School for the deaf, at $642.20, and the Manitoba School for boys,

at $550.[21] In many instances, inspectors found raw sewage in sleeping and eating quarters of the children. Underfunding also meant poorly trained and underpaid staff that used harsh physical discipline of children, including humiliation, often leading to physical abuse.[16,21,136] According to the Truth and Reconciliation Commission of Canada[21], the only evidence of a nation-wide discipline policy for these schools was issued in 1953. The failure to implement and enforce a national policy on this matter meant that Indigenous students were subject to disciplinary measures that would not be tolerated in schools for non-Indigenous students.[21] This sent a message that there were no set boundaries on what could be done to Indigenous children within the walls of residential schools. This allowed significant physical, emotional, and sexual abuse of students.[21]

Emotional Abuse

Missionaries and government officials held prejudiced beliefs against Indigenous peoples and their cultural practices. These beliefs were the foundation for the discriminatory policies that dictated order in residential schools. This created an atmosphere that consistently and relentlessly attacked the children's traditional language and cultural practices. Removed from their homes, stripped of belongings, and separated from their families, children attending residential schools were exposed to a world dominated by fear, loneliness, and lack of affection. Several accounts from residential school survivors recalled constant humiliation during class and fear being instilled in them. Children learned quickly that in order to survive, they had to harden their hearts. There are many accounts of children crying that did not result in any comfort; instead, crying resulted in being teased or shamed. One residential school survivor told the Truth and Reconciliation Commission: "There was no love, there was no feelings, it was just supervisory."[137(p.42)] The schools instilled an environment that neglected the children's

emotional needs for caregivers' warmth and nurturing. The schools ensured children gave up their Indigenous identity through emotional abuse, often through humiliation.[17,136]

Physical Abuse

Physical abuse was also often used on children as a form of discipline. Residential school survivors have strong memories of being punished for speaking their Indigenous language. One Elder attending Battleford school recalled: "Students caught speaking their own language were given a close haircut."[137(p.81)] Another Elder accounted: "I couldn't speak a word of English. I talked Cree, and I was abused for that, hit, and made to try to talk English."[21(p.82)] A majority of students entered residential schools fluent in an Indigenous language and knowing little or no understanding of English or French.[21,136] This was a common trend well into the post-war period.

Sexual Abuse

From the early nineteenth century, both the government and the churches were aware of the risk that school staff were sexually abusing the students, but it was not until the 1980s that the widespread sexual abuse that occurred in residential schools was brought to public awareness.[1,19,21] Complaints were often ignored, and in the rare occasion where Indian Affairs acted on the allegations, it would often result simply in dismissal, allowing the staff member to avoid prosecution in order to protect the school's reputation.[21,138] New students were especially vulnerable to abusive staff, as they were traumatized by separation from their parents and the alien rule of the school. These staff sought to win the student's trust through what initially appeared to be simple kindness, but often was the prelude to a sexual harassment that left the student scared and confused.[21] These patterns continued well into the late twentieth century.

Emotional Neglect: Nutritional Experiments

In addition to the several forms of abuse, nutritional experiments were also revealed to have taken place at several schools. During the post-war period, 5-year nutritional experiments were launched by nutritional experts in Canada.[139] The goal was to investigate the effects of different nutritional interventions, such as added dairy and vitamin supplements, on the children's diet.[139] The studies also included a control group for each intervention, and these children were given placebos. Consent was not given to the researcher(s), as children and parents had no knowledge of these experiments taking place. The results did not improve the conditions at the schools, nor was it made public knowledge that these experiments took place in residential schools.[139] More alarming, these experiments were conducted following the creation of the Nuremburg Code, which was implemented in response to the human experimentation that occurred in Nazi concentration camps.[140] The purpose of this international law was to prevent humans from human experimentation and to create ethically correct research.[140]

Overall, the abuse experienced by Indigenous children at residential schools can be referred to as child maltreatment, which will be defined and discussed next. The result of residential school and, in general, Indigenous populations' history of trauma has led to recognition of past violence and, in Canada, to a formal apology from the government, processes of compensation, and the creation of the Truth and Reconciliation Commission.[4,20] The legacy of residential schools and the political and legal policies and mechanisms surrounding their history continue to this day, which is reflected in the significant educational, income, health, and social disparities seen between Indigenous people and non-Indigenous people of Canada.[21]

Main Pathway of the Mediation Model: Impacts of Child Maltreatment on Allostatic Load

A definition of child maltreatment and its impact on the health of individuals is presented at the beginning of this section. Next, the brain will be discussed: specifically, the stress systems and how child maltreatment influences the development and function of the brain. I then end this section with discussion about child maltreatment in residential schools and how allostatic load can be used to explain the biological impacts as well as how this can be passed on to subsequent generations.

Child Maltreatment

Child maltreatment has been defined by the American Psychological Association in their *Diagnostic and Statistical Manual of Mental Disorders IV and V* as exposure to actual or imaginable death, serious injury, or sexual abuse, and it includes experiences of direct trauma, witnessing trauma, or learning about trauma that occurred to acquaintances.[44,141] Social and physical environments have powerful impacts on the body and brain. Early life events related to maternal and paternal care in humans also have a powerful role in mental and physical health later in life.[142,143] Research has shown that stressors experienced early in life during sensitive developmental periods can result in enduring influences on health later in life.[26] Researchers investigating the rodent mother-infant interactions resulted in ground-breaking findings of the effect of prolonged maternal separation, novelty exposure and consistency of maternal care, prenatal stress, postnatal maternal abuse, and maternal anxiety on subsequent neural and behaviour development.[144–147] Research has demonstrated a strong link between traumatic childhood events and higher rates of health issues, including mental health issues.[29,30,148] Recent data have further supported this claim, including evidence that adults diagnosed with

depression had a history of maltreatment in childhood and were twice as likely to have higher CRP levels compared to controls.[149]

Social factors such as socioeconomic status have also been shown to have tremendous effect on the developing brain.[42,142,148] For example, parental education and income were shown to have important influences on the rate of maturation on selected brain regions of their child.[148] Children living in disadvantaged environments are more likely to experience conflictive and harsh parental behaviour and have relatively fewer positive experiences, including reading, interactive conversation, and after-school activities.[150,151]

Research has shown that there are four periods during development when the body, and specifically the brain, is sensitive to the environment, termed biological embedding.[69,80,81] Biological embedding illustrates how gene expression can be modified in response to environmental cues and that biological and behavioural traits can even be maintained across multiple generations.[81,152] These four important periods of sensitivity include the following: (1) the prenatal period[153–155], (2) the neonatal period[145,147,156], (3) early childhood[157–159], and (4) adolescence.[18,160,161] For the purpose of this thesis, only early childhood and its importance in epigenetic processes is discussed in more detail.

The Brain and its Interaction with Stressors

Once seen as a static organ, only in the last few decades has the brain been recognized as being able to undergo constant change as a function of experience.[162–164] The brain is the central organ of adaptation to daily experiences, including stress, as it constantly interacts with stimuli from the environment. The brain possesses tremendous capacity for reversible structural plasticity, which is the ability to change based on stimuli in the internal and external environment.[66,81,163] It determines which experiences are

stressful and chooses appropriate behavioural and physiological responses, which can be either detrimental or positive to an individual's health.[81] Ideally, after exposure to adversity, the brain should have the ability to return back to its homeostasis state, termed resilience.[81,165]

Exposure to an adverse event or repeated adverse events activates the body's stress response systems.[44,100,101] The stress response is a complex process involving multiple mediators, including the brain-derived neurotrophic factor, which is an important mediator of plasticity that works with glucocorticoids excitatory amino acids, hormones, and multiple systems of the body, including autonomic, neuroendocrine, metabolic, cardiovascular, and immune.[164,165] Further, an individual's stress systems interact and work together to guide the body's attention toward protecting the individual against environmental life threats and to shift metabolic resources away from homeostasis and toward "flight or fight."[44] A traumatic event is first processed by the body's sensory system via the thalamus, followed by activation of the amygdala, which is the brain's main fear detection and anxiety centre.[73,166] Cortisol then increases through transmission of fear signals to neurons in the prefrontal cortex, hypothalamus, and hippocampus, and activity also increases in the SNS.[44] This leads to changes in catecholamines, which contribute to change in heart rate, metabolic rate, blood pressure, and alertness.[28,101]

The HPA axis also plays a key role in regulating the stress response of individuals. Activation of the HPA axis triggers the hypothalamus to secrete corticotropin-releasing factor (CRF), which activates the pituitary to release adrenocorticotropic hormone.[101] The adrenocorticotropic hormone then binds to G-protein-coupled receptors in the adrenal cortex, causing the release of cortisol, activating glucocorticoid and mineralocorticoid receptors throughout the brain.[167,168] Glucocorticoid

receptors act as transcription factors and regulate gene expression for several bodily functions, including cognitive and brain development, metabolism, and immune roles.[44,169]

Cortisol regulates the stress response system, both in the hippocampus and the prefrontal cortex, where it mitigates the stress response, and in the amygdala, where it functions to increase the stress response via CRF-1 receptors.[146] Through negative feedback, cortisol controls its secretion and inhibits the HPA axis, resulting in the body returning back to homeostasis.[44,146] Cortisol possesses a diurnal pattern; levels are typically high in the morning upon awakening, peak 20 minutes afterwards, then decrease progressively throughout the day.[99,103] Typically, cortisol and pituitary volumes are expected to increase with age as well.[44] In summary, this illustrates the typical scheme of how the stress response responds to stress, but if the stress becomes chronic or repeated, this can lead to dysregulation of the stress response.

Important Factors to Consider

Although research has demonstrated the impacts of stress on the brain, there are some critical factors to consider. The first is gender. Research has increasingly shown that there are important gender differences on how stress can impact biological systems.[44,81] One study, involving men and women who experienced trauma early in life, demonstrated a stronger association between trauma and increased corticotrophin releasing factor levels in men compared to women.[170] The second factor to consider is individual or genetic differences, which encompass an individual's behavioural and emotional responses.[42,44,148] Additionally, an individual's level of resiliency or vulnerability to chronic or repeated stress will determine the extent of adaptive or maladaptive changes in the brain and body systems.[165] Another important factor to take into consideration is

duration and/or timing of stress. Timing of adversity, whether it is a single event or chronic, age when adversity occurs, and stage of development influence cortisol levels following the event.[44] For example, low morning and daytime cortisol levels were shown in prepubertal children living in orphanages, suggesting that these children may be more sensitive to negative feedback of cortisol compared to older children who showed increased cortisol levels.[171–173] It is important to acknowledge and consider these factors, as research is still unraveling the possibilities and limits of child maltreatment.

Child Maltreatment and HPA Axis

Child maltreatment has been an expanding area of focus by researchers due to evidence showing its impact on the developing neural architecture.[31,174] Research also has shown that experience of adversity in childhood can cause major disruptions of regulatory processes of the HPA axis over a lifespan.[44,144,175]

Animal models have provided considerable insights into the differential responsivity to stress among different brain regions during early life. In one study, maternal care experienced by rat pups was investigated, and it was shown that the nature of maternal care could alter the response of the HPA axis.[175] The regions most affected included the amygdala, hippocampus, and prefrontal cortex, which are responsible for emotional behaviour, learning and memory, and aspects of executive functioning respectively.[42,148] These regions are most sensitive to stress when an abundance of glucocorticoid receptors are present, and exposure to prolonged stress has shown to alter the size and neuronal architecture of these areas.[148,176] In another study, CRF injections were found to produce delayed cognitive function, decreased number of CA3 hippocampal neurons, and decreased branching of hippocampal pyramidal neurons.[44,177]

Taken together, research has demonstrated early life adversity can lead to disruption in normal development.

Human studies have also shown how early life trauma can impact the brain. For example, children in the Helsinki birth cohort who were evacuated to temporary foster care during World War II showed higher rates of cardiovascular disease and depression compared to children who were not placed in foster care.[178,179] Research has also shown that child maltreatment and poverty are associated with heightened immune responses in adulthood that are now known risk factors for the development of diseases, including diabetes, asthma, cardiovascular disease, and chronic lung disease.[110,180] Children from lower socioeconomic background were also shown to have heightened activation of the stress response systems.[181,182] Not only has the early social environment been shown to play a formative role in the cognitive and socio-emotional development for that individual, research has also shown that this can impact subsequent generations.[42,81] There is growing evidence that trauma experienced in early life affects later generations, even though later generations never experienced those adverse situations.[81] Although there is mounting evidence between the link of childhood maltreatment and development of disease later in life, the underlying mechanisms that account for these developments are still being determined.[148] Researchers have postulated that early life adversity could affect adult health through two mechanisms: (1) accumulating damage over time, and (2) biological embedding. The first mechanism was previously described via the life-course perspective, and the second mechanism will now be discussed in more detail.

Epigenetics of Allostatic Load

Epigenetics was first coined by Waddington, who defined it as "above the genome" that regulates expression of genetic information without actually altering the

DNA sequence.[164] There are three main mechanisms under which epigenetic changes can occur: (1) DNA methylation, (2) histone modification, and (3) microRNA.[41,81,164] One area of epigenetics focused on assessing the effects of child maltreatment has revealed that increased methylation of CpG residues in the glucocorticoid receptor (GR) promoter results in lower GR expression and, hence, reduced capacity for glucocorticoid-mediated allostasis.[164,183] Further, biological embedding is the process by which gene expression can be altered due to environmental factors. There is a strong scientific consensus that the etiological environment modulates the expression of one's genotype.[148,166] Researchers have begun to explain the mechanisms through which adversity can alter one's genome as well as how they can be transferred to subsequent generations. Biological embedding via early life adversity is believed to lead to gene-environment interaction by modifying the neural circuits and physiological responses to stimuli later in life.[81,148]

Both animal studies and human evidence have provided greater insight on the mechanisms of transgenerational programming. Liu et al.'s study showed that maternal care experienced by rat infants could alter GR expression in the brain and alter the response of the HPA axis.[175] Subsequent work also showed that maternal care could also result in hyper-methylation of the GR promoter in the hippocampus and, therefore, alter GR expression and the sensitivity of the hippocampus to glucocorticoids.[44,154] Weaver et al. also demonstrated that increased pup licking and grooming (LG) and arched-back nursing (ABN) by rat mothers altered the offspring's epigenome at the GR promoter in the hippocampus. Specifically, they found that variations in maternal care directly modifed methylation of the exon 1_7 promoter of the GR gene, which was maintained into adulthood and associated with alterations in GR expression and HPA response to stress.[184] Building on this, McGowan et al. found alterations in the neuron-specific

glucocorticoid receptor (NR3C1) promoter of post-mortem suicide victims with a history of childhood abuse. In particular, when comparing to controls, suicide victims with a history childhood abuse had decreased levels of glucocorticoid receptor mRNA and mRNA transcripts bearing the glucocorticoid receptor 1_F splice variant, as well as increased cytosine methylation of the NR3C1 promoter.[183] Thus, research has continued to show how maternal care and early life experiences could potentially alter neural circuits and their response to stimuli in the environment through epigenetic modifications.[81] This can be applied to the Indigenous populations. The harsh environments of residential schools created adverse realities for the children.

Residential Schools as a Form of Maltreatment

Indigenous children were forced into residential schools at a young age by government law.[35,138] The extent of child maltreatment that occurred in these schools is now well known by scholars and the general public.[21] The range of the maltreatment included maternal separation; emotional, physical, and sexual abuse; and neglect.[21,138,185] The children were also underfed and suffered malnutrition, as schools were severely underfunded from the beginning.[137] Taken together, residential schools were quite traumatic for the children attending and have produced lasting impacts on survivors' health as well as subsequent generations.

It has been shown extensively that childhood is a critical period in the development of the brain. If trauma, such as the maltreatment experienced by residential school attendees, is experienced during childhood, this can have huge implications on their neural development, their health later in life, and the health of subsequent generations.[138,186] Stressors experienced in sensitive developmental periods also have enduring influences on allostasis and allostatic load.[26] Research has shown that childhood

stress predicts neurobiological, metabolic, and immune changes related to the development of disease later in life.[26,81] The underlying biological mechanisms at play need to be investigated more thoroughly in order to fully understand the process that is occurring. One way this can be explored is through the allostatic load framework, which was used for this thesis to explain the impacts of residential school stress.

What made the allostatic load model appealing is that it captures stress-associated risk beyond traditional stress-disease conceptualizations by combining cumulative stress and metabolic-associated risk that also incorporates behavioural health effects.[128] Ultimately, the ability of the allostatic load model to detect subtle changes in metabolic and neuroendocrine function and the associations of these markers with social disadvantage made allostatic load an attractive framework to target unequal distribution of disease burden, such as observed within the Indigenous populations.[128,130]

Although extensive literature discussed the extent of the trauma experienced by Indigenous children at residential schools, there has been little to date offering the biological impacts of residential school experience on the Indigenous population. This has highlighted a key gap in the literature. Based on this, the first two research questions for this thesis were: (1) *does parental residential school attendance result in a higher allostatic load score of their adult offspring*, and 2) do *offspring who believe the parenting they received as a child was negatively impacted by residential school have a higher allostatic load score?*

In summary, the interaction between the body and the brain with incoming stimuli from the environment involves many components, including several body systems, hormones, mediators, and excitatory amino acids, which is a very complex process. Hormones play a critical role in brain plasticity and represent an important channel of

communication between the brain and the body.[81,100] However, stress hormones progressively impair brain function, which increases cortisol levels and furthers impairment.[166] The concept of allostasis and allostatic load (AL) emphasize both protective and damaging effects of these hormones. These two concepts have helped researchers integrate the biology of stress with the psychosocial factors that promote stress-related health issues.[166] AL and the construction of its score by researchers provides predictive power in understanding how childhood trauma can *get under the skin* and affect health. In addition, the progressive work in the field of epigenetics compliments the work of allostasis and AL, showing how these neural changes can be stored in the genome's memory and passed on to subsequent generations.[187]

However, research has also revealed that behavioural responses can be passed along generations. Research has shown that individuals who experience adversity in childhood can later pass on behaviours to their children. This phenomenon can be explained via adverse childhood experiences.

Third Variable: Adverse Childhood Experiences

The treatment of Indigenous children in residential schools denied them a positive environment, which lacked positive parenting; additionally, the process stripped the children of a positive sense of identity and self-worth.[138] Residential school attendees have acknowledged being exposed to strict and regimented disciplines in the schools, resulting in them having difficulty being loving parents in the future.[21] Research has shown that individuals who show harsh or negative parenting style often have a history of adverse childhood experiences (ACEs).[23] This umbrella term encompasses child maltreatment, which will be explained in more detail. How ACEs can be passed on and

result in the intergenerational transmission of parenting behaviour will be explained in this section.

Background

The term ACEs is an umbrella term that includes child maltreatment as well other household dysfunctions. For the purpose of this report, ACEs are defined as an exposure to the following categories of experiences during an individual's childhood: (1) childhood abuse, which includes physical, emotional, or sexual abuse; or (2) exposure to household dysfunction, which includes exposure to mental illness, violent treatment of mother (or stepmother), and criminal behaviour.[29] That is, the concept of ACEs has been defined as childhood events that vary in severity and are often chronic or occur within a child's family or social environment that cause harm or distress, thereby disrupting the child's physical or psychological health and development.[174] This concept was first investigated in the United States. It was a cohort study that examined, both retrospectively and prospectively, the long-term impacts of abuse and household dysfunction during childhood.[29] Felitti et al. used a survey to collect data from participants. The ACE questionnaire was constructed using questions from various published surveys, including Conflicts Tactics Scale, Wyatt, The National Health Interview Survey, and Behavioural Risk Factor Surveys among others.[29]

Operationalization of Adverse Childhood Experiences

The original ACE study created what is now known as the ACE score.[29] This was used to indicate the total amount of adversity one was exposed to during childhood, and it showed that as the number of ACEs increased, the risk for a specific health problem increased as well.[29,188]

Dube et al.'s results showed that particular experiences are major risk factors for the leading causes of illnesses, including alcohol abuse, depression, illicit drug abuse, smoking, and suicide attempts.[189,190] Researchers illustrated well what an expanding body of research is suggesting: Childhood serves as a critical time in one's life, and if exposed to adversity, this can lead to a variety of problems, including substance abuse and behavioural issues later in life.[26,35,66]

In summary, research has shown a clear association between ACEs and their implications for adult health. In addition, the more adversity a child experiences, the greater the effect on physical and psychiatric health as well as behaviour.[29,174] As alluded to earlier, children attending residential school experienced poor parenting figures. This resulted in children often being abused and neglected, which resulted in children having high ACE scores. It is argued in this thesis that children attending residential school resulted in Indigenous children passing on their ACE scores, adopting those poor parenting behaviours, and passing them on with their offspring later in life, which will now be explored in further detail.

Intergenerational Transmission of Parenting Behaviour

Parenting style or behaviour is an important factor early on in their offspring's life. Parents bring their personality and personal history to their interactions with their children, which can influence their opinions and expectations about parenting and their parenting practices.[23,191] Individuals are highly sensitive to their social environment during early childhood. This period is characterized by children's rapidly developing brains, which are highly sensitive to social input, especially nurturing social experiences.[23] On the other hand, children are especially susceptible to adverse social experiences. One source of adversity can result from a parenting style that is harsh,

inconsistent, non-sensitive, or aggressive.[23] Parenting behaviour is particularly important in the early years of their offspring, when the motivation of neurophysiological systems make them receptive to and dependent on sensitive parenting care for their emotional and behavioural needs.[192] Growing literature has demonstrated that one of the most dominant predictors of parenting behaviours is how parents, mainly mothers, were parented themselves.[23]

A number of studies illustrated the intergenerational transmission of parenting style. In 1995, Knutson reported that a significant amount of mothers who were abused as children went on to abuse their own children compared to mothers who did not report abuse during childhood.[193] In another study, it was reported that mothers who were sexually abused in early life were less interested in becoming mothers themselves, and when they did, they demonstrated impaired parenting skills, including child neglect, diminished confidence in their parenting skills, increased negative self-appraisal as a parent, and greater use of physical punishment.[194] In 2008, Scaramella et al. conducted a prospective study of human participants and revealed that parenting in the first generation and second generation showed a significant amount of continuity in both harsh and positive parenting among males and females across the two generations.[195] This study was influential, in that it was an informative prospective study of intergenerational parenting that eliminated any bias typically associated with retrospective reports and was also valuable as it had a relatively large sample size.[23]

Animal models have also been used to study the transmission of parenting behaviour. Research has shown that rat pups who were artificially reared were shown to demonstrate typical maternal behaviour with their offspring, such as nesting, licking, and grooming of their offspring, and they displayed hovering, crouching, and nursing

behaviour, but when compared to the control rats, they exhibited these behaviours less frequently.[196,197]

Overall, animal and human studies have illustrated the intergenerational transmission of parenting behaviour to their children.[23,24] Children at residential schools were exposed to poor parenting models while attending. They grew up being exposed to ACEs, especially child maltreatment. The third research question of this thesis was: *Do ACE scores explain the association between parental exposure to residential school and allostatic load scores among the offspring of residential school survivors?*

Summary and Research Questions

Historically, colonial laws and their practices have been linked to health effects observed in Indigenous People. This literature review summarized what previous research has reported as well as highlighted some gaps. There is extensive knowledge about allostasis and AL and its implications with health, but there is a need for more research focused within Indigenous populations. Furthermore, research has acknowledged the devastating impacts of residential schooling on the Indigenous population, but little research has tried to link the residential school with ACEs and AL—as well as their roles on the development of intergenerational trauma within this population. While research has extended knowledge on these phenomena, it has failed to provide a biological explanation. This thesis has built on what was already been identified, by linking the impacts of residential schooling on the AL score of adult children of residential school survivors, not only through a possible direct relationship, but also through a possible mediator: ACEs to explain this complex association (Figure 1, Chapter 1). Lastly, not only does this illustrate the need for more research in this area, it can also potentially provide a basis for future research investigating the link between AL and the high amount

of health inequities observed in the Indigenous population. As mentioned previously, the research questions for this thesis were:

1. Does parental residential school attendance result in a higher allostatic load score of their adult offspring?
2. Do offspring who believe the parenting they received as a child was negatively impacted by residential school have a higher allostatic load score?
3. Do ACE scores explain the association between parental exposure to residential school and AL among the offspring of residential school survivors?

Chapter 2 Tables

Table 2-1. List of Original 10 Biomarkers Used in the MacArthur Study

10 Biomarkers	Cutoff
Systolic Blood Pressure/ Diastolic Blood Pressure	≥ 148/83
Waist-to-hip ratio	≥ 0.94
Ratio total Cholesterol (TC/HDL-C mg/dL)	≥ 5.92
Glycosylated hemoglobin (Hb_{AIc} %)	≥ 7.10
Urinary cort (ug/g cr)	≥ 25.7
Urinary NE (ug/g cr)	≥ 48
Urinary EPIN (ug/g cr)	≥ 5.0
HDL Cholesterol (mg/dL)	≤ 37
DHEA-S (ng/dI)	≤ 350.0

Table 2-2. List of Biomarkers for Allostatic Load Score			
1	Diurnal cortisol	Neuroendocrine	Salivary kit
2	Dehydroepiandrosterone (DHEA)	Neuroendocrine	Salivary kit
3	C-reactive protein (CRP)	Immune	Salivary kit
4	Systolic blood pressure	Cardiovascular	Blood pressure monitor
5	Diastolic blood pressure	Cardiovascular	Blood pressure monitor
6	Waist circumference	Metabolism	Measuring tape
7	Body mass index	Metabolism	Scale

CHAPTER 3: METHODS

Participants

Ethics approval was granted from the Human Research Committee at the University of Lethbridge (U of L). All participants (*N=100)* were post-secondary students who self-identified as First Nations, Inuit, or Métis, aged 18 years and older. Recruitment occurred via three methods: (1) posters; (2) Eaglesnest, which is a list-serve for Aboriginal students attending U of L; and (3) to a lesser extent using, the snowball effect. All participants were volunteers and had the option of stopping their participation in the study at any time

Study Design

This was a cross-sectional study that used mix-methods. Data were collected in a private office located on campus, as well as participants' homes. The study had three components: (1) an in-office survey and physical/biological measurements, (2) an at-home component, and (3) a qualitative survey. Participants were compensated $50 for the first component, $50 for completing the at-home component, and $25 for participating in the qualitative survey for a total honorarium of $125 for completion of the entire study.

Procedure

In-office data collection

At the initial meeting participants attended an in-office appointment during which they completed consent procedures. Physical and biological measures were then collected (i.e., height, weight, waist circumference, blood pressure, and saliva samples), and they completed a paper-and-pencil survey. The survey was divided into three sections. This was done to allow for physical measurements (i.e., blood pressure and salivary samples) to be taken at regular intervals during survey completion. During the data collection,

saliva samples were stored in the in-office freezer and transferred immediately to the lab freezer, which stored the samples at -80°C.

At-home data collection

After in-office data collection, participants were asked to provide at-home saliva samples over 2 days and wear an ActiLife accelerometer for a week. Instructions on how to collect the at-home samples and wear the accelerometer were provided to participants orally and in written form during their in-office visit (see Appendix A).

Saliva samples

Saliva samples were collected at three designated times during the appointment. Each time, participants were asked to fill 4 micro centrifuge tubes to the 1 mL line for a total of 12 tubes. Participants were provided with a saliva collection aid (Salimetrics, LLC, Carlsbad, CA, USA), which was inserted into the top of the tube to help transfer the saliva. Participants were asked to provide samples using the passive drool method[198] to ensure proper saliva samples were given.

The at-home saliva sample procedure was different from the in-office procedure. Participants were asked to place a cotton swab (Salimetrics, LLC, Carlsbad, CA, USA) under their tongue for 3 minutes, and then place the swab in a labeled tube. They were asked to store the samples in their freezer for the remainder of the week. The participants were asked to do the saliva samples upon wakening, half an hour after waking, and at bedtime. This was to be completed on 2 consecutive days when they woke up at similar times. Participants were also sent home with a small ice pack, which helped keep the samples cold when returning them. After one week, participants returned the saliva samples and accelerometer to the campus office. During this visit, they were asked to provide 4 final in-office saliva samples. These samples were collected using the in-office

procedure described previously. At-home saliva samples were stored in an in-office freezer during this procedure, and then transferred immediately to a lab freezer. The accelerometer and qualitative data were not used for this thesis as they did not pertain to my topic

Anthropometrics

Height, weight, and waist circumference were measured together towards the end of the appointment. Height and weight were measured using a Health O Meter Professional physician scale. This was used to calculate body mass index. To measure waist circumference, participants were asked to place their thumbs at the top of the iliac crest. The research assistant would then use measuring tape to measure the participant's waist in centimeters.

Blood pressure

Blood pressure was taken twice during the appointment. The study used a Life Source blood pressure monitor, and research assistants placed the cuff approximately two finger widths from the participant's elbow for each reading. Participants were also asked to rest their hands on the table to ensure an accurate reading.

Ethical Considerations

An Aboriginal Advisory Committee (AAC) was created for the main study and was utilized for this thesis project. The committee was comprised of key Elders and members of the Aboriginal community in the Lethbridge area. The purpose of this committee was to ensure that the data collection, and research project in general, was conducted in a culturally sensitive and respectful manner. The AAC was involved in the planning stage before the main study started; as well, they were consulted with any major decisions and/or changes.

Researchers have often conducted research on, instead of alongside, Indigenous people, with little regard to local cultural protocols and languages as well as not seeking consent from communities.[199] A number of studies have been published that have used blood samples taken from Indigenous peoples in ways that were not sanctioned by the Indigenous communities providing those samples.[200,201] Blood is considered a sacred element in many Indigenous cultures and must be respected in deep ways if it is to be used in research.[202] This belief ties in with Indigenous holistic beliefs about the body, self, culture, and nature and the idea that DNA is sacred.[202] Consultations with the AAC provided guidance on this study; the investigators selected saliva rather than blood for data collection.

As saliva is also a substance that comes from the body, a system was put in place to ensure the wishes of Indigenous participants were honoured. The consent form provided participants with the opportunity to have either their saliva samples returned to them upon analysis or to have their saliva samples included in a ceremony that would return the samples back to the Earth in a traditional Indigenous ceremony. Both options were optional. Participants recorded their choice on the consent form (see Appendix B). Overall, 16% chose to have their saliva returned to the Earth in ceremony, while approximately 2% requested their saliva be returned to them. Saliva is increasingly recognized as a valuable biospecimen for psychoneuroendocrinological research. It can provide information pertaining to a wide range of systems while still being less invasive than blood samples.[203,204]

Measures

Exposure Variable 1: Residential School Attendance

To examine the impacts of residential school on the offspring of survivors, participants were asked: "Did you have any family members attend residential school (check all that apply)." Participants could select mother, father, 1 or both grandmothers, 1 or both grandfathers, or no relatives attended.

Exposure Variable 2: Parenting Impacted by Residential School

The second variable was focused on the impacts of residential school on the parenting offspring received. This was examined by asking offspring: "Do you feel the way you were parented as a child was impacted by residential school?" Responses to this question were yes and no. Participants who attended residential school were removed prior to statistical analyses.

Outcome Variable: Allostatic Load Score

The most common method to calculate AL scores is a simple count of the number of biomarkers for which a participant falls into the highest risk quartile of each biomarker's sampling distribution.[80,80,130] Other methods include *z*-scores, bootstrapping, canonical correlations, recursive portioning, k-means cluster analysis, genetic programming, based symbolic regression algorithms and grade of membership methods.[80] For this thesis, seven biomarkers from four domains (i.e., cardiovascular, endocrine, metabolic, and immunological) were used to construct an AL score (see Appendix C).

AL scores were calculated using 75^{th} percentiles and, in some cases where biologically relevant for health, 25^{th} percentiles. Participants with a biomarker score above the 75^{th} percentile (or below the 25^{th} percentile where relevant) were given an AL score of 1. All other participants with non-missing values for a biomarker were given a

score of zero. The following 7 biomarkers were included in this score: (1) blood pressure: diastolic, (2) blood pressure: systolic, (3) body mass index (BMI), (4) waist circumference, (5) cortisol, (6) c-reactive protein (CRP), and (7) dehydroepiandrosterone sulfate (DHEA-S). A brief summary on the importance of each biomarker is provided.

1. Blood pressure: Diastolic blood pressure (BP) is a good indicator of future cardiovascular health outcomes, such as hypertension and cardiovascular disease.[91] The healthy range for this marker is not gender-based. A value of 80 mmHg is considered normal for both males and females. Typically, a diastolic BP of 90 mmHg is considered abnormal; however, the 75th percentile was used to determine the cut-off to be consistent throughout the construction of the AL score

2. Blood pressure: Systolic was collected as a second measure of the cardiovascular system function. All other participants with non-missing values were given a score of zero. Both diastolic and systolic blood pressures were measured twice for each participant, and only the second measure was used in the analysis.

3. Body mass index (BMI): height and weight were collected in order to calculate BMI. Height was measured to the nearest 0.5cm and weight was measured to the nearest 0.1Kg to ensure measurement sensitivity. BMI is calculated as the ratio of weight to height squared (kg/m^2).

4. Waist circumference is a marker for visceral adipose tissue, which is linked to the development of diabetes.[90] Waist circumference is gender dependent. A waist circumference of 94 cm or more in men and 80 cm or more in women indicates the need for weight management and suggests an increased risk for cardiovascular disease.[83]

5. Cortisol is a marker of hypothalamic-pituitary-adrenal axis (HPA axis) functioning.[167] For this thesis, the awakening response was used, which is referred to as

the cortisol awakening response (CAR). CAR is characterized by a substantial increase in cortisol is normally observed 30 minutes after awakening (50-160%), and an ensuing decline is observed over the remainder of the day.[97,205] This was selected over other methods, as it provides a better overall sense of potential abnormal cortisol levels and, hence, HPA axis dysfunction. Cortisol was measured using the Enzyme-linked Immunosorbent assays (ELISAs) from Salimetrics LLC, Carlsbad, CA, USA.

The at-home samples were used to calculate participant CAR values, utilizing the percentile method to assign a 0 or 1 for their AL score. Both the 25th and 75th percentiles were used to capture cases that had abnormal low and high CAR values. Cortisol was taken in-office, but also had an at-home component. Prior to determining the percentiles, cases above 2 standard deviations were removed (μ = 8:12 am, *SD* = 1:57). A total of 2 cases were removed, as they had a wake up time after 12:06 pm. Cases who had a time difference greater than 45 minutes between waking up (sample B-1) and his/her second sample (B-2) were removed. A total of 9 cases were removed.

6. C-reactive protein (CRP) is a marker of inflammation and immune system functioning. High levels of circulating CRP (> 10 mg/L) are an indication of acute infections or inflammatory disease[113], whereas intermediate levels of CRP are associated with chronic inflammation and increased risk of cardiovascular disease.[114,115] CRP was measured in-office only and was obtained via participant's saliva. CRP was measured using the Enzyme-linked Immunosorbent assays (ELISAs) from Salimetrics LLC, Carlsbad, CA, USA.

7. Dehydroepiandrosterone sulfate (DHEA-S) is useful in understanding the regulation of the neuroendocrine system given it acts to counter-regulate cortisol.[117,125] For DHEA-S, the 25th percentile was used because lower values in the body indicate

abnormality. That is, healthy individuals should have higher DHEA-S levels. DHEA-S was obtained via participants' saliva and was also measured in-office only. DHEA-S was measured using the Enzyme-linked Immunosorbent assays (ELISAs) from Salimetrics LLC, Carlsbad, CA, USA.

Potential Mediation Variable: Adverse Childhood Experiences

Adverse childhood experiences (ACEs) were examined as a potential mediator. Using the standard measure of ACEs by Felitti et al.,[29] 10 questions addressed the following experiences among participants in their first 18 years of life. Response options were yes and no: Physical abuse (in the form of being pushed, grabbed, slapped, or having an object thrown at them); sexual abuse; emotional abuse (including being sworn at, insulted, put down or humiliated); emotional neglect; physical neglect; parental substance abuse; parent incarceration; witnessing abuse of a female caregiver; and parental separation. The ACE score constitutes the summed number of yes responses.[29,206]

Covariates

Sociodemographic factors examined included age, gender, perceived household income (i.e., upper income, upper-middle income, middle income, lower-middle income, and lower income), and parent's education (i.e., Grade 9 or less, some high school, high school diploma, some college or university, or college and university degree). Income was asked in this manner to improve validity, given university students may not know their household income while living with their parents, but may have an understanding of their perceived socioeconomic status. Given that recruitment was mainly of post-secondary students, participants' level of education was not asked, but instead, participants were asked whether they were in full- or part-times studies.

Statistical Analysis

All analyses were conducted using SPSS 24. Descriptive analyses were used to examine sample characteristics. Demographic information and trends were presented via means, modes, standard deviation, and cross-tabs.

Initially, linear regression models were going to be used for the analyses, but upon the initial stages of the analyses it was discovered that the outcome variable was skewed toward low scores. One of the assumptions for linear regression is normality of data.[207] Due to this violation, multinomial logistic regression was decided on instead and data were collapsed into terciles. Participants with a total AL score of 0 or 1 were classified as *low allostatic load score*s. Those with a score of 2 or 3 were categorized as *mid allostatic load scores*. Those with a total score of between 4 and 7 were classified as *high allostatic load scores*.

The mediating variable, adverse childhood experiences, was skewed to low scores as well. The total adverse childhood experiences scores were collapsed into three groups based on terciles. The *low ACEs* group consisted of people who had a score of 0 through 2. The *mid-ACEs* group included people who had a score of 3 through 5. The *high ACEs* group included people with a score of 6 through 10.

Parental Residential School Attendance and Offspring Allostatic Load

To examine the first research question and the first exposure variable, multinomial logistic regression and 95% confidence intervals were used to assess the association between parental residential school attendance and the AL score of offspring. The low-AL score group (0-1) was used as the reference, given the focus was to examine the factors associated with an increased AL score. Two multinomial logistic regression models were derived; the first without adjustment for confounders, and the second

adjusted for confounders selected a priori (i.e., age, gender, parent education, and perceived socioeconomic status).

Parenting Impacted by Residential School and Offspring AL

To examine the second exposure variable, two sets of multinomial logistic regression models and 95% confidence intervals assessed the association between parenting being impacted by residential school and the AL score of offspring. Again, the low-AL score group was used as the reference. The first model was unadjusted. The second model was adjusted for age, gender, parent education, and perceived socioeconomic status. Potential confounders were tested for effect modification before entry into main effects model; none were indicated. Data were not replaced for participants with missing data; these individuals were excluded from the analyses.

Mediation Model

A mediation analysis is used to investigate the processes underlying the observed relation between an independent and dependent variable once a relation has been established between the two variables.[208] Although regression models establish an association between the independent and dependent variable, it does not translate into a deep understanding of this relationship.[209] A mediation model helps to understand why an association between *X* and *Y* may be occurring by examining how *X* exerts its effect on *Y* and when *X* affects *Y*.[208,209]

The third research question was meant to determine whether the passing on of ACEs mediates the pathway through which residential school attendance influences AL scores. That is, I wanted to test the extent to which ACEs explain the association between residential school attendance and the AL score of offspring (Figure 1-1, Chapter 1). I chose to use a mediation model to test whether there are direct impacts of residential

school attendance on AL scores of offspring after accounting for the impacts of residential school on the parenting behaviour of survivors. An adjusted multinomial logistic regression model was selected to test an association between ACEs and AL scores.

Given ACE scores were skewed towards the low end, they were collapsed into terciles for mediation testing. Perfectly sized terciles could not be achieved given the distribution of scores. As a result, 38% of the samples were categorized into a low ACE score group, 39% into a mid-ACE score group, and 23% into the high ACE score group.

In summary, a mediation model was utilized to examine:

1. Whether there is an association between exposure variable "parental residential school attendance" and the mediator (ACEs), which is quantified by path *a* (Figure 1-1, Chapter 1);
2. If the mediator is associated with the outcome variable, *Y* (AL score), which is quantified by path *b*; and
3. To examine whether the mediator (ACEs) accounts for the *X*-*Y* association, which is pathway *a***b*, (the indirect effect representing the pathway from *X* to *Y* through *M*.[25])

The Hayes method[25] was selected for the mediation analyses, as it provides a single test of mediation (*a***b*).[210] Previous approaches using the Baron and Kenny method examined the reduction of the *c* path estimate when the variance provided by the *a* and *b* path are removed (i.e., *c´* path).[210,211] With this method, if an independent variable has a strong effect on a mediator (*a* pathway), there could be limited possibility for the mediator to be significantly associated with the dependent variable.[210] In addition, the Sobel test was the most used statistical tool to test for the indirect effect, but it is

conservative and overly sensitive with small to moderately sized samples.[210,212] This is due to the Sobel test assuming a normal sampling distribution. The Hayes method makes no assumption regarding the underlying sample distribution, given bootstrapping is used to determine significance.[25,210] Bootstrapping is a non-parametric method based on resampling with replacement from the data set. As a result, data are treated as a population from which smaller samples are utilized, which is done numerous times (e.g., 5,000x) from each of the samples.[213] The indirect effect is calculated, and a sampling distribution is then empirically generated.[25] The estimate of the indirect effect was the mean *a*b* value calculated over the samples, with 95% confidence intervals determined from the *a*b* scores.[210] If the upper and lower bounds of these bias-corrected confidence intervals did not contain zero, then the indirect effect was considered significant.[25,210,212]

CHAPTER 4: RESULTS

Sample Description

The mean age of the sample was 28 years (*SD* = 8.4, range = 18 to 57 years). Initially the sample size was *N* = 114, but 11 cases were removed for not complying with guidelines for at-home samples, which were used for cortisol. An additional 13 cases were removed for individuals who attended residential school, leaving the sample *n* = 90. As shown in Table 4-1, the sample (*N* = 90) was 77% female. Please note that tables are presented at the end of this chapter. The majority of participants identified as First Nations (63%). Approximately 50% of participants were single, with almost two-thirds growing up in lower-middle or low-income households. One-quarter of participants' fathers, and almost one-third of participants' mothers had completed a post-secondary degree. Approximately 37% of participants were raised in a First Nations community, with 89% having treaty-status.

Parental Residential School Attendance Variables

Overall, 85% of participants had at least one family member attend residential school. Within this subsample, 28% reported 1 family member had attended, while 16% reported at least 4 family members had attended (*Mean* = 1.88, *SD* = 1.28). Two participants did not know if their relatives had attended residential school; they were excluded from the analysis. As shown in Table 4-2, 42% of participants indicated their mother had attended residential school, and 86% of participants in this subgroup were raised by their mother. Almost a third of participants indicated their father attended residential school; 68% of participants in this sub group were raised by their father. The breakdown of parental residential school attendance is shown in Figure 4-1.

When asked, more than half (59%) of all participants who had family members attend residential school felt the parenting they received as a child was negatively impacted by this experience. There were 13 valid skips for this question, representing participants who did not have family members attend residential school.

Allostatic Load

The most common method to calculate AL scores is a simple count of the number of biomarkers for which a participant falls into the highest risk quartile for a biomarker's sampling distribution.[76] This is the method used for this thesis. Seven biomarkers were collected and participants with a biomarker score above the 75th percentile (or below the 25th percentile where relevant) were given an AL score of 1. All other participants with non-missing values for a biomarker were given a score of zero. Participants were most likely to fall into the high-risk quartile for the following biomarkers: cortisol awakening response (43%), waist circumference (31%), and body mass index (30%). Participants were least likely to fall into the high-risk quartile for DHEA-S (20%). Information on the percentage of participants who were categorized in the high-risk quartile for each biomarker, stratified by age and gender is provided in Table 4-3.

AL scores ranged from 0 to 6 in this study (*median* = 2.0, *SD* = 1.51). Almost two-thirds of participants (62%) had an AL score of 2 or less. Only two participants (2%) received a score of 6. The AL score was skewed toward the lower end of the distribution, and not normally distributed, which is one of the assumptions for linear regression.[207] Scores were collapsed into terciles to address this issue. Perfectly sized terciles could not be achieved given the distribution of scores. Thus, 38% of the samples were categorized into the low AL group, 40% into the mid-AL group, and 22% into the high AL group.

The breakdown of AL scores is shown in Figure 4-2. As shown in Table 4-4, older participants were significantly more likely to be in the high AL group, as compared to younger participants, which is expected and underlines the importance of controlling for age as a confounder.

Research Question 1. Parental Residential School and Offspring Allostatic Load

The first research question examined whether adult offspring who had parents attended residential school had higher AL scores than adult offspring who did not have parents attend residential school. To examine research question 1, multinomial regression was used to test associations between parental residential school attendance and offspring AL score. The reference groups were parents (mother or father) who did not attend residential school (see Table 4-5).

Maternal Residential School Attendance

In an unadjusted model, participants whose mother attended residential school were 5.0 times more likely to have an AL score in the mid-range (score 2 to 3) than the low range (score 0 to 1), as compared to participants who did not have a mother attend residential school (*OR* = 5.0, 95% *CI* = 1.70, 14.5). After controlling for age, gender, mother's education, and perceived socioeconomic status growing up, participants who had a mother attend residential school were 12.6 times more likely to have an AL score in the mid-range than the low range (*OR*= 12.6, 95% *CI* = 2.94, 53.8) as compared to participants who did not have a parent attend residential school. Participants who had a mother attend residential school were not significantly more likely to have an AL score in the high-range than the low range (*OR*= 2.70, 95% *CI* = 0.59, 12.42), as compared to participants who did not have a mother attend residential school in unadjusted or adjusted models. Further, for individuals who had a grandmother attend residential school there

was no significant association with offspring AL scores in unadjusted or adjusted models. The breakdown results can be found in table 4-5

Paternal Residential School Attendance

The mean AL score for individuals who had a father attend was 2.5 (*SD* = 1.80) compared to individuals whose father did not attend 1.98 (*SD* = 1.33). In unadjusted and adjusted multinomial logistic regression models, father's residential school attendance was not significantly associated with offspring AL score. Individuals who had a grandfather attend residential school had a mean AL score of 2.3 (*SD* = 1.48) compared to individuals who did not have a grandfather attend residential school 2.0 (*SD* = 1.56). However, grandfather residential school attendance was not significantly associated with offspring AL scores in unadjusted or adjusted models. The breakdown results can be found in table 4-5.

Research Question 1: Post Hoc Analysis

I decided to conduct post hoc testing given not all participants who had parents attend residential school were raised by their parents. A goal of my thesis is to examine the physiologic impacts of residential school on the offspring of residential school survivors operationalized through AL score. It may be theorized that the traumatic stress experienced by the majority of residential school survivors may be passed down to their offspring through transgenerational processes, given the strength of epigenetic research in this area to date.[214,215] If this is the case, it would not matter whether offspring were actually raised by residential school survivors – their AL scores would be affected regardless. However, it is more probable to theorize that traumatic stress may be passed down to offspring via epigenetic *and* behavioural pathways. That is, having a parent attend residential school and being raised directly by that parent may impact offspring AL

score more strongly given residential schools survivors have been shown to experience severe mental health consequences (e.g. PTSD, addictions),[21] which may impact their interactions with their offspring.

To examine this, I separated participants who had a parent attend residential school into two groups based on whether they were raised by those parents. First, I looked at caregiver mothers. Participants who had a mother attend residential school but were not raised by that parent were removed from the analysis (n = 14). Two multinomial regression models were then used to examine whether being raised by a mother who attended residential school was associated with an increased AL score, as compared to being raised by a mother who did not attend residential school (N = 76). The first model was unadjusted, and the second model adjusted for offspring age, gender, perceived socioeconomic status, and mother's education. In an unadjusted model, participants who were raised by a mother who attended residential school were 4.7 times more likely to have an AL score in the mid-range (score 2 to 3) rather than a AL score low range (score 0 to 1), as compared to individuals who did not have a mother attend residential school. In an adjusted model, individuals who had a caregiver mother attend residential school were 12.3 times more likely to have an AL score in the mid-range rather than the low range, as compared to being raised by a mother who did not attend residential school. Participants who were raised by a mother who attended residential school were not significantly more likely to have an AL score in the high-range than the low range (OR= 2.17, 95% CI = 0.43, 11.0) as compared to being raised by a mother who did not attend residential school in unadjusted or adjusted models.

In summary, after adjusting for confounders individuals who had a mother attend residential school were 12.6 more likely to have an AL score in the mid-range (score 2 to 3) rather than a AL score low range (score 0 to 1), as compared to individuals who did not have a mother attend residential school. In addition, in an adjusted model, individuals who had a caregiver mother attend residential school were 12.3 times more likely to have an AL score in the mid-range (score 2 to 3) rather than a AL score low range (score 0 to 1), as compared to individuals who did not have a mother attend residential school. Overall, the results of this post-hoc tests suggest the impacts of maternal residential school attendance on offspring AL score were similar. Whether offspring were actually raised by their mother or not had little impact on the results.

These post hoc tests were repeated for the fathers of offspring in the sample. The first multinomial regression model was unadjusted, and the second adjusted for offspring age, gender, perceived socioeconomic status, and father's education (n = 72). Non-caregiver fathers were removed prior to analysis (n = 18). In an unadjusted model, individuals who were raised by a father who attended residential school were not significantly more likely to have an AL score in the mid-range (*OR* =1.07, 95% *CI* = 0.31, 3.67) nor the high-range (*OR* = 2.88, 95% *CI* = 0.72, 11.5) compared to individuals who were raised by a father who did not attend residential school. In an adjusted model, individuals who had a caregiver father attend residential school were not significantly more likely to have an AL score in the mid-range (*OR* =0.78, 95% *CI* = 0.19, 3.15) nor the high-range (*OR* = 1.49, 95% *CI* = 0.26, 8.73) compared to a caregiver father who did not attend residential school.

Research Question 2: Negative Impacts of Parental Residential School and Offspring Allostatic Load

My second research question sought to examine whether offspring who believed the parenting they received as a child was negatively impacted by residential school had a higher AL score then other participants in the study. Findings indicate almost 60% of participants believed the parenting they received as a child was negatively impacted by the residential school experiences of their parent or grandparent caregiver. The mean AL score for individuals who believed the parenting they received was negatively impacted by their caregiver's attendance was 2.26 (*SD* = 1.55), compared to the rest of the sample 2.03 (*SD*= 1.50). Multinomial logistic regressions were used to examine the association between participants who felt the parenting they received as a child was negatively impacted by parental residential school attendance and their AL scores. In an unadjusted multinomial model there was no significant difference in AL score between individuals who felt the parenting they received was negatively impacted as compared to the rest of the sample. As shown in Table 4-7, adjustment for offspring age, gender perceived socioeconomic status and parent's education did not impact these results.

Research Question 3: Mediation by ACEs

My third research question examined whether the parental impacts of residential school attendance on offspring AL score could be explained by higher adverse childhood experiences (ACEs) among offspring. It is well documented that parents who experience harsh discipline and abuse in childhood, which was the norm in residential school[21], often experience mental distress and addictions in adulthood, and some may also discipline their children in similarly harsh ways given this is the way that parenting was modeled to them.[216] Thus, I hypothesized that a potential pathway through which parental residential

school attendance could impact offspring AL was through higher ACE scores among offspring.

ACEs were measured by asking participants if they experienced any of the following during childhood: emotional neglect, physical neglect, emotional abuse, physical abuse, sexual abuse, parental substance abuse, parent incarceration, witnessing abuse of a female caregiver, parent suffering from mental health, and parental separation. Participants received a score of 1 for each item endorsed (maximum score 10). The mean ACE score for the full sample was 3.76 (*SD* = 2.59, range = 0 to 10), with the majority endorsing a score of 5 or less. As shown in Table 4-8, 38% had a score between 0 and 2, while approximately one quarter had high scores (≥6). Only two participants endorsed the maximum score of 10. The most frequent experience was living with a parent struggling with substance misuse (71%). The second most frequent ACE was parental separation (66%). The least frequent ACE was physical neglect, with only 17% responding yes to this item.

Among participants who had family attend residential school the mean ACE score was 4.03 (*SD* = 2.61, range, 0 to 10). This was higher than participants who did not have family attend residential school (*M* = 2.38, *SD* = 1.98, range = 0 to 9). The most frequent ACEs reported by participants who had family attend residential school were a parent struggling with substance misuse (74%), parental separation (67%), and parent suffering from mental health (49%). The least frequent ACE was physical neglect, with only 15.7% responding yes.

Mediation Testing

Given ACE scores were skewed towards the low end, they were collapsed into terciles for mediation testing. Perfectly sized terciles could not be achieved given the distribution of scores. As a result, 38% of the samples were categorized into a low ACE score group, 39% into a mid-ACE score group, and 23% into the high ACE score group. As shown in Figure 4-3, the mediational model involved three steps using the Preacher and Hayes Method.[209] First, mediational analyses of the association between parental residential attendance and offspring's AL scores began with a test of the hypothesized *a* pathway. Second, the testing of the *b* pathway between offspring's ACE scores and their AL scores. The final mediation step is the analysis of the indirect *ab* pathway.

Mediation Step 1 (*a* pathway)

A multinomial logistic model was used to determine if there was an association between caregiver residential school attendance and ACEs. After controlling for age, gender, mother's education, and perceived socioeconomic status growing up, participants who had a caregiving mother attend residential school were 4.6 times likely to have an ACE score in the high-range (6 to 10), rather than an ACE score in the low range (0 to 2), as compared to the rest of the sample. Participants who had a caregiver mother attend residential school were not significantly more likely to have an AL score in the mid-range than the low range (*OR*= 2.52, 95% *CI* = 0.66, 9.66) as compared to participants who did not have a caregiver mother attend residential school

Mediation Step 2 (*b* pathway)

A multinomial logistic model was used to determine if there was an association between ACEs and AL scores. After controlling for age, gender, parent's education, and perceived socioeconomic status growing up, it was found that ACEs were not

significantly associated with AL scores in the mid-range (*OR* = 0.95, 95% *CI* = 0.76, 1.19), nor the high range (*OR* = 1.02, 95% *CI* = 0.77, 1.34), indicating that ACEs are not associated with AL scores. Typically with mediation, linear regressions are used to test associations between the variables.[209] In instances, where categorical variables are being used, it's been suggested to use logistic regression as an alternative to linear regression.[217] Multinomial logistic regression is just an extension of logistic, and was used instead, as it allows for more than two categories in the outcome variable.[213]

Mediation Step 3 (*C'* pathway)

The final mediation step is the analysis of the indirect *ab* pathway. This was not tested given pathway b is not significant. As a result, mediation could not proceed.[209]

Chapter 4: Tables and Figures

Table 4-1. Characteristics of sample

Characteristic	*N* = 90
Gender	
Men	21 (23.3%)
Women	69 (76.7%)
Age	
18-24	38 (42.2%)
25-34	32 (35.6%)
35+	20 (22.2%)
Aboriginal Group	
Aboriginal	19 (21.1%)
First Nation	57 (63.3%)
Metis	14 (15.6%)
Marital Status	
Married	9 (10.0%)
Common law	29 (32.2%)
Widowed/Divorced/Separated	7 (7.8%)
Single	45 (50.0%)
Mother's Education	
Less than secondary grad	14 (15.7%)
Secondary grad	14 (15.7%)
Some post-secondary	29 (32.6%)
Post-secondary grad	31 (34.8%)
Father's Education	
Less than secondary grad	24 (27.3%)
Secondary grad	15 (17.0%)
Some post-secondary	19 (21.6%)
Post-secondary grad	22 (25.0%)
Household Income Growing Up	
Upper/Upper-middle	9 (10.0%)
Middle income household	28 (31.1%)
Lower-middle household	29 (32.2%)
Low income household	24 (26.7%)
Status	
Treaty or Status	80 (88.9%)
Non-Status	10 (11.1%)

Table 4-2. Comparison of residential school attendance between caregivers and non-caregivers

(*N* = 90)	Residential School Attendance		
	Caregiver	Non-Caregiver	**Total**
Caregivers			
Mother	30 (85.7%)	5 (14.3%)	35
Father	19 (67.9%)	9 (32.1%)	28
Grandmother	32 (62.7%)	19 (37.3%)	51
Grandfather	16 (40.0%)	24 (60.0%)	40

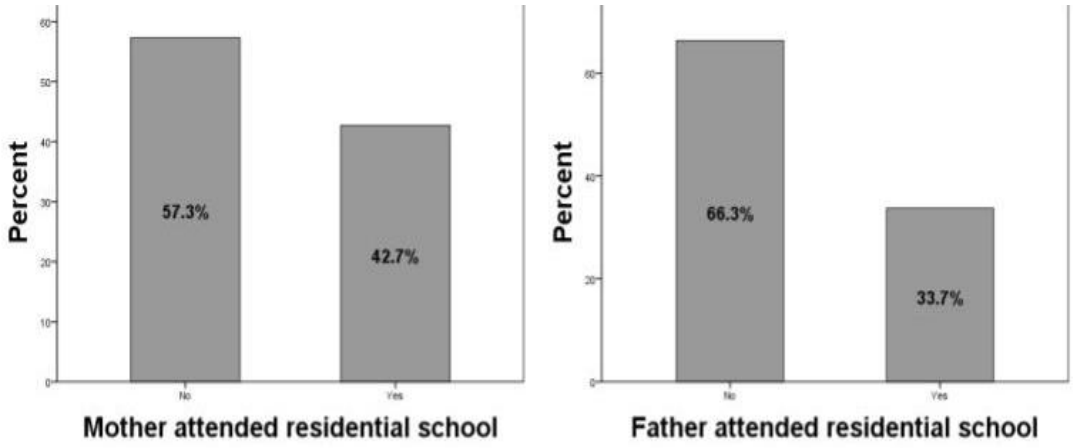

Figure 4-1. Parental residential school attendance

Table 4-3. Breakdown of individual allostatic load (AL) markers by frequency of participants who received a score of 1 for each

	Gender		Age Groups		
	Males	Females	18-24	25-34	35+
1) Cortisol Awakening Response	9 (47.4%)	26 (41.9%)	16 (44.4%)	12 (41.4%)	7 (43.8%)
2) Waist Circumference	7 (33.3%)	21 (30.4%)	5 (13.2%)	11 (34.4%)	12 (60.0%)
3) BMI	4 (19.0%)	23 (33.3%)	6 (15.8%)	11 (34.4%)	10 (50.0%)
4) Diastolic Blood Pressure	7 (33.3%)	17 (24.6%)	5 (13.2%)	8 (25.0%)	11 (55.0%)
5) Systolic Blood Pressure	9 (42.9%)	15 (21.7%)	6 (15.8%)	9 (28.1%)	9 (45.0%)
6) C – Reactive Protein	4 (19.0%)	18 (26.1%)	12 (31.6%)	6 (18.8%)	4 (20.0%)
7) DHEA-S	4 (19.0%)	17 (20.3%)	7 (18.4%)	6 (18.8%)	5 (25.0%)

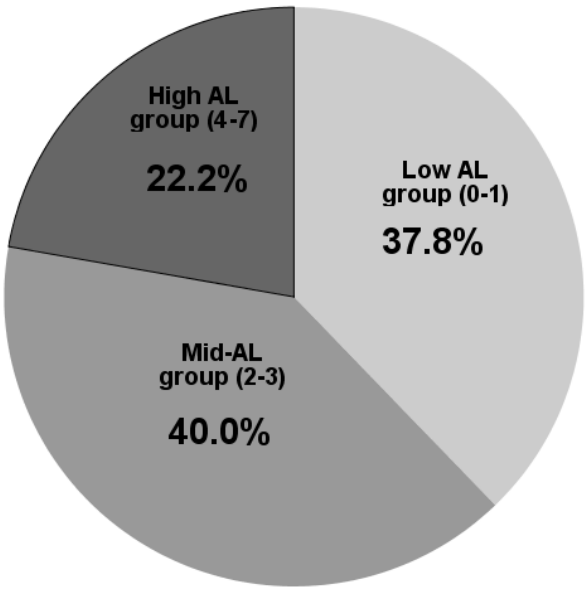

Figure 4-2. The AL scores of participants categorized into three groups.

Table 4-4. AL scores stratified by gender and age

	Allostatic Load Category			
	Low	Mid-Range	High	Significance
Total sample (*N=90*)	34 (37.8%)	36 (40.0%)	20 (22.2%)	
Gender				
Males	8 (38.1%)	9 (42.9%)	4 (19.0%)	
Females	26 (37.7%)	27 (39.1%)	16 (23.2%)	
Age groups				
18-24	18 (47.4%)	18 (47.4%)	2 (5.3%)	X^2 (4, *N*=90) = 19.40, *p* = 0.001
25-34	13 (40.6%)	12 (37.5%)	7 (21.9%)	
35+	3 (15.0%)	6 (30.0%)	11 (55.0%)	

Table 4-5. Unadjusted and adjusted odds ratios of allostatic load by parental residential school attendance (*N* = 90*)*

Variables	Model 1				Model 2			
	Mid AL scores OR (95% CI)	SE	High AL scores OR (95% CI)	SE	Mid AL scores OR (95% CI)	SE	High AL scores OR (95% CI)	SE
Mother attendance	**5.0 [1.70, 14.53]**	0.55	0.65 [0.21, 2.03]	0.59	**12.6 [2.94, 53.84]**	0.74	2.70 [0.59, 12.40]	0.78
Age					**1.15 [1.04, 1.28]**	0.05	**1.24 [1.10, 1.39]**	0.06
Gender					0.63 [0.16, 2.44]	0.69	1.94 [0.33, 11.30]	0.82
Mother's Education					**2.12 [1.23, 3.68]**	0.28	1.61 [0.96, 2.72]	0.27
SES Growing Up					1.05 [0.55, 2.03]	0.33	1.42 [0.66, 3.04]	0.39
Father attendance	0.77 [0.27, 2.21]	0.54	2.81 [0.89, 8.90]	0.59	0.59 [0.18, 1.97]	0.62	1.55 [0.38, 6.37]	0.72
Age					1.05 [0.97, 1.14]	0.04	**1.18 [1.08, 1.30]**	0.05
Gender					0.66 [0.20, 2.25]	0.62	1.85 [0.30, 11.5]	0.84
Father's Education					1.33 [0.94, 1.89]	0.18	0.89 [0.58, 1.35]	0.22
SES Growing Up					0.81 [0.45, 1.45]	0.30	0.92 [0.42, 2.02]	0.40
Grandmother attendance	2.06 [0.77, 5.54]	0.51	1.24 [0.38, 4.04]	0.60	1.74 [0.61, 4.96]	0.53	0.91 [0.22, 3.75]	0.72
Age					1.05 [0.97, 1.13]	0.04	**1.18 [1.08, 1.30]**	0.05
Gender					0.87 [0.26, 2.87]	0.61	1.93 [0.35, 10.8]	0.88
SES Growing Up					0.69 [0.40, 1.19]	0.29	1.02 [0.51, 2.06]	0.36
Grandfather attendance	1.07 [0.41, 2.73]	0.48	1.06 [0.35, 3.23]	0.56	1.19 [0.45, 3.17]	0.50	1.71 [0.68, 7.98]	0.66
Age					1.05 [0.98, 1.13]	0.04	**1.19 [1.09, 1.30]**	0.05
Gender					0.73 [0.23, 2.34]	0.59	2.01 [0.37, 10.9]	0.86
SES Growing Up					0.64 [0.37, 1.11]	0.28	1.02 [0.51, 2.04]	0.36

* Significant results ($p < 0.05$) are provided in **bold**. Outcome variable (AL scores) used the low AL scores as the reference group for analysis. An unadjusted estimate of the association between parental residential school attendance and allostatic load scores is presented in Model 1. An estimate adjusted for age, gender, perceived socioeconomic status growing up, and parent's education is presented in Model 2.

Table 4-6. Unadjusted and adjusted odds ratios of allostatic load by caregiver's residential school attendance (*N = 76*)

	Unadjusted Model 1				Adjusted Model 2			
	Mid AL scores OR [95% CI]	SE	High AL Scores OR [95% CI]	SE	Mid AL scores OR [95% CI]	SE	High AL Scores OR [95% CI]	SE
Caregiver Mother's Attendance	**4.67 [1.48, 14.8]**	0.59	0.55 [0.16, 1.89]	0.60	**12.3 [2.59, 58.5]**	0.80	2.17 [0.43, 11.01]	0.83
Age					**1.18 [1.05, 1.31]**	0.06	**1.25 [1.11, 1.41]**	0.06
Gender					0.65 [0.16, 2.63]	0.71	3.62 [0.48, 27.49]	1.00
Perceived SES growing up					0.78 [0.39, 1.53]	0.35	1.06 [0.51, 2.21]	0.38
Mother's education					**1.98 [1.09, 3.62]**	0.31	1.43 [0.78, 2.62]	0.31
Caregiver Father's Attendance	1.29 [0.42, 3.95]	0.57	2.57 [0.68, 9.68]	0.68	0.78 [0.19, 3.15]	0.71	1.49 [0.26, 8.73]	0.90
Age					1.05 [0.96, 1.16]	0.05	**1.26 [1.11, 1.43]**	0.06
Gender					0.84 [0.23, 3.13]	0.67	2.11 [0.27, 16.74]	1.06
Perceived SES growing up					0.76 [0.41, 1.41]	0.32	0.92 [0.35, 2.41]	0.49
Father's education					**1.53 [1.04, 2.26]**	0.20	1.03 [0.61, 1.73]	0.27

* Significant results ($p < 0.05$) are provided in **bold**. Outcome variable (AL scores) used the low AL scores as the reference group for analysis. An unadjusted estimate of the association between parental residential school attendance and allostatic load scores is provided in Model 1. An estimate adjusted for age, gender, perceived socioeconomic status growing up, and parent's education is provided in Model 2.

Table 4-7. Unadjusted and adjusted odds ratio of AL for participant's who believe the parenting they received was impacted by residential school (N= 90)

Variables	Model 1				Model 2			
	Mid AL scores OR (95% CI)	SE	High AL scores OR (95% CI)	SE	Mid AL scores OR (95% CI)	SE	High AL scores OR (95% CI)	SE
Felt Parenting was impacted by RS	1.30 [0.49, 3.40]	0.49	0.66 [0.20, 2.16]	0.60	1.08 [0.36, 3.22]	0.56	0.89 [0.20, 3.96]	0.77
Age					1.06 [0.98, 1.15]	0.04	**1.21 [1.09, 1.34]**	0.05
Gender					0.67 [0.18, 2.45]	0.66	1.80 [0.28, 11.78]	0.96
Mother's Education					**1.66 [1.03, 2.66]**	0.24	1.49 [0.89, 2.49]	0.26
Father's Education					1.19 [0.83, 1.71]	0.18	0.85 [0.56, 1.31]	0.22
Perceived SES Growing Up					0.89 [0.48, 1.64]	0.31	1.06 [0.47, 2.41]	0.42

* Significant results ($p < 0.05$) are provided in **bold**. Outcome variable (AL scores) used the low AL scores as the reference group for analysis. An unadjusted estimate of the association between parental residential school attendance and allostatic load scores is presented in Model 1. An estimate adjusted for age, gender, perceived socioeconomic status growing up, and parent's education is presented in Model 2.

Table 4-8. Characteristics of adverse childhood experiences among sample

	Adverse Childhood Experiences		
	Low ACEs (0-2)	Average ACEs (3-5)	High ACEs (≥6)
Total sample (*N=90*)	34 (37.8%)	35 (38.9%)	21 (23.3%)
Gender			
Males	9 (42.9%)	7 (33.3%)	5 (23.8%)
Females	25 (36.2%)	28 (40.6%)	16 (23.2%)
Age groups			
18-24	15 (39.5%)	17 (44.7%)	6 (15.8%)
25-34	14 (43.8%)	11 (34.4%)	7 (21.9%)
35+	5 (25.0%)	7 (35.0%)	8 (40%)

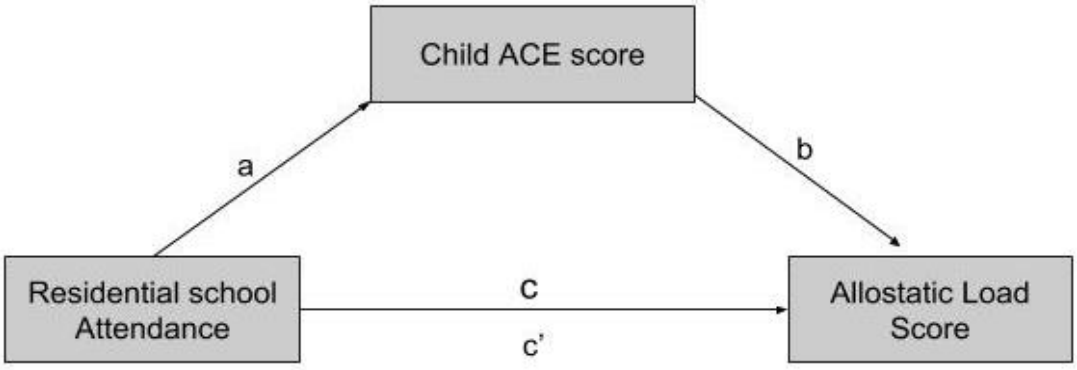

Figure 4-3. Proposed mediation model.

Table 4-9. The adjusted odds ratio of pathway A: ACEs by caregiver's residential school experience

Variables	Mid ACE Scores OR (95% CI)	SE	High ACE Scores OR (95% CI)	SE
Caregiver Mom	2.52 [0.66, 9.66]	0.70	4.59 [1.10, 19.2]	0.73
Age	0.97 [0.90, 1.05]	0.39	1.00 [0.92, 1.08]	0.04
Gender	2.24 [0.56, 8.96]	0.71	2.00 [0.44, 9.11]	0.77
Mother's Education	0.96 [0.60, 1.53]	0.24	0.93 [0.56, 1.54]	0.26
Perceived SES Growing Up	**2.52 [1.29, 4.91]**	0.34	**2.41 [1.14, 5.07]**	0.38

* Significant results ($p < 0.05$) are provided in **bold.** Outcome variable (ACE scores) used the low ACE scores as the reference group for analysis.

CHAPTER 5: DISCUSSION

This thesis had three key findings. First, participants who had a mother attend residential school were five times likely to have an AL score in the mid-range (2 to 3) than the low-range (0 to 1), as compared to participants who did not have a mother attend residential school. This association was not found for fathers. Second, 60% of participants indicated that the parenting they received as a child was adversely affected by their parent's residential school experience; however, this did not impact offspring AL score. Third, parental residential school attendance was associated with increased adverse childhood experiences among their offspring. However adverse childhood experiences were not associated with AL score. Before discussing these findings in detail, I will first review results related to the main outcome in this study, AL.

Allostatic Load

AL was calculated using 7 biomarkers. Overall, 62% of participants had an AL score of 2 or less. The mean age for the sample was 28.1 years, indicating a fairly young population. Low AL scores in this sample are consistent with previous findings, including a systematic review, showing that AL increases progressively with age.[21876] A high AL score is theorized in the literature to represent cumulative multisystem biological dysregulation resulting from repeated cycles of activation and deactivation of allostasis over a lifespan.[27] Thus, the relatively low AL scores in this young adult sample were expected.[27] Biomarkers that contributed most strongly to AL scores in the sample were cortisol awakening response (CAR), waist circumference, and body mass index (BMI), which will now be discussed in more detail.

Cortisol awakening response

Overall, 43% of this sample were below the 25th percentile or above the 75th percentile on CAR. Research has increasingly used CAR to examine the functioning of both the HPA axis, and more generally the neuroendocrine system.[205,219] Overall, research has shown that an abnormal CAR, both atypically large and small, appear to be consistent indicators of HPA dysfunction.[96] In 2007, Miller et al. published a meta-analysis on chronic stress and HPA axis outcomes to determine the specific stress conditions that resulted in cortisol levels that were atypically elevated or reduced.[102] They found cortisol release in the morning was elevated in situations where individuals experienced a social stressor, potentially controllable stress, and in instances that caused shame (e.g. sexual abuse).[102] Reduced cortisol output in the morning was found among individuals who experienced traumatic stress, uncontrollable stress, or bereavement.[102]

Research has also provided extensive evidence on the impacts of elevated/decreased cortisol and HPA dysregulation in terms of health. Normally after a stressful situation has passed, cortisol levels return back to normal via a negative feedback loop.[101,146] However, if stress is chronic, cortisol production can become dysregulated .[97,167] Dysregulated cortisol production can contribute to health issues, including heart disease, hypertension, diabetes, as well as mental health disorders such as depression, PTSD, and substance abuse.[220] Of particular interest to this study, research has also shown that cortisol dysregulation can go beyond the individual experiencing the trauma to impact cortisol functioning in their offspring.[35,220]

Waist circumference

Overall, 31% of the sample were above the 75th percentile of 110 cm for waist circumference. The average waist circumference for males and females in this sample was 98.3 cm and 97.9 cm, respectively. Waist circumference for males in this study was slightly higher than the Canadian male average of 95.1 cm, and considerably higher for females relative to the Canadian female average of 87.3 cm. [221] A large waist-circumference has been linked to an increased risk of diabetes, coronary heart disease, and hypertension, the elevated levels of waist circumference observed in this young sample may be a health concern.[221]

Body Mass Index

The First Nations Regional Health Survey reported that approximately 35% of First Nations adults living within Indigenous communities were obese using the World Health Organization (WHO) definition of 30 to 39.9 kg/m^2.[222,223] That study did not include Metis and Aboriginal people living off-reserve. The sample used for this study included all of these groups and found 30% had a BMI greater than 34.2 kg/m^2 (which was the 75th percentile cut-off used to receive an AL score of 1 for this marker). Thus, the BMI-related findings documented in this convenience sample of Indigenous university students are similar to other BMI data for Indigenous peoples more generally in Canada. The Canadian Community Health Survey (CCHS) also found that 25% of Canadians generally met criteria for obesity, suggesting obesity within this sample was approximately 5% higher than the Canadian average.[221]

Residential School Experience and Offspring Allostatic Load

Research Question 1

The first research question examined the association between parental exposure to trauma (operationalized as residential school attendance) and AL scores in their offspring. Results indicate that adult offspring who had a mother attend residential school were 5.0 times more likely to have a mid-range AL score rather than a low-range AL score, but were no more likely to have a high-range AL score, than adult offspring who did not have a mother attend residential school. It is possible that this observation is due to age and education. As mentioned previously, AL scores typically increase with age, and since the sample was fairly young, it could be hypothesized that their AL scores are more likely to rise to the mid-range rather than the high-range in the presence of a significant stressor because they are protected by their relatively young age. Research has demonstrated a positive association between education and health.[40] In addition, education has been found to be inversely associated with AL.[78] The sample consisted of post-secondary students, and as a result it can speculated that education is also contributing to this observation of significance of AL scores in the mid-range, but not the high-range.

Education also appeared to contribute to the association between residential school attendance and the AL scores. The strength of the association between parental residential school attendance and offspring AL increased after controlling for age, gender, mother's education, and the perceived socioeconomic status of adult offspring when they were growing up. These associations were not significant for adult offspring who had a father or grandparents attend residential school.

Post hoc testing was used to better understand the association between maternal residential school attendance and AL score in this study. Participants were removed who had a parent attend residential school but were not raised by that parent from the sample, and re-ran the regression model. It was expected that comparing participants who did not have a mother attend residential school to participants who had a mother attend residential school and were also raised by that mother would increase the size of the effect, given the behaviour of a residential school survivor as a parent could contribute to biological stress in their offspring beyond any biological embedding that may have taken place. Surprisingly, the size of the odds ratio did not increase. Participants raised by a mother who attended residential school were 4.7 times more likely to have an AL score in the mid-range rather than the low-range, as compared to participants raised by a mother who did not attend residential school. This post hoc test was also repeated for paternal residential school survivors and was not significant.

Research on the biological impacts of the Dutch famine and the Holocaust on survivors and their offspring provided convincing evidence that parental exposure to severe stressors in childhood can have deleterious impacts on future offspring.[215,224] Within the context of residential school attendance, Bombay et al. found offspring who had a parent attend residential school had significantly elevated depressive symptoms.[35] The present study builds on previous research by highlighting that it may be *the maternal childhood experience* of residential school that plays the most important role in determining offspring AL scores, rather than the impacts of residential school on *maternal behaviour* toward her later offspring. This hypothesis is supported by the research highlighting the ways in which psychological trauma may be biologically

embedded within the body, and passed to subsequent generations through epigenetic processes.[12,18-19] Both animal and human models have provided great insight on these epigenetic processes. Using an animal model, Babenko et al. found that there are critical periods when epigenetic programming can occur.[226] Specifically, they demonstrated that there are specific periods when offspring are highly susceptible to ancestral and prenatal stress impacting their health over a lifetime.[226] Further, using a rat model, Korosi et al. found that early maternal separation resulted in lifelong epigenetic changes in their hippocampus.[227] Specifically, the ability of a transcriptional repressor to bind to corticotropin releasing factor (CRF) was reduced due to increased methylation, which was linked to inability of the offspring to appropriately respond to and cope during stressful situations as adults.[227] Building on this, Yeduda et al. demonstrated that Holocaust exposure had an impact on *FKBP5* methylation that was observed in both exposed parents and their unexposed offspring compared to control subjects and their offspring who had lower methylation.[228] This provides evidence of a link between preconception parental trauma with epigenetic alterations in both parents and offspring. Future research that incorporates the collection of epigenetic data, specifically in Indigenous populations, may contribute to a deeper understanding of these associations.

It is interesting that paternal residential school attendance had no impact on offspring AL score either in main hypothesis testing or post hoc testing. To date, most studies on the transgenerational transmission of trauma effects highlight maternal influences.[229] For example, maternal PTSD has been shown to be more strongly associated with cortisol dysregulation in the offspring of Holocaust survivors than paternal PTSD.[20-21] Subsequent research has shown that this effect is due to increased

glucocorticoid receptor sensitivity among these offspring.[22] Research by Yehuda et al., who examined the epigenetic impacts of parental PTSD among the offspring of Holocaust survivors found different epigenetic mechanisms were involved in the intergenerational transmission of trauma-related vulnerabilities to the offspring of maternal and paternal Holocaust survivors with PTSD.[23] Future research is needed to examine adult offspring of residential school survivors using blood samples so that changes in epigenetic processes can be identified.

Research Question 2

The second research question examined adult offspring who believed that the parenting they received as a child was impacted by parental residential school attendance. Approximately half of participants responded yes to this item, which is similar to data collected for the 2002 First Nations Regional Longitudinal Health Survey, which found 43% indicated yes to a similarly worded survey item.[24] Contrary to my hypothesis, participants who believed the parenting they received as children was negatively impacted by their parents' residential school attendance did not have significantly elevated AL scores. It could be speculated that the question was too broad, and that a more specific inquiry could have led to different findings. Future research could examine whether this is true or not.

Mediation

Research Question 3

The third research question examined whether adverse childhood experiences (ACEs) could partially explain the association between being raised by a mother who attended residential school and offspring AL scores. Fathers were not examined given the

association was not significant. It was hypothesized that ACEs would provide a behavioral link between residential school attendance and offspring AL scores. For ACE scores to be tested as a mediator, it first had to tested whether ACE scores were associated with the independent (maternal residential school attendance) and dependent variable (offspring AL score). Results indicated that adult offspring who were raised by maternal residential school survivors were 4.6 times more likely to have an ACE score in the high-range (6 to 10) than the low-range (0 to 2), as compared to adult offspring who were raised by mothers who did not attend residential school, thus indicating that ACE scores were impacted by maternal residential school attendance. This finding has also been documented by Bombay et al. (2011) who found parental residential school attendance was associated with higher ACE scores in their offspring.[35]

Surprisingly, ACEs were not significantly associated with the dependent variable (AL scores) in this sample. Given that this association was not significant, formal mediation testing could not take place. This finding contravenes a recent study highlighting an association between childhood trauma and AL scores in middle-aged adults.[25-27] However, the present study was focused on young adults rather than middle-aged adults, which may help to explain this discrepancy. It is plausible that the impacts of offspring ACEs on AL are still developing, and as previous research has suggested, could potentially become evident in later years. Social desirability bias may have also resulted in an artificial reporting of lower ACE scores in this study. This bias is present when participants are unwilling or unable to report accurately on sensitive topics in order to avoid embarrassment or socially unacceptable answers.[28-29] Given the sensitivity of ACE questions, it may be that some participants did not answer questions about their own

childhood experiences reliably. Participants were informed of the confidentiality of the data collected in the consent form, and that processes were in place to ensure the information they shared could not be lined back to them. However, research has shown that the individual collecting the data can influence whether a respondent presents their answer in a socially acceptable manner.[30] I am Indigenous and I am from a nearby First Nations community. Given I collected the majority of the data from participants in this study, this may have influenced participant answers on sensitive ACE questions, as some participants were also from this community.

Strengths and Limitations

These results were limited by the use of a cross-sectional design, which prevents causal interpretations. Although these findings may be suggestive of the intergenerational transmission of residential school trauma to the subsequent generation, caution is needed in the interpretation of these results, given blood samples and DNA information were not collected. Thus epigenetic processes could not be directly examined. As mentioned previously, the sample consisted of post-secondary students. This was a limiting factor as education and health are positively associated[40], which could help explain the observed low ACE and AL scores. The use of at-home saliva samples proved to be somewhat challenging. It was difficult to determine how accurate participants were completing the samples based on the provided guidelines. The timing of the samples was important as CAR is time sensitive. To resolve this issue, medication event monitoring system ([MEMs], Aprex Corp., Fremont, Calif.) caps were implemented. MEMs caps are a medication bottle cap with a microprocessor that records the incidence and time of each

bottle opening.[230] This allowed us to determine if the at-home saliva samples were being completed accurately. The caps were implemented part way through the study.

Typically, the temporal sequence of an association cannot be assumed in a cross-sectional design, but in this case, we know parents attended residential schools prior to having their children, making the temporal sequence of documented associations less of a concern. Recall bias remains a concern given self-report measures were used. It is believed that social desirability bias also played a role in the reporting of ACE scores, and potentially other sensitive information. The sample size may have also been a limitation, as indicated by the width of some confidence intervals in this study.[31]

It should also be noted which confounders had the biggest contributions. Confounders selected a priori were age, gender, parent education, and perceived socioeconomic status. Controlling for age and parental education played the biggest role with the results. These findings highlight the importance of controlling for these confounders in future studies.

Conclusion

A key finding in this study is that Indigenous adult offspring who had a mother attend residential school had an elevated AL score, which may suggest biological dysregulation in this young adult population. Whether participants were raised by these parents had little impact on the strength of this association. This study contributes to a growing body of research focused on the intergenerational transmission of trauma-related vulnerabilities, and builds on our current knowledge by examining the contributions of maternal childhood experiences of trauma and maternal parenting behaviour on offspring AL.

The findings also highlight several of the TRC's calls to action, which were created to advance the process of reconciliation between Indigenous and non-Indigenous populations in Canada.[231] In particular, Call to Action No. 21 recommend funding for existing and new healing centres to address the impacts of residential schools.[231] The current study's findings speculate that current generations are being impacted physiologically by their parents' residential school attendances, which support the need for innovative health and healing strategies to address these issues. The findings have not only demonstrated the biological impacts of residential schools, but as well summarised the literature illustrating the complex relationship between the current health status of Indigenous populations and how the unique history of this population has effected their health. As noted by Call to Action No. 24, more work needs to be done to educate students in medical and nursing schools about these issues. It is important that future health professionals are educated on the history of Indigenous populations, and how it impacts their health.

The implications of this study also raise a number of opportunities for future research. For instance, more research would be necessary to refine and further elaborate on these findings. A better understanding of the neurobiological and genetic components of trauma stemming from residential schools can lead to a better understanding of health inequities within Indigenous populations, and how to best intervene to interrupt the legacy of the residential school system within this population.

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APPENDICES

Appendix A: Take Home Instructions

Thank you for participating in this study – you are making an important contribution that will help us better understand how everyday experiences impact stress and health.

Saliva Samples

Please choose 2 days that will be typical of your normal schedule to collect 3 saliva samples over the course of the day (6 total samples to be returned) - Preferably the 2 days before your scheduled return appointment as samples need to go into a special low temperature freezer as soon as possible. It is important that samples are frozen and do not thaw before returning to the university.

General Instructions for Completing Each Sample

- Please **rinse your mouth** with water before each sample. Avoid eating or drinking immediately before taking a sample.
- Open the **white bottle and remove ONLY the appropriate sample tube** (purple vial) as indicated below – labelled as A1, A2, A3 (Day 1) and B1, B2, B3 (Day 2).
- **Replace the lid on the white bottle** immediately after taking sample tube out.
- Place the **cotton swab from the tube under your tongue for 3 minutes**. Do not chew on it.
- Put the cotton swab into the sample tube and **place in the freezer for the remainder of the week**. **Do not put completed sample(s) back in the white bottle**
- **Record the date & time** you took each sample on Pg. 2 along with some information about your day. It is very important that we get the **exact time each sample** was taken!
- **The white bottle *must not* go in the freezer!!**

DAY 1:

1. **Sample 1 (A1) -** As soon as you wake up (keep a cotton swab kit by your bed)
2. **Sample 2 (A2) -** 30 minutes after you wake up (after you have showered for example)
3. **Sample 3 (A3) -** Before you go to bed at night

DAY 2:

Repeat the same steps as Day 1 for the remaining samples: B1 – upon waking; B2 – 30 minutes after you wake up; & B3 – before bed)

When all 6 samples are complete: Return samples in the lunch kit provided **with the frozen ice pack**. Also return your completed Day 1 & Day 2 log sheet (Pg. 2) and accelerometer (see p. 3 for instructions). In exchange you will be compensated $50 for your time.

Appendix B: Consent Form

Aboriginal Health Study: Main Consent Form

University of Lethbridge
Faculty of Health Sciences

4401 University Drive
Lethbridge, Alberta, Canada
T1K 3M4

Phone 403.329.2699
Fax 403.329.2668

http://www.uleth.ca/hlsc

Dear Sir or Madam:
You are being invited to participate in a study to better understand how social experiences influence stress in the body. Participation is voluntary and will involve the following:

- You will be asked to complete a survey about social experiences you have had in childhood and adulthood, your current levels of physical activity, and your psychological well-being. This will take about 1.5 hour. You may take a break when you would like.
- We will also collect physical measurements associated with stress and health. This includes measuring your blood pressure, weight, height, and waist measurements, and 3 saliva samples to examine how much stress your body is experiencing. You will receive a $50 cash gift as a thank you for being in the study today.
- When you leave, we would like to invite you to take a small kit home to collect 3 samples of saliva a day over the next 2 days. We will ask if you would like to take part in this segment of the study when we are completed here today, and give you instructions. This segment of the study is also voluntary.
- When you leave we will also invite you to wear a motion sensor known as an accelerometer for 7 days. It is a small lightweight device worn on a belt and can be worn over or under your clothes. It is worn at all times except while sleeping, showering or swimming. This segment of the study is also voluntary.
- When you return the saliva samples and motion sensor you will receive a $50 cash gift as a thank you.

You will likely not benefit directly from being in this study, however you will be making an important contribution to research that will help us understand the effects of social experiences on stress and health. **Participating in the study will not be linked to any courses you are taking at the University of Lethbridge or impact your grade in any way**. If some of the questions we ask, or physical measures we would like to take make you feel uneasy, you can ask to have those questions or measurements skipped. If you feel stressed, you can talk to someone about how you are feeling after the interview. To do this, you can call the Canadian Mental Health Association line at 403-327-7905 to talk to someone about how you are feeling.

All information you provide is confidential. Only the research team will see your answers. All research assistants will be required to sign confidentiality agreements. All data will be stored on a secured computer or in a locked cabinet for 7 years. After this time, it will be destroyed along with all consent forms.

Saliva samples will be kept in a freezer in a locked laboratory at the university for 5 years, after which they will be destroyed. All saliva samples will be labeled by a number only, which cannot be linked to you. If you would prefer, we can return your saliva samples to you several months after you have completed the study, or include your sample in a ceremony to return it to the earth in a traditional way. If you would prefer either of these options, we would

link your name to your study ID on this consent form to ensure we return the correct samples to you or include the correct samples in a ceremony to return it to the earth. This form will be kept in a locked cabinet separate from the sample; your name would not appear on the sample itself. The results from this study will be reported in general terms in the form of presentations and publications. Your personal information, including your name, will be kept confidential and will not be distributed in any way.

You may also withdraw from the study at any time without a reason. If you choose to withdraw, all of the information you have shared will be destroyed.

If you have questions about this research please contact the Principal Investigator: Cheryl Currie at cheryl.currie@uleth.ca or 403-332-4060 at the University of Lethbridge. If you have any other questions regarding your rights as a participant in this research, you may also contact the Office of Research Ethics at the University of Lethbridge at 403-329-2747 or research.services@uleth.ca.

I have read the above information regarding this research study on social experiences and stress. I consent to participate in this study.

_____ Printed Name of Participant

_____ Signature of Participant

_____ Signature of Research Assistant

_____ Date

Optional:

Please check this box if you would like your saliva sample returned to you: ☐

Please check this box if you would like your saliva sample included in a ceremony that will return it to the earth ☐

Appendix C: List of Biomarkers for Allostatic Load Score

1	Diurnal cortisol[1]	Neuroendocrine	Salivary kit	25th & 75th
2	Dehydroepiandrosterone (DHEAS)	Neuroendocrine	Salivary kit	25th percentile
3	C-reactive protein (CRP)	Immune	Salivary kit	75th percentile
4	Systolic blood pressure (mmHg)	Cardiovascular	Blood pressure monitor	75th percentile
5	Diastolic blood pressure (mmHg)	Cardiovascular	Blood pressure monitor	75th percentile
6	Waist circumference (CM)	Metabolism	Measuring tape	75th percentile
7	Body mass index	Metabolism	Scale	75th percentile