THE EPIDEMIOLOGY OF STRESS AND OBESITY OVER THE LIFE COURSE

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Lay Abstract

Stress takes several forms across the life course and is a risk factor for several chronic diseases, including obesity. Examples of stress include adversity during childhood or exposure to disasters such as the COVID-19 pandemic. The mechanistic pathways to disease development following stress exposure are not well understood, however, a suspected pathway includes nutritional patterns. Stress is a risk factor for obesity, but it has also been found that obesity may also increase the risk of stress. This thesis contributes a life course research perspective investigating the epidemiology of stress and obesity, and how they are interrelated.

Abstract

Background: Obesity and stress share a complex relationship. It has been found that obesity and stress are constantly influencing each other, sharing a cyclical association. Stress can be caused by psychological, social, or physical determinants. Understanding this relationship is particularly of interest as a high proportion of people in Canada have obesity, and obesity is not only a disease itself but is a risk factor for several other diseases.

Objectives: The objectives of this thesis were: 1) To understand the impact of disasters, including pandemics, on obesity and cardiometabolic risk; 2) To describe stress during the COVID-19 pandemic by socioeconomic factors; 3) To determine how early life adversity and obesity impacted stress during the COVID-19 pandemic; 4) To evaluate the association between early life adversity and adulthood obesity, and to determine if this association was mediated by nutrition.

Methods: To address objective 1 a systematic review was conducted. For objectives 2-4, data from over 50,000 adults aged 45 and older from the Canadian Longitudinal Study on Aging (CLSA) was used. This study is unique as it is a nationally representative cohort with comprehensive measures of both obesity and stress, including adverse childhood experiences (ACEs), as well as in-depth data from the COVID-19 pandemic. For objective 2, a cross-sectional study was conducted and for objectives 3 and 4, longitudinal studies were conducted. Multivariable Poisson, negative-binomial and multinomial logistic regression models were used to evaluate associations. To address objectives 3 and 4, novel epidemiologic methods were applied, including effect modification, evaluated on

the additive and multiplicative scales and mediation evaluated using causal mediation methodologies.

Results: Overall the results of these theses studies support a strong bidirectional relationship between stress and obesity This was observed for various stressors at different periods throughout the life course. The systematic review identified that the indirect harms of disasters, including pandemics, have lasting effects on cardiometabolic outcomes, including obesity. Stress experienced during the COVID-19 pandemic varied across several socioeconomic factors, and obesity was associated with stress experienced during the pandemic. Although ACEs did not modify this association, it was found to independently be associated with stress during the COVID-19 pandemic. ACEs were found to be strongly associated with adulthood obesity, but there was no evidence to suggest this was mediated by nutrition in later life.

Conclusions: The findings from this thesis confirm that regardless of the type of stress, or the timing of exposure, obesity and stress are strongly associated. Using a life course perspective allows for a comprehensive assessment of potential risk factors of experiences that occur during adulthood, such as disease development or experiences during a stressful event. People are susceptible to worse experiences during adulthood, which may be related to a variety of factors including adversity during childhood, socioeconomic factors or chronic disease. This should be considered when developing prevention strategies and interventions targeting those at the highest risk.

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List of all Abbreviations and Symbols

ACEs	Adverse Childhood Experiences
AMI	Acute myocardial infarction
AOR	Adjusted Odds Ratio
BF	Body fat
BMI	Body mass index
BP	Blood pressure
CDN	Canadian
CESD	Center for Epidemiologic Studies Short Depression scale
COVID-19	Coronavirus disease
CLSA	Canadian Longitudinal Study on Aging
CHD	Coronary heart disease
CHOL	Cholesterol
CI	Confidence interval
CM	Centimeter
CT	Computed tomography
CVD	Cardiovascular disease
CVE	Cardiovascular events’
DCS	Data collection sites
DNA	Deoxyribonucleic acid
DOHaD	Developmental Origins of Health and Disease
DXA	Dual-energy X-ray absorptiometry
HIREB	Hamilton Integrated Research Ethics Board
HDL	High-density lipoproteins
HR	Hazard ratio

JBI	Joanna Brigs Institute
KCAL	Kilocalories
KG	Kilogram
L	Litre
LDL	Low-density lipoproteins
M	Metre
MMHG	Millimeters of Mercury
MMOL	Millimole per litre
MRI	Magnetic resonance imaging
N	Number
NA	Not applicable
NCD	Noncommunicable diseases
OR	Odds ratio
PASE	Physical Activity Scale for the Elderly
PHAC	Public Health Agency of Canada
PMNS	Prenatal Maternal Stress
PMOL	Picomoles per litre
PR	Prevalence ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PTSD	Post-traumatic stress disorder
PURE	Prospective Urban Rural Epidemiological
RERI	Relative excess risk due to interaction
RR	Relative risk
RRR	Ratio of relative risk
SARS-CoV-2	Severe Acute Respiratory Syndrome-Coronavirus-2

SD	Standard deviation
SDQ	Short Diet Questionnaire
SE	Standard Error
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
TRIG	Triglycerides
WHO	World Health Organization
%	Percent

Declaration of Academic Achievement

This is a "sandwich thesis" comprised of 6 chapters. All work contained within this thesis meets the requirements for inclusion in a Doctor of Philosophy dissertation.

Chapter 1 is unpublished. VD is the sole author.

Chapter 2 is published in BMJ Open. VD led the conceptualization of the project, as well as the registration of the review, developing the search, screening, data extraction, synthesis of data, manuscript writing, submission of the manuscript and manuscript revisions. JL, MSA, YYM, ATA, ES, SI, JDM and RR were the secondary screeners and data extractors. SENS, EA, EA and LNA also assisted with the conceptualization of the project. All authors revised and approved the final version.

Chapter 3 is published in CMAJ Open. VD conceptualized the research question and study objectives, as well as, applying for data access, analyzing data, manuscript preparation, manuscript submission, and revisions of the manuscript. LNA, JK, MDG, YJ, UEO, NEB, SK, CW, LEG, and PR provided methodological and content expertise throughout the project and contributed to revising the manuscript. All authors approved the final version of the manuscript.

Chapter 4 has been accepted to the International Journal of Obesity and is in press. VD conceptualized the research question and study objectives, as well as, applying for data access, analyzing data, manuscript preparation, manuscript submission, and revisions of the manuscript. AG, MDG, YJ, UEO, JET, NEB, SK, CW, LEG, PR and LNA provided methodological and content expertise throughout the project and contributed to revising the manuscript. All authors approved the final version of the manuscript.

Chapter 5 has been submitted to a journal and is under peer review. VD conceptualized the research question and study objectives, as well as, applying for data access, analyzing data, manuscript preparation, manuscript submission, and revisions of the manuscript. AG, JET, LEG and LNA provided methodological and content expertise throughout the project and contributed to revising the manuscript. All authors approved the final version of the manuscript.

Chapter 6 is unpublished. VD is the sole author.

Chapter 1: Introduction

Obesity and stress share a complex relationship. It has been found that obesity and stress are constantly influencing each other, sharing a cyclical bidirectional association (1). Stress can be both acute and chronic and may be caused by psychological, social, or physical determinants (2). Understanding this relationship is particularly of interest as the prevalence of obesity has been on the rise since 1985 (3). Obesity is not only a disease but is also a risk factor for several other diseases including cardiovascular diseases, diabetes and cancer (4) and can also increase the risk for stress (1).

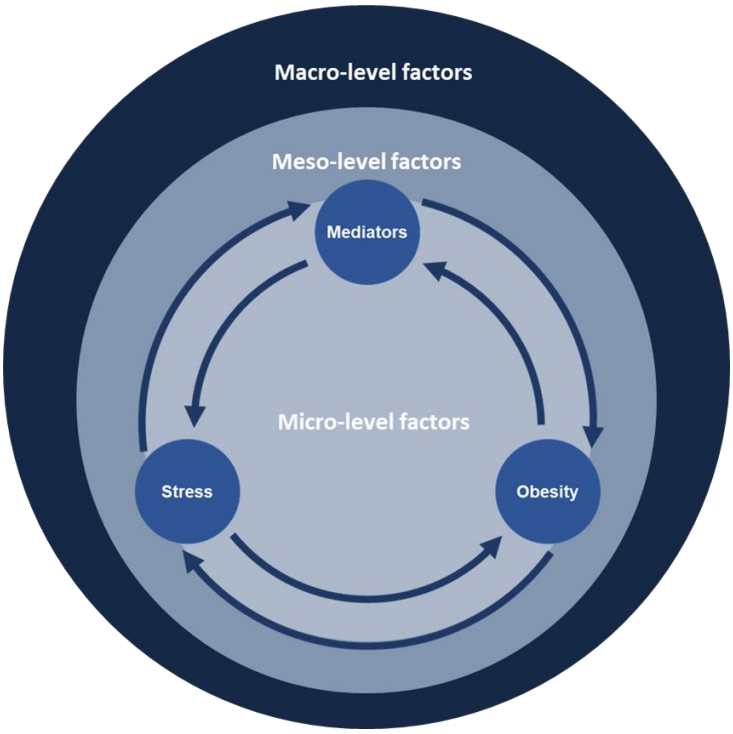

Figure 1. Adapted conceptual framework by van der Valk et al., (1) and Bronfenbrenner's Social Ecological model (5) depicting the bidirectional association shared by stress and obesity

Note: This figure has been modified from the original publication by van der Valk ES, Savas M, van Rossum EFC. Stress and Obesity: Are There More Susceptible Individuals? Curr Obes Rep. 2018;7(2):193–203, published under Creative Commons License (6)

Obesity

Obesity is defined as a complex condition that is characterized by excess or an accumulation of body fat or adipose tissue that leads to health complications (4,7–9).

The burden of obesity in Canada

In Canada, the rates of obesity rapidly increased from 1985 to 2016 (4). Since then, rates of obesity have been found to have plateaued, however, the prevalence of obesity remains high with 26.4% to have reported having obesity, which is equivalent to about 1.9 million Canadian adults (4). This is alarming as obesity dramatically impacts the life of a person with this disease. Obesity impacts a person's quality of life and increases the risk of developing other diseases including type II diabetes, gallbladder disease, liver disease and several cancers including colon, kidney and esophagus in both males and females, and endometrium and postmenopausal breast cancer among females (4,8,10). Along with the increase in the prevalence of obesity, there has been an increase in those with the most severe type of obesity, which is concerning as those with the highest excess fat are at the greatest risk of complications associated with obesity (4).

Obesity not only causes significant health complications but is costly to the broader healthcare system (7). Direct and indirect costs associated with obesity and obesity-related illnesses have been estimated to be around $7.1 billion in 2010 (3). Given the high prevalence of obesity and the associated costs, it signifies the importance of developing targeted prevention strategies and intervention strategies.

Risk factors for obesity

There are several well-established risk factors for obesity. The Public Health Agency of Canada (PHAC) and the Canadian Institute for Health Information (CIHI) released a comprehensive report on determinants of obesity among Canadians (3). Generally, these factors include genetic, behavioural, social, cultural, and neighbourhood/community-level determinants (3,4). It is important to recognize that these are often interconnected and are not independent when impacting obesity risk (11). Briefly, examples of modifiable risk factors for increased risk of obesity include physical inactivity, poor diet, increased screen time and lower income (3). Neighbourhood factors also play an important role in understanding the risk of obesity. For instance, obesity was more prevalent in areas that were more deprived and had a lower socioeconomic status (3).

It is apparent that several factors play a role in obesity risk, and when thinking more specifically about obesity in adulthood, it is important to use a life course perspective and identify factors from early life that may increase the risk of developing adulthood obesity. At each stage of the life course, beginning with pre-conception to death, there are unique factors that influence obesity development (12).

Although there is significant research on potential risk factors for obesity, in 2020, the Canadian Adult Obesity Clinical Practice Guidelines included a key message that there is a need for continued non-experimental research on biopsychological and environmental causes and contributors to obesity (8). This call for continued research will help to better refine current interventions and to inform the development of new prevention and intervention strategies.

Measurement of obesity

Several measures are used to define obesity. Anthropometric measurements that are commonly used in epidemiologic research include body mass index (BMI) and waist circumference (13). More advanced methods, such as the use of magnetic resonance imaging (MRI), dual-energy X-ray absorptiometry (DXA) or computed tomography (CT), are used in research to measure body composition, more specifically fat mass (13,14). Although these are gold standard measurement tools, they are not often used as they are expensive (13). The above measures all require different techniques or procedures to obtain measurements. Once researchers obtain the measures, standard cut-offs are applied to define obesity.

BMI: BMI is a ratio of a person's height and weight (15). It is the most often used measure to define obesity in epidemiologic research as it is easy to use, not costly and can be used on people of any sex or age (13). To define obesity using BMI, the World Health Organization (WHO) has established standard cut-offs (9). These include:

- Underweight: < 18.5 kg/m^2
- Normal weight: 18.5-24.9 kg/m^2
- Overweight: 25-29.9 kg/m^2
- Obesity: ≥ 30 kg/m^2

Obesity can be further classified as:

- Obesity class I: 30-34.9 kg/m^2
- Obesity class II: 35-39.9 kg/m^2
- Obesity class III: $\geq$40 kg/m^2

Although BMI is commonly used and is correlated with measures of body fat taken from DXA, however, it does not provide an indication of fat or more specifically abdominal obesity (16). This measure may also be skewed as it does not consider muscle mass, bone density, overall body composition, or differences by sex or race (16).

Waist circumference: Waist circumference is an important measure as it provides information on abdominal obesity and the distribution of fat. Having a higher waist circumference, meaning increased abdominal obesity, is concerning as this has been linked to worse health outcomes (17). Similar to BMI, standard cut-offs are used to define obesity (9,18). These include:

- Normal weight: Male: < 102 cm; Female: < 88 cm
- Obesity: Male: ≥ 102 cm; Female: ≥ 88 cm

Body fat: To measure body fat, CT, DXA or MRI are considered to be gold standard assessments (13). Each of these used different processes to obtain measures. A major limitation associated with both CT and MRI is that it is difficult to get body composition measures for people who have a larger body size, such as those who are overweight or have obesity (14). This factor, along with the high costs, time and software needed to interpret results make these methods not often used in epidemiologic research (13). DXA scans have become a popular measurement tool to assess body composition when researchers are interested in validating or determining the accuracy of other anthropometric measures (19). To define obesity using DXA, percent body fat is often

used, however, there are no standard cut-offs that are established by the WHO. Cut-offs that are often cited in the literature include (20):

- Normal weight: Males: ≤25%; Females: ≤35%
- Obesity: Males: >25%; Females: >35%

Comparison of anthropometric measures: Previous work in the Canadian Longitudinal Study on Aging (CLSA) (21), explored the variation in defining obesity using different measures of adiposity relative to percent body fat, which was the gold standard measure. For both males and females, BMI and waist circumference were highly correlated with percent body fat, whereas the waist-to-hip ratio had a low degree of correlation. These findings are somewhat consistent beyond this sample, where it has been noted that BMI has a sensitivity of 51.4% (95% CI: 38.5-64.2%) and specificity of 95.4% (95% CI: 90.7-97.8%), and waist circumference has a sensitivity of 62.4% (95% CI: 49.2-73.9%) and specificity of 88.1% (95% CI 77.0-94.2%) compared to imaging techniques to determine obesity (19). This systematic review and meta-analysis also found that there is limited evidence that supports using the waist-to-hip ratio as a better tool than BMI or waist circumference (19).

Stress

Stress is a broad term describing an event that interrupts or disturbs a person's daily functioning and the inability to effectively cope with the psychological and physiological demands associated with it (2). Prolonged and repeated exposure to stress is associated

with negative health outcomes and chronic diseases (2). Stress can be acute, meaning the immediate response to a stressful event or stimuli, or chronic, which means exposure to stress stimuli for a prolonged period (22).

Measurement of stress

To measure stress, generally, three approaches are followed: the epidemiological, the psychological and the biological (23). It is becoming more common to see these three approaches be used together, combining techniques to measure stress.

Epidemiological approach (23)*:* This approach uses an objective approach, where stress is considered through the number of stressful events an individual has encountered throughout their life. Specific scales or interviews are sometimes administered to estimate the cumulative stress a person has encountered throughout the life course. In this method, people are sometimes asked about specific stressors they encountered, including the loss of a job, or a person close to them dying, or more generally asked about events that may have occurred throughout a person's life. When measuring the influence of a specific stressor or stressful event, in the epidemiological tradition, a person is considered to have been exposed to stress if they have experienced a stressful event or stressor and were required to adapt to these situations. Often, a list of stressors relevant to a stressful event may be administered where people can select all that they have experienced (24).

Psychological approach (23)*:* This approach recognizes that a single stressful event, likely will not have the same impact or associated stress for every individual, and how people experience an event will vary. Given that it is assumed people have varied

experiences with different stressors, an appraisal of stress is used which means the level of stress associated with a specific event is measured in relation to how a person infers or perceives the specific event and their ability to cope. A stress appraisal considers the length, intensity, ability to control or manage an event, and the resources available to adapt to a stressful event. To measure stress using this approach, people are often asked how they perceived a stressful event, or the consequences associated with it (24).

Biological approach (23)*:* The biological approach to measuring stress considers the physiological response within the body following exposure to stress stimuli (23). A physiological response includes immune, neuroendocrine, neural, or autonomic (2). It is assumed the body is typically at homeostasis, meaning a state of stability (25). Exposure to stress or an event that induces stress can cause the body to no longer be in a constant state. For an acute stressor, the body may adapt but prolonged exposure can lead to a constant state of dysregulation (23). Using hematological, cardiometabolic and clinical biomarkers, a measure of accumulated stress can be calculated, which is called an allostatic load index (26). This index uses high-risk cut-offs of several biomarkers to estimate accumulated stress, where a higher score indicates higher accumulated stress (27). Another biological method of assessment includes measures of cortisol, which measures stress related to the neuroendocrine system within the body (28).

It is apparent there are different approaches to measuring stress, however, across all approaches research has found stress to predict health outcomes and mortality (23). When a researcher is considering measuring stress, it is important to conceptualize stress in relation to the research question to ensure the most appropriate measure is selected (2).

Another consideration that should be made is the specific sample being studied to determine if validated scales or tools exist (2). Researchers may also select the specific measure of stress based on the timeframe of the study, including the life stage in which stress is being measured or they may consider the cost of different tools. In some cases, researchers may find adapting or creating new tools to fit their research question or the target population the most optimal approach (2).

Adverse childhood experiences (ACEs)

An example of stressors that occur in early life is adverse childhood experiences (ACEs). ACEs are traumatic experiences or a negative environment that occur before the age of 18 (29,30). These include but are not limited to physical, sexual or emotional abuse, neglect, exposure to intimate partner violence, parental divorce or separation, death or incarceration of a parent, or someone within the family having mental health or substance use problems (30–32).

Population-based studies have found that 47-59% of people experienced at least one ACE (33). More specifically, in Canada, a study conducted using participants from the Canadian Longitudinal Study on Aging (CLSA) found 61.1% of people to have experienced one or more ACE (34). ACEs impact a significant proportion of the population, signifying the importance of understanding how this may impact a person beyond their childhood. Following exposure to ACEs, the body typically activates a stress response which interferes with the homeostasis of the body (35). Prolonged exposure to these stressors can lead to dysregulation of several systems within the body creating biological changes which lead to damage to the immune, metabolic, and cardiovascular

systems (35,36). This constant state of imbalance increases the risk of developing disease and worse physical health, mental health and social outcomes (31,34).

The COVID-19 pandemic

In March 2020, a global pandemic was declared in response to the coronavirus disease (COVID-19). This is viewed as a major stressor as daily life was completely altered across the globe. Public health preventive measures were implemented to slow the transmission of the virus (37). Aside from the morbidity and mortality associated with the virus, these measures created a shift in daily functioning, leading to increased stress (38). Studies reported that up to 81.9% of people reported feelings of stress throughout the COVID-19 pandemic (38). In Canada, there has been limited work throughout the pandemic exploring stress experienced during the pandemic, and how this may have varied by different sociodemographic characteristics.

In previous disasters, an indirect consequence that has been noted is increased stress in addition to the direct harm associated with the disaster itself (39,40). The stress experienced varied based on several different factors, including sex, age race, socioeconomic status, and family factors, such as having children (40). The COVID-19 pandemic is a stressful event unlike any other disaster in the modern day, given the wide-scale implications. However, experiences during the COVID-19 pandemic likely varied in several characteristics. Few studies from early in the pandemic (January 2020-May 2020) identified differences in experiences of stress by sex, age, unemployment, chronic condition or a psychiatric illness (38,41,42), however, were limited by small sample sizes and lack of generalizability.

In disaster research, to measure stress a combination of the different approaches (epidemiological, psychological and biological) are often used. Several studies have been conducted that aimed to understand how stress during a disaster impacted different health outcomes (24,43–47).To measure stress in these studies, perceived scales (physiological approach), lists of stressors (epidemiological approach) or measures of cortisol (biological approach) were used. Given the unexpected nature of most disasters, when conducting research to understand their impact, researchers may use different measurement tools informed by previous literature or gold-standard tools, with modifications often made to better address the unique characteristics of the disaster of interest (24).

The complex relationship between stress and obesity

Obesity and stress share a complex relationship as they are said to be interrelated (1). Stress is not only a predictor of obesity, but obesity also is a predictor of stress. This indicates this relationship is not linear but rather is cyclical and bi-directional (1). Although stress and obesity are constantly influencing each other, several factors can play a role in this relationship. As depicted in Figure 1, applying a social-ecological framework (5) can better explain the different levels of influence. These include micro-level factors such as genetics, physical health, unhealthy lifestyle, mental illness and medication use (1). At the meso-level, including interactions and supports from family and friends, and at the macro-level, government or system-level policies can exacerbate or alleviate this relationship, such as policies or legislation aimed at improving support,

such as economic supports for families (48). Consideration of these different levels of influence is imperative to comprehensively evaluate and understand why the complex relationships between obesity and stress exist. Although there is literature establishing the relationship between stress and obesity, and vice versa, it is important to recognize stress can take many different forms. Using a life course perspective it is apparent stress can occur throughout different stages of life, for instance during childhood and extending into older adulthood, and these different experiences may still influence obesity (22). Research is needed to isolate and focus on specific associations involving different stressors or stressful events throughout the life course and the subsequent impact on obesity, and consequently how obesity may impact experiences of stress.

ACEs and obesity

ACEs have a lasting effect following exposure, and research has found that people with ACEs are at a greater risk of developing obesity later in life (49). A systematic review and meta-analysis conducted in 2020 found those with ACEs to be 46% more likely to have obesity in adulthood (pooled OR: 1.46; 95% CI: 1.28-1.64; n=118,691) (49). This review noted previous systematic reviews that were conducted in 2010 (50) and 2014 (51,52) that also found adversity or child maltreatment also increases the odds of obesity in adulthood (pooled OR range: 1.12-1.39) (50–52). However, these reviews did not identify potential pathways to disease development. The systematic review conducted in 2020 identified potential mediators such as social disruptions, health behaviours (e.g., smoking, diet, physical activity, sleep patterns), and mental health problems (49). This systematic review called for future research to continue exploring this association using

large, population-based samples and to continue exploring potential mechanisms between ACEs and obesity (49).

Using a life course epidemiology framework, exposure to risk factors can start the pathway to disease development from as early on as gestation (53). Two potential pathways include nutrition and stress (54). ACEs have been linked to a poor diet (55) and stress (56), which are subsequently linked to obesity (1,57). It is possible these lie on the mechanistic pathway and plays a role in disease development. There has been limited literature that has specifically explored these pathways given the difficulties associated with the availability of data (49).

The COVID-19 pandemic and obesity

The COVID-19 pandemic completely shifted everyday functioning. The preventive measures and lockdowns that were put in place to slow the spread of SARS-CoV-2 also significantly impacted behaviours and factors that influence weight (58). For instance, sedentary behaviours increased given most people shifted to working from home and virtual learning, as well as an increase in time spent watching television and an increase in consumption of processed foods (59–61). In addition, the stress associated with the pandemic may have also influenced short-term weight changes throughout the pandemic (58,62). It is hypothesized that these societal changes, albeit short-term, will have lasting effects on future rates of obesity (63).

Although it is hypothesized and has been reported that changes in behaviours and increased stress throughout the pandemic influenced weight during the pandemic and are

expected to impact future weight gain, the impact of obesity on experiences of stress during the pandemic has not yet been explored. Given the understanding that obesity and stress share a cyclical relationship (1), it signifies the importance of studying how obesity impacted experiences during the pandemic.

Mechanistic pathway

Given the interrelated relationship between stress and obesity, and obesity and stress, it is important to recognize the possible mechanistic pathway that explains the relationships. In response to a stressful event, the body activates cortisol, which is a glucocorticoid stress hormone (1). The chronic increase in cortisol leads to an accumulation of adipose in the abdominal region of the body and an increased appetite, which in turn leads to the development of obesity (1). When a person has obesity, they often face a significant amount of stigma, potentially hindering their mental health, and increasing stress. For instance, during the COVID-19 pandemic, it was particularly challenging for those with obesity, as obesity was identified as a risk factor for increased morbidity and mortality from COVID-19. This messaging led to significant for people with obesity, likely leading to worse experiences during the pandemic (64). There are several potential pathways where stress may lead to obesity, and vice versa, however, it is apparent regardless of the pathway, when a person is exposed to stress, they are at a greater risk of obesity development, and having obesity also leads to stress (1).

Exploring the relationship between stress and obesity using advanced epidemiologic methods

To continue to explore the relationship obesity and stress share, using different measures of stress at different points throughout the life course, it is important to apply different novel epidemiologic methodologies. For instance, previous research has called for the use of population-based samples to continue exploring the association between ACEs and obesity and to identify potential variables that lie on the mechanistic pathway (49). Mediation and effect modification are epidemiologic approaches that allow researchers to study various aspects of an association between an exposure and an outcome.

Mediation

To better understand how stress, specifically ACEs, impacts obesity and to allow for future intervention or preventive measures to be implemented, the pathway to disease development must be further explored (49). Mediation analysis is often used to better understand the mechanistic pathway between an exposure and outcome, however, these methodologies are not often used in epidemiology (65). Traditional approaches to mediation analysis are often used in sociology or psychology. However, these methods fail to consider all potential confounding variables, making it difficult to make causal inferences (65). To overcome these limitations, causal mediation analysis is more commonly used. Causal mediation analysis ensures all confounders are accounted for. These include exposure-outcome confounding, mediator-outcome confounding, and exposure-mediator confounding (65). Once these confounders are accounted for, the total effect can be decomposed into direct and indirect effects.

Total effect: The total effect of an exposure on an outcome. The total effect is the sum of the direct effect and indirect effect (66).

Direct effect: The effect the exposure has on the outcome when the mediator is absent (66).

Indirect effect: The effect the exposure has on the outcome through the mediator (66).

Another strength of this methodology is the ability to allow for an exposure-mediator interaction. An exposure-mediator interaction means the effect the exposure has on the outcome varies by different levels of the mediator (65). This allows for a better decomposition of the total effect. Causal mediation analysis is a relatively new methodology, and few studies have applied it (67). Given research has established an association between ACEs and obesity risk in adulthood (49–52), it further confirms the importance of applying causal mediation methodologies to allow for the pathway to disease development to be better understood, contributing to prevention and intervention strategies.

Effect modification and interaction

To understand if an association between an exposure and an outcome is modified or varies by a third variable, epidemiologists will frequently use effect modification or interaction (66). Although these two concepts are often used interchangeably, they do use different statistical techniques to understand variation in association with an outcome (68).

Effect modification: Effect modification is when the magnitude of an association between an exposure and outcome varies across strata of a third variable. If effect modification is present, the effect is heterogeneous across strata, if it is not present, the effects are homogenous (66). To estimate effect modification, analyses are often stratified by the third variable or statistical interaction is assessed.

Interaction: Interaction is when the joint effect of two exposures or variables on an outcome is of interest (66). To study interaction, researchers can estimate the effect on either the additive or multiplicative scales. There is growing evidence that studying interaction using both scales allows for better inferences at the public health level to be made (69).

When investigating interaction using both the additive and multiplicative scales, only one scale needs to be significant to suggest interaction is present. Using both scales has greater public health relevance as they both have advantages. The additive scale can be used to inform if an exposure impacts an outcome in the presence or absence of another variable, explaining possible mechanistic interaction rather than just statistical interaction (68). Whereas interaction on the multiplicative scale is often easier to obtain using statistical software, and researchers can answer more causal questions on this scale (68). In the context of the interrelated relationship between stress and obesity, the use of advanced interaction methodologies to explore how this association is modified by past experiences of stress is novel, as we know stress and obesity are constantly influencing each other.

Summary and rationale for thesis

Independently obesity and stress are complex. When aiming to understand the relationship they share, it becomes increasingly more difficult. Given the high prevalence of obesity, and that obesity is not only a disease but a risk factor for several other chronic conditions, there is a need for research on risk factors. This was further exemplified by the call for continued research made in 2020 by the Canadian Adult Obesity Clinical Practice Guidelines. Using a life course perspective allows for different examples of stress to be identified from early life extending into older adulthood. This is important given the cycle obesity and stress share, where they are constantly impacting each other. ACEs are a known stressor occurring in early life, and the COVID-19 pandemic is a global stressful event. There are apparent gaps in the literature when thinking about the relationships stress and obesity share, specifically in the context of the COVID-19 pandemic. Given the unexpected nature of the pandemic, it is difficult to determine differences in peoples' experiences. The proposed lasting effects of the pandemic make research in this area even more imperative.

This thesis uses a quantitative, epidemiological approach to better understand how stress and obesity are interrelated. In this thesis, stress is measured using two distinct examples: ACEs and stress during the pandemic. Recognizing stress can take several different forms and focus on these two examples of stressors at different stages of the life course is a novel contribution to the literature. Given the lasting effects ACEs have on future outcomes, it is important to continue researching and understanding pathways to disease

development allowing for prevention and intervention strategies to be developed. Consequently, the COVID-19 pandemic completely altered daily life across the globe. Understanding how experiences during the pandemic varied by socioeconomic factors, chronic disease (e.g., obesity), and past adversity (e.g., ACEs) can inform who may be at the greatest risk of worse outcomes beyond the pandemic. As the COVID-19 pandemic subsides, it's important to consider how the effects beyond the direct health-related outcomes associated with the SARS-CoV-2 may impact future outcomes, including chronic disease development.

Objectives of thesis

The overarching objective of this thesis is to understand complex relationships between obesity and stress, including the COVID-19 pandemic and early life adversity, while applying novel epidemiologic methodologies using a population-based sample. More specifically the objectives of this thesis are:

1) To understand the impact of disasters, including pandemics, on obesity and cardiometabolic risk;
2) To describe stress during the COVID-19 pandemic by socioeconomic factors;
3) To determine how early life adversity and obesity impacted stress during the COVID-19 pandemic;
4) To evaluate the association between early life adversity and adulthood obesity, and to determine if this association is mediated by nutrition.

Thesis manuscripts

This thesis is a sandwich thesis where each subsequent chapter is a manuscript. Below is a brief overview of each manuscript.

Manuscript 1: The impact of disasters, including pandemics, on cardiometabolic outcomes across the life course: A systematic review

Manuscript 1 reviewed the literature to understand the long-term impacts of disasters, including pandemics, on future cardiometabolic outcomes, such as obesity. The secondary aim of the paper was to determine methods of reducing the impact of disasters and to identify subgroups that may be at the greatest risk of worse health outcomes. This paper informs the potential long-term health risks beyond the COVID-19 pandemic.

Manuscript 2: Stressors and perceived consequences of the COVID-19 pandemic among older adults: A cross-sectional study using data from the Canadian Longitudinal Study on Aging (CLSA)

Given the wide-scale implications of the COVID-19 pandemic, few studies in Canada were able to collect information on stress during the pandemic on large population-based samples. Manuscript 2 explores how stressors and the perceived consequences of the COVID-19 pandemic varied by different socioeconomic factors, using a cross-sectional study design.

Manuscript 3: The association between adverse childhood experiences, adulthood obesity and stress during the COVID-19 pandemic: An analysis of the Canadian Longitudinal Study on Aging

In Manuscript 3, the associations between ACEs and obesity, and stress during the pandemic were explored. Various multivariable regression models were used to estimate measures of effect to better understand how these influenced experiences during the COVID-19 pandemic. To understand if ACEs modified the association between obesity and stress during the pandemic, interaction on the additive and multiplicative scales were used.

Manuscript 4: A longitudinal study evaluating adverse childhood experiences and obesity in adulthood using the Canadian Longitudinal Study on Aging (CLSA)

Manuscript 4 uses a longitudinal study design to explore the association between ACEs that occurred before the age of 18 and adulthood obesity and to determine if nutrition mediates this association, using causal mediation methodologies. Obesity was defined using BMI, waist circumference, and percent body fat which were all measured by trained research assistants.

Duplication across thesis

Manuscripts 2 through 4 use data from the CLSA. Across the papers, there may be overlap in methodologies explained, including the description of the sample and the data source, the variables used and how these were described, and a discussion about strengths and limitations associated with the data source. For instance, in manuscripts 2 and 3 stress defined by stressors and the perceived consequences of the pandemic may have similar descriptions. In manuscripts 3 and 4 obesity is defined by various anthropometric

measures. There is some overlap in these measures across these two papers and thus variable descriptions may be similar. Although there is this slight overlap in methodology for each of these papers, they each answer distinct research questions, and thus are each an important contribution to the literature.

Chapter 2: The impact of disasters, including pandemics, on cardiometabolic outcomes across the life course: a systematic review

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Chapter 2 Summary

Disasters, including pandemics, alter daily functioning and may also have long-term implications on cardiometabolic outcomes, such as obesity. Given the wide-scale implications of the COVID-19 pandemic, understanding the implications that past disasters had on long-term outcomes, can help to provide an understanding of the lasting effects the COVID-19 pandemic may have. The purpose of this study was to review the literature to determine the impact of disasters, including pandemics on the risk of cardiometabolic outcomes, including obesity, across the life course, and to determine how to reduce the impact of chronic disease outcomes following a disaster and to identify populations at highest risk of cardiometabolic outcomes following a disaster. It was apparent that the burden of disasters extends beyond the known direct harm of disasters and had lasting effects on cardiometabolic outcomes.

ABSTRACT

Background: Disasters are events that disrupt the daily functioning of a community or society and may increase the long-term risk of adverse cardiometabolic outcomes, including cardiovascular disease, obesity, and diabetes. The objectives of this study were to conduct a systematic review to determine the impact of disasters, including pandemics, on cardiometabolic outcomes across the life course.

Design: A systematic search was conducted in May 2020 using two electronic databases, EMBASE and Medline. All studies were screened in duplicate at title and abstract, and full-text levels. Studies were eligible for inclusion if they assessed the association between a population-level or community disaster and cardiometabolic outcomes ≥ 1 month following the disaster. There were no restrictions on age, year of publication, country, or population. Data were extracted on study characteristics, exposure (e.g., type of disaster, region, year), cardiometabolic outcomes, and measures of effect. Study quality was evaluated using the Joanna Briggs Institute critical appraisal tools.

Results: A total of 58 studies were included, with 24 studies reporting the effects of exposure to disaster during pregnancy/childhood and 34 studies reporting the effects of exposure during adulthood. Studies included exposure to natural (n=35; 60%) and human-made (n=23; 40%) disasters, with only 3 (5%) of these studies evaluating previous pandemics. Most studies reported increased cardiometabolic risk, including increased cardiovascular disease incidence or mortality, diabetes, and obesity, but not all. Few studies evaluated the biological mechanisms or high-risk subgroups that may be at a greater risk of negative health outcomes following disasters.

Conclusions: The findings from this study suggest that the burden of disasters extends beyond the known direct harm, and attention is needed on the detrimental indirect long-term effects on cardiometabolic health. Given the current COVID-19 pandemic, these findings may inform public health prevention strategies to mitigate the impact of future cardiometabolic risk.

PROSPERO registration: CRD – 42020186074

Strengths and limitations of this study:

- This systematic review is one of the first to review the literature on disasters, including pandemics, and subsequent cardiometabolic outcomes throughout the life course.
- A comprehensive search strategy was used to identify studies that covered a range of disasters (e.g., famine, war, terrorism, natural disasters, and infectious disease epidemics), periods of exposure from pregnancy, childhood to older adulthood, and a wide breadth of cardiometabolic outcomes.
- Only studies published in English were included and a search of the grey literature was not conducted.
- Due to the heterogeneity of studies, a meta-analysis could not be conducted, and results were only synthesized narratively.
- Limited evidence was available on the impact of pandemics specifically, and few studies evaluated proposed mechanisms or risk modification across subgroups of the populations.

BACKGROUND

Disasters, as defined by the World Health Organization (WHO), are events that disrupt the daily functioning of a community or society causing material, economic or environmental losses, and overwhelming local capacity (1). Disasters can be categorized into natural disasters, human-made disasters, and hybrid disasters (2). Natural disasters include natural phenomenon above and beneath the earth's surface (e.g., tsunamis or landslides), meteorological phenomenon (e.g., tornadoes or floods) or biological phenomenon (e.g., epidemics and pandemics) (2). Human-made disasters include adverse transportation incidents, technological events (e.g., fire or toxic leaks), terrorism, warfare or conflict (2). A hybrid disaster results from both human and natural forces, such as the clearing of a jungle that results in a landslide (2). All types of disasters can result in public health emergencies as they typically impact a significant proportion of people (3). Epidemics, defined as a greater than expected increase in cases of a disease, and pandemics, which cross countries and continents, are types of natural disasters with far-reaching global disruption (4). The COVID-19 pandemic is a present-day example of a global disaster that is unlike any disaster in recent history. Understanding the potential long-term health implications of the current COVID-19 pandemic and resulting public health mitigation strategies is urgently needed.

Previous systematic reviews have focused on acute outcomes, specifically on the psychological impact of quarantine during pandemics (5), the impact on health outcomes after disasters in older adults (6), medically unexplained physical symptoms following disasters (7), and chronic medical interventions following a natural disaster (8). It is

biologically plausible that exposure to a disaster may lead to long-term or chronic outcomes that could arise many years later and this may be modified by the time of exposure across the life course. Consistent with established models of life course epidemiology there may be critical periods of exposure (e.g., during development in childhood), where exposure to a disaster substantially increases later life disease risk, or exposure to a disaster may contribute to a chain of risk or accumulation of risks across the life course (9,10). There is currently no review on the long-term impacts of disasters, or more specifically, epidemics and pandemics on cardiometabolic outcomes across the life course. Noncommunicable diseases (NCDs), including cardiovascular disease (CVD), obesity, and diabetes, are the leading cause of morbidity and mortality worldwide (11,12). NCDs are attributed to 71% of all global deaths annually, with approximately 14 million CVD-related deaths and 1.6 million diabetes-related deaths (12). Findings from the Global Burden of Diseases Study indicate that CVD and diabetes account for over 20% of the global burden of disability, with diabetes recently emerging as the fourth leading cause of disability globally (11). Exposure to disasters may cause cardiometabolic outcomes to emerge or worsen through several different mechanistic pathways including stress exposure (13), lack of access to health services (14), food security and behavioural changes such as alterations in physical activity, sleep, and diet (15). It is important to understand the impact of disasters on the incidence of new cardiometabolic diseases and changes in disease status in all populations and age groups. Particular subgroups of a population may be more or less susceptible to cardiometabolic outcomes and understanding this can inform targeted interventions. The primary objective of this review

was to determine the impact of disasters, including pandemics on risk of cardiometabolic outcomes across the life course. The secondary objectives were to determine how to reduce the impact of chronic disease outcomes following a disaster and to identify populations at highest risk of cardiometabolic outcomes following a disaster.

METHODS

A systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (16). This review was registered on PROSPERO (CRD – 42020186074).

Search strategy

A systematic search was conducted in May 2020 using the electronic databases EMBASE and MEDLINE. The health research librarians at McMaster University assisted in developing the search strategy. The search broadly captured two concepts: disasters and cardiometabolic outcomes (e.g., diabetes, obesity, hypertension). The complete search strategy for EMBASE can be found in Table 1. The search strategy for MEDLINE can be found in the Appendix (Table A1). Reference lists of eligible studies and relevant systematic reviews were hand searched to identify additional articles.

Eligibility criteria

Studies were eligible for inclusion if they assessed the relationship between a population-level or community disaster and the risk of future cardiometabolic outcomes

including CVD, diabetes or obesity or cardiometabolic risk scores (17). CVD included myocardial infarction, stroke, hypertension and angina. There were no restrictions on year of publication, country of disaster, or population. Only studies evaluating the impact of real-world disasters in humans were included. Due to the research team's capacity, only studies published in English were included. Observational and quasi-experimental study designs, including case-control, cohort and other longitudinal study designs or natural experiments were included. Outcomes that were not cardiometabolic-related or acute cardiometabolic events, such as an immediate complication (defined as <1 month after disaster), were excluded. Studies that assessed the exposure to a chemical as a result of the disaster, were excluded, as we were not interested in outcomes resulting from chemical exposure. Earthquake studies were also excluded since a systematic review was published in 2018 that assessed the impact of earthquakes on cardiometabolic outcomes (18).

Study selection

After running the search, all identified studies were imported into Covidence and duplicates were removed (19). Studies were screened at title and abstract-level, and then at full-text by any two of the following independent reviewers VD, JL, MSA, YYM, ATA, ES, SI, JDM, RR LNA. Conflicts were resolved by a third reviewer who made the final decision regarding eligibility for inclusion.

Data extraction

A data extraction template was created, and pilot tested prior to data extraction. Data were then extracted from all studies by any two of the following independent abstractors VD, JL, SMA, YYM, ATA, RR, ES and conflicts were resolved by a third independent abstractor. Study characteristics including year of publication, study design, country of disaster, sample size, and length of study were extracted where reported. Specific information on the exposure and outcome in each study were extracted including the type and name of the disaster, country and year of the disaster, the outcome of interest, and how the exposure and outcome were measured. Finally, any information on subgroups including age, population, sex and disaster type were also extracted, if applicable.

Critical appraisal

Critical appraisal was conducted using the Joanna Briggs Institute (JBI) Critical Appraisal Tools (20). This tool was chosen due to the availability of checklists for a wide range of study designs, including cohort, cross-sectional and quasi-experimental designs (20). The quasi-experimental study design checklist was used for natural experiments including time-series studies and pre/post designs, as it was decided this was the most appropriate tool. All studies were critically appraised independently by any two of the following individuals VD, JL, MA, YYM, ATA, ES, SI and a third individual was consulted for any discrepancies.

Data analysis

Data from the included studies were narratively synthesized. Results are presented by exposure period (perinatal/childhood versus adulthood) and by cardiometabolic outcome (obesity, CVD, and diabetes). Characteristics of studies are presented as frequencies and percentages. Due to the heterogeneity of studies, a meta-analysis was not conducted.

RESULTS

A total of 4830 studies were identified through the electronic database search. An additional 12 studies were identified through manual searching of the reference lists of relevant studies. After removing duplicates (n=439), 4403 studies were screened at title and abstract level. After applying inclusion and exclusion criteria, 4068 studies were excluded, leaving 335 studies screened for full-text eligibility. A total of 58 studies were eligible for inclusion into the review. The complete screening process is described in Figure 1.

Description of studies

Table 2 provides a summary of included studies. Of 58 included studies, 24 studies (15,21–43) investigated exposure to disasters during pregnancy or childhood while the remaining 34 studies (14,44–76) investigated exposure to disaster during adulthood. Almost all studies (n=49) assessed cardiometabolic outcomes during adulthood, only two studies assessed outcomes during pregnancy (27,28) and seven studies assessed outcomes during childhood and adolescence (15,21–26). The length of

studies, including prospective follow-up and retrospective assessment, ranged from one month to 95 years. Most studies (n=36) focused on disasters that occurred in North America (14,21–28,38,39,42,45–49,51,52,54,55,57–60,63–65,67–72,75,76), followed by Europe (n=13) (29–33,35,41,43,53,62,73,74). The remaining disasters occurred in Asia (n=7) (15,37,40,44,50,56,61) and Africa (n=2) (36,66). The characteristics of included studies and key findings are provided in Table 3 for disaster exposure during the perinatal period and childhood, and Table 4 for exposure during adulthood.

Exposure to disaster in the perinatal and childhood period

Of the 24 studies that evaluated perinatal and childhood exposure to disaster, 12 studies evaluated human-made disasters (29–35,40,41,47) and the remaining 12 evaluated natural disasters (15,21–28,38,39,42) of which two were pandemics (38,39). Most studies (n=15) assessed the disaster as the main exposure of interest (24,28–33,35,36,39–42). The remaining studies evaluated stress (e.g., maternal stress, disaster-related PTSD, subjective stress, objective hardship) (21–25,27,47), maternal weight and maternal nutrition status (15,34), cognitive appraisal (26), and coping strategies (27) that were the result of the disaster as the exposure variable. The age when cardiometabolic outcomes were assessed varied across studies, with two studies evaluating pregnancy outcomes (27,28), 8 studies evaluating outcomes among children and youth (15,21–26,47), four studies assessed outcomes during young to mid adulthood (>18-40 years of age) (27,29,36,37), and 10 during later adulthood (≥50 years of age) (30,32–35,38–42). One study did not specify the exact age, rather evaluated outcomes throughout adulthood, from 18-63 years of age (31).

Detailed characteristics and findings of all studies that assessed perinatal and childhood exposures to disasters can be found in Table 3.

Within the 10 studies that evaluated perinatal or childhood disaster exposure in relation to pregnancy, childhood, or youth outcomes, one study evaluated a human-made disaster (the World Trade Center Attacks) and the other nine studies evaluated natural disasters (including ice storms, floods and hurricanes) and the findings were mixed. The one study that evaluated a human made disaster found limited evidence of any increased cardiometabolic risk and a small decrease in both BMI and zBMI was observed for children exposed to the World Trade Centre attacks compared to those who were not but found no differences in triglycerides or lipids (47). Within the eight studies that evaluated exposure to a natural disaster during the perinatal and childhood period and cardiometabolic outcomes in later childhood, there were six studies that evaluated measures of child growth and four of these studies reported increased BMI or adiposity in later childhood (21,23,25,26), one study was null (22) and one study reported increased wasting or malnutrition following exposure to a flood (15). Importantly, the one study where increased wasting was observed was in Bangladesh, whereas all of the studies that observed increased risk of obesity were in North America. Of the studies that evaluated childhood cardiometabolic outcomes other than growth, one study found increased insulin concentrations at age 13 (24). There were two studies that evaluated exposure to a natural disaster (Hurricane Katrina and Hurricane Sandy) during pregnancy and both found increased incidence or hospital visits for gestational hypertension and diabetes (27,28).

There were 14 studies that evaluated exposure to a disaster in pregnancy or childhood in relation to the subsequent onset of adult cardiometabolic conditions; 11 of these studies evaluated exposure to human made disasters and three evaluated natural disasters. Within the 11 studies that evaluated human made disasters, one study found no association between exposure to the Dutch famine and coronary artery disease in older adulthood (32). While the remaining 10 studies all found some evidence of increased cardiometabolic outcomes in adulthood following perinatal or childhood exposure, the results were mixed with many null results depending on outcome or exposure. For example, prenatal exposure to famine was associated with higher LDL and CHD approximately 28 years later, however no difference was found for glucose, insulin, BMI or other lipids (29). The results were not consistent across outcomes, for example, increased risk of hypertension was found in three studies (29,36,40) but not in two studies (35,37). Within the three studies that evaluated adult cardiometabolic outcomes following exposure to a natural disaster, all three studies found increased risk of cardiovascular diseases or mortality following prenatal exposure to famine or the 1918 influenza pandemic (38,39,42).

Studies on adult exposure to disaster and subsequent cardiometabolic outcomes

Thirty-four studies investigated the effects of exposure to disasters during adulthood on cardiometabolic outcomes. The length of follow-up ranged from one month to 13 years. There were 23 studies that examined natural disasters (14,44–46,48,51,52,54–56,58–61,64–67,72–76), and 11 studies that examined human-made disasters (43,49,50,53,57,62,63,68–71). Of these studies, only one evaluated the impact of

an infectious disease epidemic (66). Most studies (n=27) considered the disaster as the main exposure of interest (14,43–46,48,50,52,54–56,58–66,68,71–76). The remaining seven studies assessed disaster-related stress (53,57,67,69), including post-traumatic stress disorder (PTSD) and psychological strain, unemployment rates as a result of the disaster (51) and exposure to damaged or collapsed buildings during the World Trade Center disaster (70). Detailed characteristics and findings of all studies that assessed adult exposures to disasters are included in Table 4.

The studies that assessed exposure to human-made disasters (n=11) during adulthood reported mixed results in terms of associations with outcomes and statistical significance. Three studies assessed PTSD related to disasters and found an increased association with stoke (69), heart disease (57) and cardiovascular/vascular problems (53), two of which were exposure to the World Trade Centre disaster and the third was a Fireworks depot explosion. Two studies assessing exposure to the World Trade Centre disaster and Amsterdam Air disaster found an increased association with cardiovascular hospitalizations (49) and cardiovascular symptom complaints (62) in rescue workers compared to non-rescue workers. Of the remaining six studies, three studies reported an increased association with hypertension (43), systolic blood pressure (71) and CVD mortality (63), however, the exact exposure varied across studies. For instance, one study explored the level of exposure, defined as low, intermediate, or high to the World Trade Centre disaster (63), whereas another study evaluated exposure to the Volendam Pub Fire among parents who had children who were injured or died (43). The final three studies assessing exposure to human-made disasters (World Trade Centre disaster and Sewol

Ferry disaster) reported mixed results with some showing a decreased association or null findings (53,68,70).

Among studies that evaluated the impact of exposure to natural disasters (n=23), six studies that evaluated exposure to Hurricanes Sandy, Katrina, Iniki, and the Flood of Saint-Jean-sur-Richelieu reported an increased association with cardiometabolic outcomes (45,46,51,58,64,72). One of these studies specifically investigated unemployment as a result of Hurricane Katrina and found those who were unemployed, compared to those who remained employed were 5.65 times more likely to have a cardiometabolic event ($p<0.05$) (51). Nine studies reported a statistically significant increase in outcomes following exposure disaster (52,54–56,61,67,73–75). For instance, one study found those who reported higher levels of psychological strain after surviving Hurricane Ike, compared to those with lower levels of psychological strain had higher mean blood glucose and obesity four months after the disaster (67). Whereas another study found a higher proportion of people experiencing worse hypertension who were living in households affected by the 2008 Hanoi flood compared to those who lived in an unaffected households in both rural and urban areas (61). Two of these studies reported an increase in incidence of AMI and AMI hospital admission pre-Hurricane Katrina, compared to post-Hurricane Katrina (54,55). The remaining six studies reported a mix of findings. Three studies found varying associations across outcomes reported within their study. For example, Fonseca et al., found an increased mean difference pre- and post-Hurricane Katrina for glycemic control, systolic blood pressure, diastolic blood pressure,

and HDL, but not for LDL and triglycerides (59). Nine studies reported mixed findings across outcomes within the study. Four of these studies found both an increase and decrease in outcomes when comparing mean difference or proportion pre- and post-disaster (14,48,66,76). One study found those with higher reports of exposure to natural disaster throughout the life course were significantly different from those with lower reports (44). The final two studies found a decreased proportion of AMI following Hurricane Katrina (65) and no significant association between exposure to the Oklahoma tornado and hospital admission for cardiovascular events (60).

Mediation and modification of cardiometabolic outcomes

Across all studies, few evaluated effect modification or subgroups of a population that may be at a greater risk of negative health outcomes following disasters. Eight studies stratified by sex (30,34,36,41,45,50,57,64), gestational timing of exposure (22,29,31–33,35,38), year of birth or age at outcome (42,64,69), urban or rural area (37), race (45,48) and socioeconomic status (67), however, results varied greatly due to the differences in exposure period, disaster type, cardiometabolic outcome and age at outcome. One study explored the possible mediators between cognitive appraisal following the Quebec Ice Storm and obesity. It was noted that negative cognitive appraisal was found to predict obesity via DNA methylation of diabetes-related genes (26). No studies evaluated or discussed possible interventions to mitigate risk of cardiometabolic disease following a disaster.

Critical appraisal

The critical appraisal assessment for all study designs can be found in the Appendix (Tables A2-A4). Among the cohort studies, most studies met all criteria included in the checklist indicating high study quality. For instance, almost all cohort studies had comparable populations that were recruited in a similar way and exposures that were assessed in the same way across populations. However, across almost all cohort studies, information on follow-up or strategies to address incomplete follow-up were unclear or not addressed. The critical appraisal results for cross-sectional studies were inconsistent with a small number of studies meeting only some checklist requirements. For quasi-experimental studies, the checklist requirement for within person comparisons were not applicable for all studies, however, all studies clearly defined the cause and effect within the study.

DISCUSSION

Principal findings

A total of 58 studies were identified and they covered a wide breadth of exposures to both natural and human-made disasters, including famine, war, terrorism, natural disasters, and infectious disease epidemics. Exposures were investigated in pregnancy and childhood exposure through to adulthood with outcomes measured 1 month to 95 years later. The reviewed studies reflect a true-life course body of literature with exposures at multiple ages and long-term exposures. A range of cardiometabolic outcomes including obesity, hypertension, myocardial infarction, diabetes, and cardiac mortality were

investigated. Given the varied nature of the studies, it was difficult to draw overall conclusions, but the vast majority of studies provided some evidence of increased cardiometabolic risk following disaster exposure. There were only 11 studies that reported no increased risk or had unclear findings. Across these studies, there was a variety of disaster exposure, outcomes, and follow-up periods, however seven of these studies did not report adjustment or consideration of any confounders.

Relation to other studies

To the best of our knowledge, this is the first review to systematically review the literature on a broad range of disasters and cardiometabolic health outcomes across the life course. Other reviews have focused on a specific population, such as older adults, specific disaster types (e.g., natural disasters only) or other health conditions (e.g., mental health) or acute outcomes (5,6,8). However, across most reviews it was apparent the heterogenous nature of included studies makes it difficult to summarize findings and make overall conclusions and recommendations. For instance, Chan et al. found exposure to natural disasters negatively affected those with chronic conditions, although authors noted limitations due to limited literature (8). Another systematic review found very heterogenous results when reviewing the literature on health outcomes after disasters for older adults with chronic disease (5). The studies included here were from multiple disciplines and utilized a variety of studies designs, assessed several different outcomes, and applied different statistical approaches. Overall, the results suggested increased risk of adverse cardiometabolic outcomes following disasters, although this was not apparent

across all included studies (6). The unexpected nature of disasters, uniqueness of population or region affected, and scale of damage lead to research studies that vary greatly. Although previous reviews and the current review have identified quite heterogenous studies, overall conclusions suggest risk of disease increases after exposure to disasters.

Biologic mechanisms

Several potential mechanisms were discussed in the included studies that may contribute to the observed associations between disaster exposure and increased cardiometabolic outcomes, include the role of both objective and subjective stress, nutritional changes, and reduced access to healthcare. One study that explored mediators in the association between stress and obesity measures identified the role of DNA methylation in this association (26). It is well postulated that the activation of a stress response following a stressful event leads to changes in the nervous, cardiovascular, endocrine and immune systems (77). Exposure to disasters including famine, war, terrorism, natural disasters, and infectious disease epidemics may activate a stress response, altering the progression of disease development (77). The repeated or prolonged exposure to various disasters, such as a pandemic spanning over months, may lead to worse health outcomes. Reduction in health services is another possible mechanism leading to worse health outcomes. Healthcare services may be directed toward the immediate response to health-related consequences caused by the disaster (e.g., illness from a pandemic, injuries associated with a terrorist attack or natural disaster), limiting access to primary care (78). This interruption to services may decrease screening or early

treatment ultimately leading to the rise in chronic diseases. Lastly, social determinants of health are known to be important risk factors for cardiometabolic conditions (79). At least one study investigated whether the observed associations were due to changes in educational attainment (42) and unemployment (51) . More investigation of the role of social determinants as modifiers or mediators of the associations between disasters and long-term cardiometabolic outcomes may be warranted. Despite numerous proposed biologic mechanisms and well-established life course frameworks, relatively few studies actually evaluated potential causal pathways using a life course framework, and this may contribute to some of the observed heterogeneity in results.

Strengths and limitations

This review had several strengths including the comprehensive evaluation of the impact of a wide range of disaster exposures on various cardiometabolic outcomes at different periods throughout the life course. The search strategy was developed in consultation with health science librarians at McMaster University to ensure the most comprehensive search was developed and relevant literature was identified. The timely findings of this synthesis are a strength of this review, given the current COVID-19 pandemic, which is affecting millions of people worldwide. While only a small proportion of the identified studies focused on pandemics and epidemics, the findings may serve to guide our understanding of expected outcomes, and to develop future research to study the effects of COVID-19 on cardiometabolic outcomes.

Although this review had several strengths, interpretation of findings should be done with caution due to limitations. First, the heterogeneity across studies restricted the

ability to conduct a meta-analysis. Studies varied in terms of study design, reported measures of effect, the comparison group (e.g., some studies did not include a comparator group), length of follow-up, timing and measurement of exposure, and primary outcomes and how they were measured. Given the multi-disciplinary nature of the identified studies, a wide range of analytic approaches were used, and measures of effect varied. These differences in addition to the lack of statistical significance across studies make it difficult to draw overall conclusions. Many of the studies used a retrospective cohort study design and relied on administrative data sources as such many studies were unable to comprehensively adjust for confounders, including social determinants of health. Measurement error and misclassification of exposure status is also possible since many studies did not objectively measure disaster exposure or degree of impact, and instead used proxy measures of disaster exposure based on time and geography.

Very few studies have evaluated the long-term impacts of pandemics and epidemics on cardiometabolic outcomes, identifying a current gap in the literature. This made it difficult to truly assess if exposure to disasters at sensitive periods of development had lasting effects much later in life. Studies also reported insufficient data on subgroups that were at increased risk of worse cardiometabolic health outcomes and interventions that were implemented to mitigate risk of cardiometabolic outcomes. In addition, results were not often explored by sex and gender, or did not apply an equity lens. It has been noted that those of different levels of socioeconomic status experience differential cardiometabolic outcomes (80,81). This signifies the importance of exploring associations between exposure to disasters and cardiometabolic outcomes stratified by

these factors. Understanding how these associations differ will also help to identify groups of people who will experience worse outcomes following a disaster.

Study implications

To the best of our knowledge, this is the first study to comprehensively explore the impact of several different types of disasters on cardiometabolic outcomes at different periods throughout the life course. The results suggest that increased risk is observed for disaster exposure at any period over the life course from the perinatal child and adult periods. These findings emphasize that the burden of disasters extends beyond the known direct harms they cause, and attention is needed on the detrimental indirect long-term effects on cardiometabolic health and chronic disease. Given the current COVID-19 pandemic, this review may be helpful in raising awareness of the potential increase in cardiometabolic health outcomes post-pandemic, to ensure appropriate public health mitigation measures are developed and implemented to prevent long term cardiometabolic outcomes at the population level.

Unanswered questions and future research

Future research should evaluate the impact of pandemics, such as COVID-19, on future cardiometabolic health throughout the life course. It may also be of interest for future research to explore the impact of implementing public health measures, such as physical distancing to reduce transmission of a virus, and the implications following a disaster with access to healthcare on health outcomes. This information would be helpful

in planning public health responses to different disasters. In addition, further investigation of possible mechanisms, such as disruptions to healthcare or medication access, and changes in dietary intake or physical activity, is needed. This would help to develop preventative strategies targeted at these mechanisms to help reduce the possible cardiometabolic consequences after experiencing a disaster. This review found insufficient evidence identifying subgroups of the population who are at the greatest risk or specific disaster related risk factors that that increase cardiometabolic disease development following a pandemic. This is an important gap that needs to be addressed by future research.

Table 1. Search strategy for EMBASE

1	social isolation.mp. or social isolation/	24963
2	quarantine.mp. or quarantine/	4752
3	*epidemic/	32686
4	*pandemic/	4387
5	disease outbreak.mp.	2321
6	disaster/	13321
7	*natural disaster/	968
8	humanitarian crisis.mp.	257
9	mass casuality.mp. or mass disaster/	3654
10	coronavirus.mp. or coronaviridae/	23106
11	cardiovascular disease.mp. or *cardiovascular disease/	357319
12	*diabetes mellitus/	210248
13	*cerebrovascular accident/	78444
14	*heart infarction/	99072
15	*angina pectoris/	22631
16	*obesity/	178134
17	public health emergency.mp.	1752
18	*body mass/	31459
19	*hypertension/	198593
20	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 17	109105
21	11 or 12 or 13 or 14 or 15 or 16 or 18 or 19	1087681
22	20 and 21	2047
23	limit 22 to human	1832

Table 2. Characteristics of included studies (n=58)

Characteristics	N (%)
Continent	
North America	36 (62%)
Europe	13 (22%)
Asia	7 (12%)
Africa	2 (3%)
Year of Publication	
2010-2020	44 (76%)
2000-2009	12 (21%)
1996-1999	2 (3%)
Study design	
Cohort/longitudinal	41 (71%)
Quasi-experimental[1]	10 (17%)
Cross-sectional	7 (12%)
Sample size	
≥10,000	19 (33%)
1,000- <10,000	10 (17%)
≤1,000	24 (41%)
Not specified	5 (9%)
Exposure life stage	
Pregnancy/Childhood	24 (41%)
Adulthood	34 (57%)
Outcome life stage	
Pregnancy	2 (3%)
Childhood [2]	8 (13%)
Adult	47 (81%)
Disaster	
Human-made	23 (40%)
Natural	35 (60%)
Cardiometabolic outcome [3]	
Cardiovascular disease [4]	41 (71%)
Diabetes [5]	11 (19%)
Obesity or BMI	12 (21%)
Mortality from cardiovascular disease	9 (16%)
Cardiometabolic risk during pregnancy [6]	2 (3%)

1. Includes pre/post study design, time series and natural experiments
2. Children defined as ≤18 years of age
3. Does not equal to 100% as studies report multiple cardiometabolic outcomes
4. Includes hypertension, coronary artery disease/heart disease, angina, heart attack/myocardial infarction, metabolic syndrome, cardiac disease related blood markers, stroke
5. Diabetes, blood glucose, metabolic syndrome
6. Gestational diabetes, gestational hypertension, pre-eclampsia

Table 3. Characteristics of included studies investigating the association between exposure to a disaster during the perinatal and childhood periods and cardiometabolic outcomes across the life course, by disaster type (n=24)

Study	Study design	Country	Name of disaster	Year	Sample size	Primary exposure and comparator	Average follow-up	Outcomes	Primary results[1]
Human-made disaster with child/youth outcome									
Trasande, 2018 (47)	Prospective cohort study	USA	World Trade Center attacks (9/11)	2001	402	New York children and youth enrolled in the World Trade Center Health Registry (birthdates: Sept 11, 1993 to September 10, 2001) compared to individuals born during the same time period who were ineligible for enrollment in the WTCHR	2 years	Youth outcomes: 1) BMI (kg/m2) 2) zBMI 3) Triglycerides (mg/dL) 4) Cholesterol (mg/dL) 5) LDL (mg/dL) 6) HDL (mg/dL)	Regression coefficient and 95% CI: 1) BMI: -1.12 (-2.11, -0.12) 2) zBMI: -0.24 (95% CI: -0.49. -0.002) 3) logTrig: 0.02 (95% CI: -0.07, 0.12) 4) logChol (0.02 (95% CI: -0.02, 0.06) 5) log LDL: 0.06 (95% CI: -0.001, 0.12) 6) logHDL: -0.04 (95% CI: -0.10, 0.03)
Human-made disaster with adult outcome									
Bercovich, 2014 (40)	Cross-sectional	Israel	Holocaust	1941-1945	300	European Jews born in 1940-1945 with exposure to the holocaust compared to European Jews during the same time period born	N/A	Adult outcomes: 1) Hypertension 2) Diabetes 3) Dyslipidemia 4) Any cardiovascular disease	1) Adjusted OR: 2.2, 95%CI: 1.2-3.8 2) Adjusted OR: 2.2, 95%CI: 1.2-4.2 3) Adjusted OR: 3.1, 95%CI: 1.7-5.7 4) Adjusted OR: 2.6, 95%CI: 1.4-4.7
de Rooij, 2007 (30)	Cohort	Netherlands	Dutch Famine	1944-1945	783	Prenatal exposure to Dutch famine defined as people born between January 7, 1945 and December 8 1945 compared to people	58 years	Metabolic syndrome at age 58	Metabolic syndrome OR: 1.2; 95% CI: 0.9, 1.7

						born before Jan 7 1945 or conceived after Dec 8 1945			
Ekamper, 2015 (31)	Cohort	Netherlands	Dutch Famine	1944-1945	41096	Male military conscripts born between Jan 1944 and 1946 and compared to military conscripts born before 1944 or after 1946	63 years	Adult outcomes: 1) Heart disease mortality 2) Cerebrovascular disease mortality 3) Diabetes mellitus mortality	Hazard ratio (HR): 1) HR: 0.94; 95% CI: 0.77, 1.15 2) HR: 1.55, 95% CI: 0.95, 2.51 3) HR: 1.61, 95% CI: 0.91, 2.86
Huang, 2010 (37)	Cohort	China	1959-1961 Chinese Famine	1959-1961	35,025	County level famine intensity for women born during 1957-1962 compared to women born post-famine in 1963	32 years	Adult outcomes at age 32: 1) BMI among rural sample 2) BMI among urban sample 3) Hypertension among rural sample 4) Hypertension among urban sample	1) Average effect = 0.92, 95% CI: 0.32, 1.51 2) Average effect = 0.03, 95% CI: -2.82, 2.87 3) Log odds = 1.23, 95% CI: -0.38, 2.84 4) Log odds = 0.37 95% CI: -2.07, 2.80
Hult, 2010 (36)	Cohort	Nigeria	Biafran Famine	1967-1970	1,339	Individuals exposed to famine during early childhood (born 1965-1967) or exposed to famine in fetal life and infancy (born 1968-Jan 1970) compared to	~40 years	Adult outcomes at age ~40 years: 1) Hypertension 2) Diabetes 3) Overweight (BMI>25 kg/m^2)	Adjusted OR (95% CI) 1) Childhood exposure OR: 1.42, 95% CI: 0.63, 3.13; Fetal-infant exposure: OR: 2.50, 95% CI: 1.19, 5.26 2) Childhood exposure OR: 1.81, 95% CI: 0.64, 5.15;

						people born between 1971 and 1973		4) Obesity (BMI>30kg/m^2)	Fetal-infant exposure OR: 2.56, 95% CI: 0.92, 7.17 3) Childhood exposure OR: 1.02, 95% CI: 0.77, 1.34; Fetal-infant exposure: OR: 1.41, 95% CI: 1.03, 1.93 4) Childhood exposure OR: 1.20, 95% CI: 0.87, 1.67; Fetal-infant exposure: OR: 1.30, 95% CI: 0.92, 1.85
Lumey , 2012[1] (32)	Cohort	Netherlands	Dutch Famine	1944-1945	1075	Infants whose mothers were exposed to famine during or immediately preceding pregnancy (born Feb 1, 1945, March 31, 1946) compared to individuals born in the same hospital before or after famine	~56-62 years	Adult outcomes at 56-62 years Coronary artery disease	Early gestation HR: 1.26, 95%CI: 0.59, 2.70 Late gestation HR: 1.31, 95%CI: 0.67, 2.57
Painter, 2006 (33)	Cohort	Netherlands	The Dutch Famine	1944-1945	975	Infants who were born between January 1945 and December 1945 who were exposed to famine in utero compared to infants born before the famine (November 1943 and January 1945) and after the famine (December 1945 and February 1947)	~50-58 years	Adult outcomes at 50-58 years: Coronary artery disease	HR: 1.9, 95% CI: 1.0, 3.8

Ravelli, 1999[2] (34)	Cohort	Netherlands	The Dutch Famine	1944-1945	741	Infants exposed to famine during different periods of gestation (late, mid and early) whose maternal daily ration was <1000 kcal (born between January 1945 and December 1945) compared to those born not during the famine	50 years	Obesity adult outcomes at 50 years stratified by sex: 1) Weight (kg) 2) BMI (kg/m2) 3) Waist circumference (cm)	Mean difference (95% CI) between exposure during late or early gestation versus nonexposed: Men: 1) late: 0.8 (-3.1, 4.7); early: 1.5 (-3.5, 6.6) 2) late: 0.4 (-3.5, 4.5); early: 0.5 (-4.6, 6.0) 3) late: 1.8 (-1.4, 4.9); early: (1.8 (-2.4, 6.0) Women: 1) Late: -1.8 (-6.1, 2.5); early: 7.9 (2.5, 13.2) 2) late: -2.1 (-7.0, 3.1); early 7.4 (0.7, 14.5) 3) late: -0.7 (-4.4, 3.0); early: 5.7 (1.1, 10.3)
Roseboom, 2001[2] (29)	Cohort	Netherlands	The Dutch Famine	1944-1945	2414	Infants who were exposed to famine in utero whose mother had a daily ration <1000 calories during any 13-week period of gestion compared to infants who were born before or conceived after the famine period (before November 1943 or after February 1947)	~28 years	Adult outcomes at 28 years; 1) Plasma glucose (mmol/l) 2) Plasma insulin (pmol/l) 3) Total cholesterol (mmol/l) 4) HDL (mmmol/l) 5) LDL (mmol/l)	Mean values of outcomes for late gestation and early gestation: 1) Late: 6.3; early: 6.1 2) Late: 200; early: 207 3) Late: 5.83; early: 6.13 4) Late: 5.83; early: 6.13 5) Late: 1.32; early: 1.26* 6) Late: 3.87; early: 3.26* 7) Late: 26.7; early: 28.1 8) Late: 2.5; early: 8.8* 9) Late: 127.4; early: 123.4 10) Late: 86.4; early: 84.8 * $p<0.05$

								6) LDL/HDL cholesterol 7) BMI (kg/m) 8) CHD 9) Systolic BP (mmHg) 10) Diastolic BP (mmHg)	
Schrier, 2011 (41)	Cohort	Finland	Winter War and Continuation War	1939-1940 (Winter War), 1941-1944 (Continuation War)	13,039	Individuals in utero who were exposed to bombings that occurred for 48 days between 1934-1944 compared to those who were not exposed in utero	~60-70	Adult outcomes: 1) Coronary heart disease 2) Cerebrovascular disease	Results are shown graphically Higher CHD survival rates among women 64+ and among men aged 50-54 exposed while in utero
Stein, 2006 (35)	Cohort	Netherlands	The Dutch Famine	1944-1945	971	Prenatal exposure to famine defined as the weeks post-last menstrual period that mother was exposed to an official ration of <900 kcal/week (gestation weeks: 1-10, 11-20, 21-30, or 31-delivery)	59	Adult outcomes: 1) systolic BP (mmHg) 2) Diastolic BP (mmHg) 3) Hypertension	Adjusted regression coefficients 1) 1-10 weeks: 1.20 (95% CI: -3.28, 5.69); 11-20 weeks: -1.19 (95% CI: -4.92, 2,55); 21-30 weeks: 1.33 (95% CI: -2.24, 4.90); 31-delivery: 2.02 (95% CI: -1.53, 5.57) 2) 1-10 weeks: 1.10 (95% CI: -1.36, 3.57); 11-20 weeks: -1.26 (95% CI: -3.32, 0.80); 21-30 weeks: 1.19 (95% CI: -0.78, 3.15);

									31-delivery: 0.71 (95% CI: -1.24, 2.66) 3) 1-10 weeks: 1.14 (95% CI: 0.62, 2.11); 11-20 weeks: 0.98 (95% CI: 0.59, 1.65); 21-30 weeks: 1.23 (95% CI: 0.74, 1.05); 31-delivery: 1.42 (95% CI: 0.86, 2.35)
Natural disaster with pregnancy outcomes									
Oni, 2015 (27)	Cross-sectional	USA	Hurricane Katrina	2005	146	Women who were pregnant during Hurricane Katrina or became pregnant immediately after hurricane compared to those who were not exposed to the hurricane; Women who experienced prenatal stress caused by Hurricane Katrina compared to those who did not experience stress	9 months	Pregnancy related outcomes: 1) Pregnancy induced hypertension 2) Gestational diabetes	1) Hurricane exposure: adjusted OR: 1.22 (95% CI: 0.81, 1.84); perceived stress: adjusted OR: 1.16 (95% CI: 1.05, 1.30); 2) Hurricane exposure: adjusted OR: 1.04 (95% CI: 0.69,1.57); perceived stress: adjusted OR: 1.13 (95% CI: 1.02, 1.25)
Xiao, 2019 (28)	Time series/Quasi-experimental	USA	Hurricane Sandy	2012	Not reported	Exposure to Hurricane Sandy lasting impacts defined as the following 12 months after Sandy (November 2012-October 2013) compared to the November to October	12 months	Outcomes in adults: 1) Emergency department visits for gestational hypertension 2) Emergency	1) Increased at 7 months: 7.3% (95% CI: 1.0%, 13.9%) 2) Increased at 8 months:26.3% (95% CI: 3.9%, 53.6%)

						in other years during November 2005 to October 2014 among women who were pregnant		department visits for diabetes or abnormal glucose	*results for 12 months reported graphically
Natural disaster with child/youth outcomes									
Cao-Lei, 2016 (26)	Cohort	Canada	Quebec Ice Storm	1998	31	Negative cognitive appraisal of the impact of the ice storm among pregnant women compared to neutral or positive appraisal	13 years	Outcomes among children at age 13: 1) Central adiposity (waist to height ratio) 2) BMI (kg/m2)	Mean (standard deviation) 1) Exposed: 20.86 (3.73); unexposed: 22.84 (5.19) 2) Exposed: 0.43 (0.04); unexposed: 0.45 (0.06)
Dancause, 2012 (23)	Cohort	Canada	Quebec Ice Storm	1998	111	Higher ~~o~~bjective PNMS scores compared to lower scores among women who were pregnant or conceived within 3 months of the storm	5.5 years	Childhood obesity at 5.5 years of age	OR: 1.37, 95% CI: 1.06-1.77
Dancause, 2013 (24)	Cohort	Canada	Quebec Ice Storm	1998	32	Higher objective hardship compared to lower hardship scores reported among pregnant women exposed to the storm	13.4 years	Childhood insulin secretion at 13 years of age	Insulin secretion: Adjusted linear regression standardized coefficient = 0.52, $p<0.01$
Dancause, 2015 (22)	Cohort	USA	Iowa Flood	2008	106	Higher reported measures of objective hardship and subjective distress compared to lower scores among pregnant women during the floods	2.5-4 years	Childhood outcomes: 1) Child BMI z-scores at age 2.5 2) Child BMI z-scores at age 4 3) Difference in	Beta coefficient (p-value) 1) -0.07 (p=0.56) 2) -0.22 (p=0.07) 3) 0.11 (p=0.41) 4) 0.00 (p=0.97) 5) -0.06

								BMI from age 2.5 to 4 4) Child adiposity (skinfolds) at age 2.5 5) Child adiposity (skinfolds) at age 4 6) Difference in adiposity from age 2.5 to 4	(p=0.72) 6) 0.03 (p=0.82)
Goudet, 2011 (15)	Cohort	Bangladesh	1998 Bangladesh Flood	1998	220	Maternal malnutrition among mothers of infants and young children following flood exposure defined as underweight (BMI<18.5 kg/m2) compared to normal (BMI>=18.5)	12 months	Child outcomes at 12-36 months of age: 1) Underweight (weight for age z-score <-2) 2) Stunted (height for age z-score < -2) 3) Wasted (weight for height z-score < -2)	1) Adjusted OR = 3.509, 95%CI: 1.022,12.048) 2) Adjusted OR: 4.447, 95%CI: 1.044,18.943 3) Adjusted OR: 2.097, 95%CI: 0.507, 8.671
Kroska, 2018 (21)	Longitudinal study	USA	Iowa Flood	2008	103	Levels of maternal stress among those exposed to Iowa floods	2.5 years	Children outcomes at 2.5 years: BMI (kg/m2)	Standardized coefficient: 0.2071 (p=0.0322)

Liu, 2016 (25)	Longitudinal study	Canada	Quebec Ice Storm	1998	52-111 at different time points	Levels of maternal stress (objective hardship and subjective stress) among those exposed to Iowa floods	5.5-15.5 years	Children outcomes at 5.5-15.5 years: 1) BMI (kg/m2) 2) Waist to height ratio	Correlation R (p-value) Age 8.5 1) Objective hardship: 0.21 (p=0.05) 2) Objective hardship: 0.23 (p=0.03) Age 15.5 1) Objective hardship: 0.34 (p=0.02) 2) Objective hardship: 0.44 (p<0.01)
Natural disaster with adult outcomes									
Mazumder, 2010[23] (38)	Cohort	USA	1918 Influenza Pandemic	1918-1919	101,068	Infants who were born during the Influenza pandemic (third and fourth quarter of 1918, and the first, second and third quarter of 1919) compared to those born in the last quarter of 1919	~ 60-82 years	Adult outcomes at 60-82 years: 1) Diabetes 2) Heart disease	Excess cases of diabetes/heart disease: 1) 1918 Q4: 7.7% excess (95% CI: -10.6, 25.9); 1919 Q1: -5.2 (95% CI: -22.9, 12.5); 1919 Q2: 36.7% excess (95% CI: 18.9, 54.4); 2) 1918 Q4: 4.6% excess (95% CI: -4.3, 13.5); 1919 Q1: 10.9% excess (95% CI: 2.3, 19.6); 1919 Q2: 6.4% excess (95% CI: -2.2, 15.1);
Mryskyla, 2013[3] (39)	Cohort	USA	1918 Influenza Pandemic	1918-1919	81,571	Infants who were born during the Influenza pandemic (born during different quarters of 1917, 1918 and 1919)	~ 63-95 years	Adult outcomes at 63-95 years: Cardiovascular mortality	1918 Q1: HR: 1.05 (95% Ci: 0.94, 1.17); 1918 Q2: HR: 1.02 (95% Ci: 0.91, 1.14); 1918 Q3 HR: 0.99 (95% CI: 0.89, 1.10); 1918

						compared to those born in 1920-1924			Q4 HR: 0.97 (95% Ci: 0.87, 1.09); 1919 Q1 HR 1.07 (95% CI: 0.96, 1.19); 1919 Q2: HR:1.06 (95% CI: 0.95, 1.19);
Sotomayer, 2013 (42)	Cohort Natural experiment	Puerto Rico	Hurrican e San Felipe and San Cipiran	1928 and 1932	11990	Those born during 1929 and 1933 were defined as exposed to the hurricanes compared to individuals born outside of these years between 1920 and 1940	Not reported (average age = 70)	Outcomes at ~70 years of age: 1) Diabetes 2) Hypertension 3) High cholesterol 4) CVD 5) AMI 6) Coronary/angina 7) Stroke	Linear regression estimates (p-value) 1) San Felipe: 5.94 (p<0.01); San Ciprian: 5.43 (p<0.01) 2) San Felipe: 4.73 (p<0.01); San Ciprian: 6.39 (p<0.01) 3) San Felipe: 8.85 (p<0.01); San Ciprian: 5.28 (p<0.01) 4) San Felipe: -1.48; San Ciprian: 1.33 5) San Felipe: 0.81; San Ciprian: 3.26 (p<0.01 6) San Felipe: 0.40; San Ciprian: -0.60 7) San Felipe: -0.25; San Ciprian: 0.58

1. Results are numbered to correspond with the numbered outcomes in the outcomes column
2. Only presenting results for early and late gestation; results for mid gestation are not included in summary table but can be found in studies
3. Not all results presented for different exposure groups

Abbreviations: AMI: Acute myocardial infarction; BMI: Body mass index; BP: Blood pressure; CI: Confidence Interval; CHD: Coronary heart disease; Chol: Cholesterol; CVD: Cardiovascular disease; HDL: High-density lipoproteins; HR: Hazard ratio; LDL: Low-density lipoproteins OR: Odds Ratio; PMNS: Prenatal Maternal Stress; Q1-Q4: quarter; SE: Standard error; Trig; Triglycerides.

Table 4. Description of studies investigating the association between exposure to a disaster during adulthood and cardiometabolic outcomes across the life course, by disaster type (n=34)

Study	Study design	Country	Name of disaster	Year	Sample size	Primary exposure and comparator	Average follow-up	Outcomes	Primary results[1]
Human-made disaster									
Brackbill, 2006 (70)	Cohort	USA	World Trade Center attacks (9/11)	2001	8,418	Adult survivors of 9/11 present at time of first airplane impact in a structure that was damaged compared to those that collapsed; time of evacuation before compared to after damage	1 year	1) Hypertension 2) Coronary heart disease 3) Angina 4) Heart attack 5) Diabetes 6) Stroke	1) Building type: adjusted OR: 1.2 ($p<0.05$); time of evacuation: adjusted OR: 0.9 (0.6, 1.3) 2) Building type: adjusted OR: 0.8 (0.4, 1.6); time of evacuation: adjusted OR: 0.5 (0.1, 2.2) 3) Building type: adjusted OR: 0.8 (0.4, 1.6); time of evacuation: adjusted OR: 0.7 (0.2, 3.1) 4) Building type: adjusted OR: 2.1 (0.9, 4.9); 5) Time of evacuation: adjusted OR: 0.7 (0.3, 1.7) 6) Building type: adjusted OR: 1.5 (0.6, 4.0)
Dirkzwager, 2007 (53)	Cohort	Netherlands	Fireworks depot explosion	2000	896	PTSD among those exposed to the fireworks disaster 19 months following the disaster compared to those with no PTSD exposed to the fireworks explosion	18 months	1) Cardiovascular 2) Vascular problems	1) Physical health problems OR: 1.23; 95% CI: 0.78, 1.94; New health problems (not present pre disaster): 1.11; 0.65, 1.89 2) Physical health problems OR: 2.12 95% CI: 1.23, 3.68; 1.92; New health problems (not present pre disaster) OR: 1.92, 95% CI: 1.04, 3.55.

Dorn, 2007 (43)	Cohort	Netherlands	Volendam Pub Fire	2001	2255	Parents of children with burns from fire parents of children without burns, bereaved parents compared to community controls who were not trapped in fire	4 years	Incidence of hypertension	Bereaved parents: OR: 2.42, 95%CI: 0.90, 6.55); parents of victims with burns: OR: 1.43, 95%CI: 0.97, 2.11; parents of victims without burns: OR:1.44, 95%CI: 0.92, 2.26)
Gerin, 2005 (71)	Pre/post design/ quasi experimental	USA	World Trade Center attacks (9/11)	2001	528	Adults 2 months before 9/11 compared to 2 months after 9/11 across 4 cities (Chicago, Washington DC, New York, and Mississippi)	4 months	Systolic blood pressure	Difference (SE) New York: 1.58 (0.82) $p<0.05$ Chicago: 2.15 (0.32) $p<0.001$ Mississippi: 2.92 (0.67) $p<0.001$ Washington DC: 8.67 (1.16) $p<0.001$
Huizink, 2006 (62)	Cohort	Netherlands	Amsterdam Air Disaster	1992	1996	Police officers and firefighters who performed at least one disaster-related task compared to professional colleagues who did not perform any disaster-related tasks	8.5 years	Cardiovascular complaints	Adulthood outcomes Police officers: OR: 1.76 (95% CI: 1.35, 2.29) Firefighters: OR: 3.3 (95% CI: 1.70, 6.41)
Jordan, 2011A (57)	Prospective cohort	USA	World Trade Center attacks (9/11)	2001	39,324	9/11-related PTSD compared to no PTSD	2.9 years	Heart disease	Women adjusted OR: 1.68 (95% CI: 1.33, 2.12) Men adjusted OR: 1.62 (95% CI: 1.34, 1.96)

Jordan, 2011B (63)	Prospective cohort study	USA	World Trade Center attacks (9/11)	2001	39324	Low, intermediate and high exposure to 9/11	2.9 years	Heart disease mortality	Intermediate exposure: HR: 1.21 (95% CI: 80, 1.83) High exposure: HR: 2.06 (95% CI: 1.10, 3.86)
Jordan, 2013[2] (49)	Cohort	USA	World Trade Center attacks (9/11)	2001	46,346	Low, intermediate and high exposure to 9/11	7 years	CVD hospitalizations	Rescue/recovery workers: women: high: adjusted HR: 3.29 (95% CI: 0.85, 12.69); men: high: 1.82 (95% CI: 1.06, 3.13) Non-rescue/recovery workers: women: high: adjusted HR: 0.88 (95% CI: 0.54, 1.43); men: high: adjusted HR: 0.94 (95% CI: 0.60, 1.47)
Kong, 2019 (50)	Pre/post design/ quasi experimental	South Korea	Sewol Ferry Disaster	2014	73,632	Exposure to the Sewol Ferry Disaster in one-week periods from May 21 through June 17, 2014 compared to the reference period (March 2015-April 2015)	8 weeks	Adulthood outcomes 1) Acute MI 2) Angina	1) 8 weeks after Sewol: IRR: 0.91 (95% CI: 0.81, 1.02) 2) 8 weeks after Seowl: IRR: 0.93 (95% CI: 0.85, 1.01)
Lin, 2010 (68)	Pre/post design/ quasi experimental	USA	World Trade Center attacks (9/11)	2001	Not reported	Areas affected by 9/11 compared to areas not affected by 9/11	10 years	Adulthood outcomes for Cardiovascular disease hospitalizations	Prevalence ratio (95% CI): 08/14–09/10: 0.51 (95% CI: 0.26, 1.00) 09/11–09/17: 0.56 (95% CI: 0.28, 1.11); 09/18-09/24: 0.77 (95% CI: 0.44, 1.32); 09/25-10/01: 0.49 (95% CI:

									0.24, 1.00); 10/02-10/08: 0.98 (95% CI: 0.53, 1.87); 10/09-10/15: 1.09 (95% CI: 0.60, 1.98); 10/16–10/22: 0.50 (95% CI: 0.26, 0.95); 10/23–10/29: : 0.45 (95% CI: 0.20, 0.98); 10/30–11/05: 0.48 (95% CI: 0.23, 0.97)
Yu, 2018 (69)	Cohort Study	USA	World Trade Center attacks (9/11)	2001	42,527	9/11-related PTSD compared to no PTSD	13 years	Stroke	Adjusted HR: 1.69 (95% CI: 1.42, 2.02)
Natural disaster									
An, 2015 (67)	Cross-sectional	USA	Hurricane Ike	2008	19	Psychological strains among Hurricane Ike survivors	3 months	1) Blood glucose (mg/dL) 2) Obesity (BMI; kg/m2)	Mean (high vs low) and standard deviation: PTSD symptom: 22.44 (4.93) vs.12.86 (10.48); p=0.014; perceived stress:23.00 (5.03) vs. 28.11 (5.07) p=0.048 2) 28.43 kg/m^2 (3.92) vs. 20.83kg/m^2 (3.92) p=0.018
Baum, 2019 (14)	Cohort study	USA	Hurricane Sandy	2012	81 544	Veterans who used Manhattan VA Medical Center before Hurricane Sandy and experienced decreased access to health care services	2 years	1) Uncontrolled hypertension 2) Systolic BP (mmHg) 3) Diastolic BP (mmHg) 4) Uncontrolled diabetes	% differential change (95% CI): 1) 6 months: 19.3 (4.5, 8.7); 12 months: 4.5 (3.1, 5.9); 18 months: 5.0 (3.5, 6.5); 24 months: 2.1 (0.5, 3.6) 2) 6 months: 3.8 (3.1, 4.5); 12 months: 2.3 (1.7, 2.9); 18

						compared to veterans who used the VA Bronx, Brooklyn or West Haven medical centers		5) Uncontrolled cholesterol (mg/dL) 6) Weight (lbs)	months: 3.1 (2.5, 3.7); 1.5 (0.9, 2.1) 3) 6 months: 2.7 (2.3, 3.1); 12 months: 2.2 (1.9, 2.6); 18 months 2.9 (2.5, 3.3), 24 months: 2.0 (1.7, 2.4) 4) 6 months: 1.9 (-0.1, 4.0); 12 months: 1.7 (-0.3, 3.6); 18 months: 0.8 (-1.2, 2.8); 24 months: -0.2 (-2.2, 1.8) 5) 6 months: 1.3 (-0.1, 2.6); 12 months: 0.6 (-0.6, 1.8); 18 months: -0.7 (-2.0, 0.6); 24 months: -0.2 (-1.4, 1.0) 6) 6 months: -0.1 (-0.5, 0.2); 12 months: 0.2 (-0.2, 0.5); 18 months: -0.2 (-0.5, 0.2); 24 months: 0.5 (0.1, 0.9)
Becquart, 2018 (48)	Time series/quasi experimental	USA	Hurricane Katrina	2005	383 552	Exposure to hurricane before, during and after among older adults in Louisiana in the affected counties	1 year	Hospitalizations due to CVD	Mean (SD) Orleans: T1: 7.25 (2.44); T2: 3.91 (1.45)*; T3; 18.47 (17.3)*; T4:13.76 (6.51)*; T5: 9.54 (2.78); T6: 4.69 (2.08) Jefferson: T1: 5.90 (1.90); T2: 5.01(1.52); T3: 8.118 (3.70)*; T4: 7.25 (2.15)*; T5: 5.26 (1.53); T6: 4.65 (1.57)* East BR: T1: 8.69 (2.74); T2: 9.11 (2.69); T3: 6.52 (2.58); T4: 6.55 (1.70)*; T5: 6.69 (2.42)*; T6: 7.39 (2.37)* * $p<0.05$

Bich, 2011 (61)	Cross-sectional	Vietnam	Historic flood in 2008	2008	781	Individuals who resided in households affected by flood in Hanoi in 2005 compared to non-affected households	1 month	Worsening hypertension after rain/flood	Rural: non flooded 33.3%; flooded: 51.2%; Urban: non flooded 20.3% flooded: 42.9%* * p<0.05
Fonseca, 2009 (59)	Cohort	USA	Hurricane Katrina	2005	1795	Adults with diabetes who were in the databases from 3 health care systems 6 months before the hurricane (Feb 28, 2005-Aug 27, 2005) compared to 6-16 months after the hurricane (March 1, 2006-December 31, 2006)	22 months	1) Glycemic control/A1C 2) Systolic BP (mmHg) 3) Diastolic BP (mmHg) 4) HDL (mg/dL) 5) LDL (mg/dL) 6) Triglycerides (mg/dL)	Difference in mean (SD) 1) 0.1 (1.6) (p<0.01) 2) 10.5 (20.4) (p<0.01) 3) 3.9 (13.1) (p<0.01) 4) 6.0 (35.5) (p<0.01) 5) -2.4 (9.2) (p<0.01) 6) -2.1 (137.5) (p=0.60)
Gautam, 2009 (55)	Retrospective cohort	USA	Hurricane Katrina	2005	396	Exposure to Hurricane Katrina compared to period before hurricane	4 years	Incidence of AMI admission	Pre-Katrina group: 150 admissions for AMI (0.71%) Post-Katrina group: 246 admission for AMI (2.18%) p<0.0001
Hendrickson, 2996 (64)	Pre/post design/ quasi experimental	USA	Hurricane Iniki	1992	Not reported	Mortality data for residents of Kauai for 5-year period 1987-1991 prior disaster compared to the year immediately following the hurricane (Oct 1 1992-Sept 30, 1993)	6 years total	Mortality by: 1) Heart disease 2) Stroke 3) Diabetes mellitus	1) RR: 0.96 (95% CI: 0.79-1.17) 2) RR: 1.20 (95% CI: 0.81-1.78) 3) RR: 2.61 (95% CI: 1.44-4.74)

Husarewycz, 2014 (72)	Cross-sectional	USA	Natural disaster/terrorism	Lifetime disaster experience	34,653	Number of times directly experienced natural disaster/terrorism compared to no experiences	1 year	1) Cardiovascular disease 2) Hypertension/arteriosclerosis 3) Diabetes 4) Obesity	1) OR: 1.28 (95% CI: 1.10, 1.49) 2) OR: 1.08 (95% CI: 0.95, 1.24) 3) OR: 1.10 (95% CI: 0.94, 1,29) 4) OR: 1.01 (95% CI: 0.90, 1.14)
Jiao, 2012 (54)	Retrospective cohort observational study	USA	Hurricane Katrina	2005	Not reported	2 years prior to the hurricane (August 29, 2003 - August 28, 2005) compared to the 3-year period post-Hurricane Katrina (February 14, 2006 - February 13, 2009)	5 years	Incidence of AMI	Pre-Katrina: 0.7% compared to post-Katrina: 2% ($p<0.001$)
Joseph, 2014 (51)	Cohort/ longitudinal	USA	Hurricane Katrina	2005	215	African Americans who experienced acute unemployment due to Hurricane compared to those who remained employed	4 years	Cardiometabolic event	Adjusted OR = 5.65, $p < .05$
Karatzias , 2015 (44)	Cross-sectional	Hong Kong	Natural disaster	Not specified	1147	Experience of natural disaster across life course compared to less or no experiences	Survey done from August to December 2012	1) Hypertension 2) Heart disease 3) Diabetes	Chi square (p-value) 1) X^2: 3.3 p=0.047 2) X^2: 3.6 p=0.056 3) X^2: 2.5 p=0.088
Kim, 2017 (58)	Pre/post design/ quasi	USA	Hurricane Sandy	2012	Not reported	The month of Hurricane Sandy (October 28, 2012-November 27, 2012)	Sandy month: Oct 28, 2012-Nov	Cardiovascular disease-related death	Sandy quarter: adjusted RR: 1.06; 95% CI: 1.02, 1.10 Sandy month: adjusted RR: 1.10; 95% CI: 1.02, 1.18

	experi mental					compared to the same month in 2009-2011; Sandy quarter (October 28, 2012-January 27, 2013) compared to the same period in 2009-2011 among elderly people	27, 2012 Sandy quarter: Oct 28, 2012-Jan 27, 2013		
Koroma, 2019 (66)	Cross-section al	Sierra-Leone	Ebola	2014-2015	10011	District facilities for six-month periods before Ebola (June-December 2012), during Ebola (June-December 2014) and post-Ebola (June-December 2015)	June-December 2012,2013 ,2014	1) Cardiovascular disease 2) Hypertension 3) Diabetes	Number of people with non-communicable diseases 1) Pre-Ebola: 355, Ebola: 300, Post-Ebola: 196 2) Pre-Ebola: 282, Ebola: 230, Post-Ebola: 457 3) Pre-Ebola: 3716, Ebola: 1851, Post-Ebola: 2463
Lawrence, 2019 (45)	Prospec tive Cohort Study	USA	Superstor m Sandy	2012	651858	Residing in counties affected by Superstorm Sandy compared to non-affected counties; Superstorm period compared to reference periods (short-term and long-term (4 and 12 months))	1 year	Emergency department visits, outpatient visits, and hospital admissions for cardiovascular disease	4 months: Superstorm sandy period: RR: 2.10 (95% CI: 2.10, 2,10); Affected counties RR: 2.62 (95% CI: 2.62, 2.63) 12 months: Superstorm sandy period: RR: 2.01 (95% CI: 2.00, 2.01); Affected counties RR: 2.64 (95% CI: 2.64, 2.65)
McKinney , 2011 (52)	Time-series/q uasi experi mental	USA	Hurricane Charley, Frances, Ivan and Jeanne and	2004	Not reporte d	Counties in 2004 directly impacted by the hurricanes, ordered evacuated regardless of the	5 years	Heart-related mortality	Results shown graphically Significantly elevated heart-related deaths

			Tropical Storm Bonnie			level of damage that occurred and adjacent to the impact zone where direct deaths were reported compared to compared to the same areas in 2001-2006			
Moscona, 2019 (75)	Retrospective cohort study	USA	Hurricane Katrina	2005	2-year pre-Katrina -21,079 10-year post Katrina - 84,751	Individuals who lived in New Orleans who went to the Tulane University Health Sciences Center compared to the two months prior to the Hurricane	12 years	1) Hospital admission for Incidence of AMI 2) Changes in CAD 3) Changes in diabetes mellitus 4) Changes in hypertension 5) Changes in hyperlipidemia	Pre-Katrina versus Post-Katrina 1) 0.7% vs 2.8% (p<0.001) 2) 36.4% vs. 47.9%, (p= 0.01) 3) 31.3% vs. 39.9% (p= 0.04) 4) 71.1% vs 80.6%, (p=0.12) 5) 45.4% vs. 59.3% (p = 0.005)
Nagayoshi, 2015 (56)	Pre/post design/ quasi experimental	Japan	July 12, 2012 heavy rain and mudslides "mountain tsunamis"	2012	583	Individuals who were admitted at Aso Central Hospital from July 12 to August 31, 2012 compared to the 3-year period before flooding	3 years	1) Hospital admission for cardiovascular outcomes 2) Cardiovascular events	1) 4.5/month before compared to 16.8/month after; p < 0.01 2) 5.1/month before compared to 16.8/month after; p < 0.01).
Ng, 2011 (73)	Cohort	United Kingdom	Flood	June, 2007	1,743	Diabetics affected by floods compared to diabetics not affected by floods	2 years	Glycemic control/HbA1c levels	Mean HbA1c before 7.6% (7.5–7.7) vs. After 7.9% (7.7–8.0); p = 0.002

Peters, 2013 (65)	Retrospective Cohort	USA	Hurricane Katrina	2005	698	Admission to Tulane University Health Sciences Centre in the 3-year period post-Katrina compared to the 6-year period pre-Katrina	9 years	Chronobiology of AMI onset	Pre-Katrina: 45% vs post-Katrina: 30.9%, p=0.002
Rey, 2007 (74)	Longitudinal	France	6 Heat Waves	1971-2003	Not reported	Time of heat wave compared to the expected mortality during the 3 years prior to the heat wave	N/A	Excess cardiovascular disease death	41% in 1975 to 23% in 2003
Sliva-Palacios, 2015 (60)	Pre/post design/ quasi experimental	USA	Oklahoma Tornado	2013	22,607	Victims of the Oklahoma Tornado Outbreaks compared to the same people pre-tornado and same period one year prior	6 Months	Hospital admissions for CVE	One year prior: PR = 1.05 95% CI: 0.91 to 1.21, p = 0.50; 3-month pre-tornado: PR = 0.96, 95% CI: 0.83 to 1.21, p = 0.63
Thethi, 2010 (76)	Cohort	USA	Hurricane Katrina	2005	1523	Individuals exposed to Hurricane Katrina compared to 6-16 months pre-Hurricane Katrina (February 28, 2005-August 27, 2005)	6 months before Katrina and 6-16 months after Katrina and follow up 1 year after the first post-	1) LDL (mg/dL) 2) HDL (mg/dL) 3) Triglycerides (mg/dL) 4) Cholesterol (mg/dL) 5) Diastolic blood pressure (mm/Hg) 6) Systolic blood pressure (mm/Hg)	Mean Pre-Katrina vs Post-Katrina: 1) 101.34 vs 107.44 2) 43.53 vs 41.08 3) 160.8 vs 158.65 4) 181.9vs 181.39 5) 70.99 vs 74.88 6) 130.73 vs 141.27

							Katrina visit		
Vanasse, 2016 (46)	Population-based retrospective cohort study with a time series design	Canada	Flood of Saint-Jean-sur-Richelieu	2011	111,317	Exposure to flood in spring 2011 and exposure to flooded area (Area 1) compared to same period in Spring 2010 and 2012 and non-flooded areas in the same town (Areas 2, 3 and 4)	4 months	Acute cardiovascular event	Spring 2010: aOR 1.25 (95%CI: 0.81, 1.92); spring 2012 aOR: 1.27 (95% CI: 0.82, 1.92); Non-flooded areas 2: aOR: 1.11 (95%CI: 0.79, 1.59), Non-flooded area 3: aOR: 0.94 (95% CI: 0.68, 1.32); Non-flooded area 4: aOR 1.08 (95%CI: 0.78, 1.47)

1. Results are numbered to correspond with the numbered outcomes in the outcomes column
2. Only results for extreme outcomes are reported in table, remaining results can be found in the study

Abbreviations: aOR: Adjusted odds ratio; AMI: Acute myocardial infarction BMI: Body mass index; BP: Blood pressure; CI: Confidence Interval; CAD: Coronary artery disease; CHD: Coronary heart disease; CVD: Cardiovascular disease; CVE: Cardiovascular events; HbA1c ; Hemoglobin A1C; HDL: High-density lipoproteins; HR: Hazard ratio; LDL: Low-density lipoproteins OR: Odds Ratio; PR: Prevalence Ratio; PTSD: Post-traumatic stress disorder; RR: Relative risk; SD: Standard deviation; SE: Standard Error; Trig; Triglycerides.; T1-T6; Time.

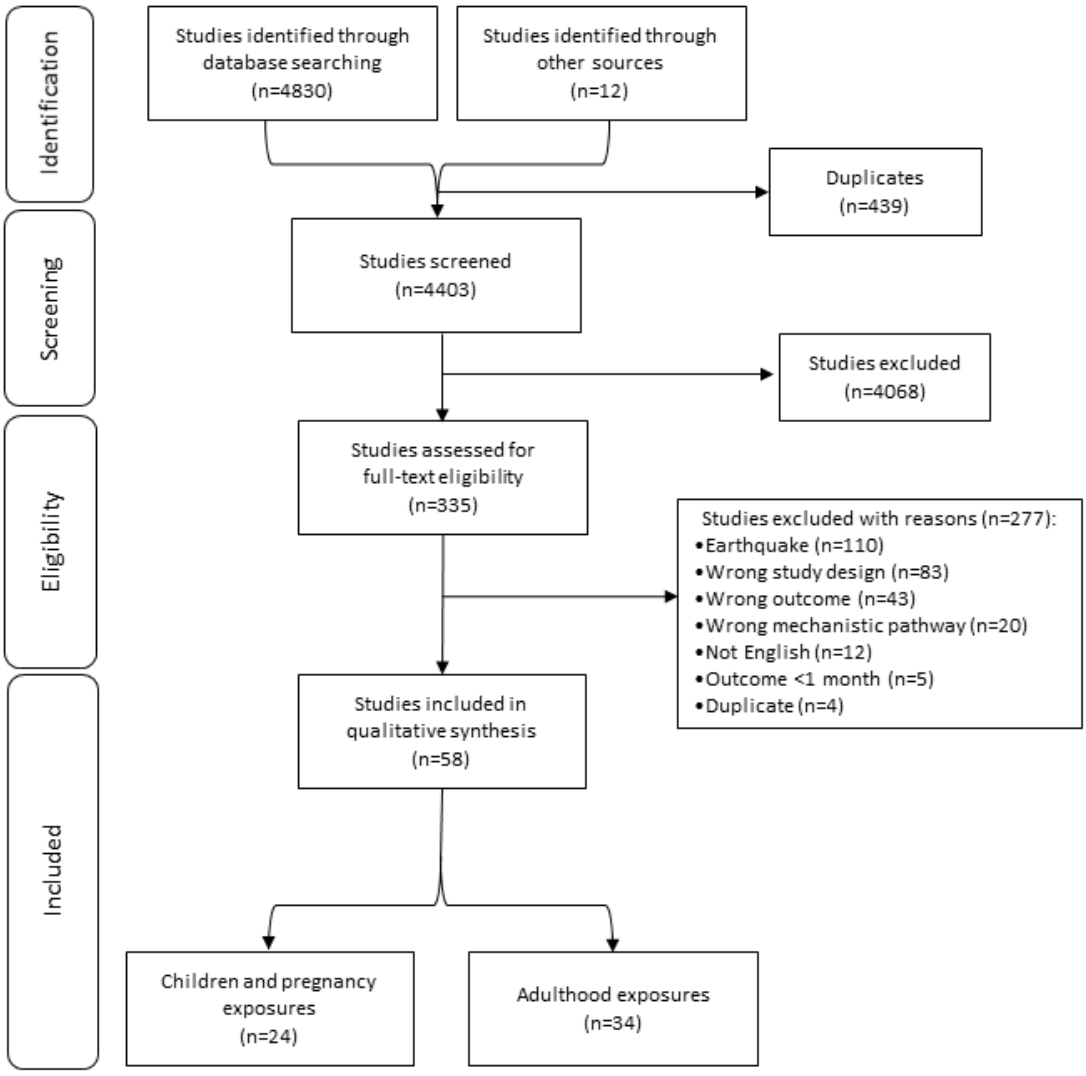

Figure 1. PRISMA flow diagram

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Supplementary Information

Table A1. Search strategy for Medline

1	"social isolation.mp." or Social isolation/	1479
2	quaratine.mp. or exp Quarantine/	5589
3	Pandemics/	7247
4	Epidemics/	10146
5	Coronavirus or coronavirus.mp.	19310
6	humanitarian crises.mp.	232
7	exp mass casualty incidents/ or exp natural disasters/	18883
8	public health emergency.mp.	1636
9	cardiovasucalr.mp. or exp Cardiovascular Diseases/	2605399
10	hypertension.mp. or exp Hypertension/	484321
11	exp Obesity/ or obesity.mp.	321847
12	body mass index.mp. or exp Body Mass Index/	236149
13	stroke.mp, or exp Stroke/	310109
14	myocardial infarction.mp. or exp Myocardial Infarction/	247417
15	angina.mp. or exp Angina Pectoris/	698186
16	diabetes.mp. or Diabetes Mellitus/	646582
17	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	3552066
18	Disasters/ or disaster.mp.	39131
19	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 18	10917
20	17 and 19	3688
21	limit 20 to humans	2998

Table A2. Critical appraisal using Joanna Briggs Institute (JBI) checklist for cohort studies by exposure period (n=41)

Author, Year	Were the two groups similar and recruited from the same population?	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Was the exposure measured in a valid and reliable way?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Were the outcomes measured in a valid and reliable way?	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	Were strategies to address incomplete follow up utilized?	Was appropriate statistical analysis used?
Perinatal											
Dancause, 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Dancause, 2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Dancause, 2015	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Unclear	Yes
de Rooij, 2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Dorn, 2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes
Ekamper, 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Goudet, 2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Huang, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Hult, 2010	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Unclear	Yes
Kroska, 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Unclear	Yes
Lei, 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Unclear	Yes
Liu, 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Unclear	Yes
Lumey, 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Mazumder, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Mryskyla, 2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Painter, 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ravelli, 1999	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Roseboom, 2001	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Schrier, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Sotomayer, 2013	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Unclear	Yes
Stein, 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adult											
Baum, 2019	Yes	Yes	Yes	Yes	Yes		Yes	Yes	Yes	Yes	Yes
Brackbill, 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Dirkzwager, 2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Fonseca, 2009	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Not applicable	Yes
Gautam, 2009	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Unclear	Unclear	Yes
Huizink, 2006	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Jiao, 2012	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Unclear	Unclear	Yes
Jordan, 2011 (A)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Jordan, 2011 (B)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Jordan, 2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes

Joseph, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Lawrence, 2019	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Not applicable	Yes
Moscona, 2019	Yes	Yes	Yes	Yes	No	Unclear	Yes	Yes	Unclear	Unclear	Yes
Ng, 2011	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Unclear	Yes
Peters, 2013	Yes	Yes	Yes	No	No	No	Yes	Yes	Unclear	Unclear	Yes
Rey, 2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes
Thethi, 2010	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Unclear	Yes
Trasande, 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Not applicable	Yes
Vanasse, 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Not applicable	
Yu, 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes

Table A3. Critical appraisal using Joanna Briggs Institute (JBI) checklist for cross-sectional studies by exposure period (n=7)

Author, Year	**Were the criteria for inclusion in the sample clearly defined?**	**Were the study subjects and the setting described in detail?**	**Was the exposure measured in a valid and reliable way?**	**Were objective, standard criteria used for measurement of the condition?**	**Were confounding factors identified?**	**Were strategies to deal with confounding factors stated?**	**Were the outcomes measured in a valid and reliable way?**	**Was appropriate statistical analysis used?**
Perinatal								
Bercovich, 2014	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Oni, 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adult								
An, 2015	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Bich, 2011	No	Yes	Yes	Yes	No	No	No	Yes
Husarewycz, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Katratzias, 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Koroma, 2019	No	No	Yes	Yes	No	No	Yes	Yes

Table A4. Critical appraisal using Joanna Briggs Institute (JBI) checklist for quasi-experimental studies by exposure period (n=10)

Author, Year	Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	Were the participants included in any comparisons similar?	Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Was there a control group?	Were there multiple measurements of the outcome both pre and post the intervention/exposure?	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Was appropriate statistical analysis used?
Perinatal									
Xiao, 2019	Yes	Unclear	Not applicable	Yes	No	Yes	Yes	Yes	Yes
Adult									
Becquart, 2018	Yes	Unclear	Not applicable	No	No	Yes	Yes	Yes	Yes
Gerin, 2005	Yes	Yes	Not applicable	Yes	Yes	Yes	Yes	Yes	Yes
Hendrickson, 1996	Yes	Unclear	Not applicable	No	Yes	Yes	Yes	Yes	Yes
Kim, 2017	Yes	Unclear	Not applicable	No	Yes	Yes	Yes	Yes	Yes
Kong, 2019	Yes	Unclear	Not applicable	Yes	No	Yes	Yes	Yes	Yes
Lin, 2010	Yes	Unclear	Not applicable	Yes	No	Yes	Yes	Yes	Yes
McKinney, 2011	Yes	Unclear	Not applicable	No	Yes	Yes	Yes	Yes	Yes
Nagayoshi, 2015	Yes	Unclear	Not applicable	Yes	No	Yes	Yes	Yes	Yes
Silva-Palacios, 2015	Yes	Unclear	Not applicable	No	No	Yes	Yes	Yes	Yes

Chapter 3: Stressors and perceived consequences of the COVID-19 pandemic among older adults: a cross-sectional study using data from the Canadian Longitudinal Study on Aging (CLSA)

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Chapter 3 Summary

The COVID-19 pandemic altered all aspects of daily functioning, and aside from the direct harms related to morbidity and mortality, how people experienced the COVID-19 pandemic is not well understood. This paper aimed to describe the stressors and perceived consequences of the COVID-19 pandemic on older adults in Canada and to evaluate differences by socioeconomic factors. Most adults reported they experienced at least one stressor during the pandemic and that they perceived the consequences of the pandemic as negative. Differences were identified across several socioeconomic factors, including age group, sex, and region of residence. It is apparent that variation existed in how people experienced the COVID-19 pandemic, and this was seen across several socioeconomic factors. These differences highlight the inequalities people face during a stressful event, and those subgroups of people are more susceptible to worse experiences.

ABSTRACT

Background: The consequences of the COVID-19 pandemic on stress in older adults is unknown. The objectives of this study were to describe the stressors and perceived consequences of the COVID-19 pandemic on older adults in Canada and to evaluate differences by socioeconomic factors.

Methods: A cross-sectional study was conducted using data from the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Exit Questionnaire (Sep-Dec 2020). A 12-item checklist was used to assess stressors (e.g., income loss, separation from family) experienced during the pandemic, and a single-item was used to measure perceived consequences. A generalized linear model with a binomial distribution and log link were used to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) for the association between socioeconomic factors, stressors, and the perceived consequences.

Results: Among the 23,972 older adults (aged 50-96 years) included in this study, most reported at least one stressor (76%) during the pandemic, with 24% experiencing three or more. The consequences of the pandemic were perceived as negative by 63%. Females were more likely to experience most stressors compared to males, such as separation from family (adjusted PR: 1.31; 95% CI: 1.28, 1.35). The perceived consequences of the pandemic varied by region; residents of Quebec, compared to Atlantic provinces, were less likely to perceive the consequences of the pandemic as negative (adjusted PR: 0.87; 95% CI: 0.84, 0.91).

Interpretation: These findings suggest that older adults across Canada experienced stressors and perceived the pandemic consequences as negative, which varied by socioeconomic factors and geography, highlighting inequalities in experiencing stress. Future research will be needed to determine the impact of stress during the pandemic on future health outcomes.

INTRODUCTION

In addition to the direct impacts of the COVID-19 the pandemic and the associated public health preventive measures, there are several indirect consequences that have also had a great impact on population health (1,2). One such indirect consequence of the pandemic is increased stress (3). Stress has a major impact on both physical and mental health, including cardiovascular disease, stroke, diabetes, anxiety, and depression (2,4–6). Previous research on population level disasters, including earthquakes and floods, has found that exposure to stress during an acute disaster has a profound impact on long-term health outcomes, including chronic diseases (7). Given the dramatic change in daily functioning throughout the COVID-19 pandemic, several factors (e.g., limited access to physical activity facilities, closures, etc.) may lead to increased incidence of obesity, cardiovascular disease and type 2 diabetes, however, it has been hypothesized that chronic stress may particularly influence disease development (8). Like other disasters, the COVID-19 pandemic can be viewed as a stressful event, as it has completely altered the daily activities of individuals across the globe (9). Measures of stress can include both objective and perceived measures (10,11). Objective measures include economic hardships and loss of possessions, family and social stressors, and loss of daily activities (12). Perceived measures of stress include an individual's perceived ability to cope with the demands or presence of a disaster (11,13).

A systematic review from early in the pandemic found a high prevalence of stress, which differed by sex, age, unemployment, and presence of chronic or psychiatric illness (14). A study conducted in the United States during the pandemic (April 2020) (15)

revealed a high proportion of participants experienced stressors such as changes to social routines (83.7%) and another study conducted in China (January-February 2020) found that people reported higher experiences of stress throughout the pandemic, compared to pre-pandemic levels (16). However, these studies noted limitations, including lack of generalizability and small sample sizes (15,16). It has also been noted that experiences of stress and coping vary among older adults, where adults in the oldest age groups have reported less mental health effects early in the pandemic although they are at risk for worse health outcomes associated with COVID-19 (17). Experiences of stress vary by socioeconomic characteristics (18,19); however, this has not been comprehensively evaluated during the COVID-19 pandemic in Canada. The objectives of this study were to describe the prevalence of stressors and the perceived consequences reported by older adults during the COVID-19 pandemic and to evaluate how they differed by socioeconomic factors.

METHODS

Study design, data source and setting

We conducted a cross-sectional analysis using data from participants in the Canadian Longitudinal Study on Aging (CLSA). The CLSA is a nationally generalizable study of community-dwelling adults aged 45-85 years at the time of recruitment. Participants were recruited from all 10 Canadian provinces and are followed-up every 3 years for at least 20 years or until death or loss-to-follow-up. Data were collected at

baseline (2011-2015) (n=51,338) and follow-up 1 (2015-2018) (n=44,817). In April 2020, the CLSA COVID-19 Questionnaire Study was implemented to collect pandemic-related data. The CLSA COVID-19 Study collected longitudinal data over a 9-month period with participants delivered by web (n=23,832) or phone (n=2,606). A baseline survey was administered from April 2020-June 2020 and the Exit Survey administered from September 2020-December 2020. Additional details regarding the CLSA methodology can be found in the Supplementary Information and have been extensively described previously (20). Ethics approval for this study was received from the Hamilton Integrated Research Ethics Board (HiREB).

Participants

Participants were selected into the CLSA following a population-based sampling strategy (20). Inclusion criteria included people who were able to complete interviews in either English or French, were cognitively able to participate on their own, were not institutionalized, and did not reside in a Canadian territory or on a Federal First Nations reserve. Individuals who were full-time members of the Canadian Armed forces were also not eligible to be included in the study. CLSA participants that were still alive, had not withdrawn, did not require a proxy to assist with completion of surveys, and had sufficient contact information were eligible to be invited to participate in the CLSA COVID-19 Questionnaire Study.

Primary outcomes of interest

Two questions in the CLSA COVID-19 Questionnaire Study Exit Survey (September 2020-Decemeber 2020) were used to assess stressors and perceived consequences during the pandemic. To measure stressors, participants were asked if they had experienced any of the items on a 12-item checklist throughout the pandemic: participant was ill, someone close to the participant was ill, someone close to the participant died, loss of income, unable to access necessary food and supplies, unable to access healthcare, unable to access usual prescriptions, increased conflict, separation from family, increased caregiving, unable to care for those who require assistance due to limitations, and breakdown in family relationships. Participants could select multiple stressors. Each stressor was considered individually, and the number of stressors was summed to create a total score reflecting the cumulative number of stressors participants had reported.

To assess the perceived consequences of the COVID-19 pandemic, participants were asked a single question, "*Taking everything about COVID-19 into account, how would you describe the consequences of COVID-19 on you and your household?",* with a 5-point Likert scale ranging from very negative to very positive (11). The development of this question is based on the Transactional Model, published by Lazarus and Folkman (1984), stating that when an individual encounters a stressful event, their ability to cope is related to whether a threat is perceived or not. If a threat is perceived, then this leads to increased stress (13). A relatively small proportion of participants reported the extreme response options, thus very negative and negative, and positive and very positive were combined. A response of neutral was combined with positive and very positive in the

regression analysis to create a binary variable, as we were most interested in understanding negative/very negative outcomes. The measures used for objective stress and perceived stress have been used to measure stress during previous disasters (10,11,21–23).

Measurement of other variables

Descriptor variables were selected from the literature as variables that may introduce variation in experiences of stress and perceptions of the consequences of the pandemic (15,24,25). The participants age group, region, urban/rural status, and essential worker status were taken from the CLSA COVID-19 Questionnaire Study Baseline Survey (April 2020-June 2020). Participant's age was grouped into 50-64 years, 65-74 years, and 75-96 years. Region was based on the province of residence at CLSA COVID-19 Baseline Survey to reflect the most up-to-date location of residence, and was categorized into Atlantic (Newfoundland, New Brunswick, Nova Scotia, Prince Edward Island), Quebec, Ontario, Prairies (Manitoba, Saskatchewan, Alberta), and British Columbia. Postal code was used to classify area of residence as urban and rural (26). Participants were asked if they usually work at a job outside of their residence and if they were considered an essential worker. This was categorized as not usually working outside the household, working as an essential worker, and working outside the household but not as an essential worker. Household income (categorized as less than $50,000, $50,000 to less than $100,000, $100,000 to less than $150,000 and $150,000 or more), and marital

status (categorized as single (never married/never lived with partner), married/living with partner in a common-law relationship, widowed, and divorced or separated) were taken from CLSA follow-up 1 (2015-2018). Participant's sex (categorized as male or female), racial background (dichotomized as white or non-white) and education level (categorized as secondary school graduation or less, some post-secondary education and post-secondary degree or diploma) were measured at CLSA baseline (2011-2015).

Statistical methods

All statistical analyses were conducted using SAS 9.4. Descriptive statistics included the frequency of each stressor, the total number of stressors, and the distribution of the perceived consequences of the pandemic overall and by selected socioeconomic variables. To evaluate the association between socioeconomic factors and the individual stressors and the binary perceived consequences variable, separately, a generalized linear model (PROC GENMOD) with a binomial distribution and log link were used. For all outcomes, an unadjusted prevalence ratio (PR) and 95% Confidence Interval (CI) (separately for each socioeconomic factor (sex, age group, urban/rural status, region, essential worker status, household income, marital status, racial background, and education) and a fully adjusted PR and 95% CI (including all socioeconomic factors) were estimated. To evaluate the association between socioeconomic factors and the total number of stressors (ranging from 0 to 12), PROC GENMOD was used with a negative binomial distribution and log link to estimate PRs and 95% CIs. A negative binomial

distribution was chosen as it was a good approximation of the distribution of the total stressor score (Figure A1). A complete case analysis was conducted as less than 6% of participants were missing data on some variables. Although sampling weights have been developed for CLSA sample at baseline, these weights can not be used for the subsample that completed the CLSA COVID-19 Questionnaire Study, thus sampling weights were not used for this analysis.

RESULTS

A total of 24,114 participants completed the CLSA COVID-19 exit survey and 23,785 had available data for this study (see flow diagram in Supplementary Figure A2). The age distribution of participants was: 35% (n=8,269) 50-64 years, 37% (n=8,705) 65-74, and 29% (n=6,811) 75-96 years of age. 53% (n=12,640) of participants were female, and the vast majority were of white racial background (n=23,091; 97%). The complete descriptive characteristics of the study sample can be found in Table 1. CLSA COVID-19 Questionnaire Study participants have previously been compared to the total CLSA study population, and were slightly more educated and had higher income, but few other differences were observed (27).

Stressors during COVID-19 pandemic

The total number of stressors reported by age group is described in Figure 1. The mean and median number of stressors were 1.7 and 1.0, respectively (standard deviation: 1.5; interquartile range: 1.0). Figure 2 presents the prevalence of each individual stressor

at the exit survey by sex. The most frequently reported stressors were being separated from family and being unable to access healthcare. Supplemental Table A1 displays the prevalence of each reported stressor by sociodemographic factors.

The adjusted PR for the associations between socioeconomic factors and each stressor are presented in Table 2. Females were more likely to experience most stressors compared to males, for example, females were more likely to report increased caregiving and separation from family. Low household income (<$50,000), compared to an income of $100,000 to $150,000, was associated with an increased likelihood of being unable to access necessary food or supplies. Most unadjusted associations were similar to adjusted associations (Supplemental Table A2).

The adjusted PRs for the association between each socioeconomic variable and the number of stressors are presented in Table 3. Older adults, compared to younger adults (aged 50-64 years), individuals residing in Quebec, compared to those in the Atlantic, and those who had a secondary school education or less, compared to those with a post-secondary degree/diploma reported less stressors Whereas individuals residing in Ontario and British Columbia reported more stressors, relative to those residing in the Atlantic provinces. Unadjusted results were very similar to the adjusted results and can be found in Supplemental Table A3.

Perceived consequences of the COVID-19 pandemic

Almost two-thirds (63%) of the sample (n=23,020) perceived the consequences of the pandemic as negative or very negative when surveyed between September and

December 2020 (Figure 3). The distribution of the self-reported consequences of the COVID-19 pandemic by socioeconomic variables is presented in the Supplemental Table A4. The perceived consequences of the pandemic varied across Canada, with the greatest proportion of participants reporting the perceived consequences as negative or very negative in British Columbia, Ontario, and the Prairies (Figure 4). Several socioeconomic characteristics were associated with perceiving the consequences of the COVID-19 pandemic as negative or very negative (Table 4). Older adults (75-96 years), compared to those aged 50-64 years, non-white adults, compared to adults who are white, and those who resided in a rural setting, compared to an urban setting were less likely to perceive the pandemic as negative or very negative. Unadjusted results can be found in Supplemental Table A5.

INTERPRETATION

This study is one of the first national studies to describe the stressors and perceived consequences experienced by older adults during the COVID-19 pandemic. Many studies have focused on the perception of the threat of the pandemic (25,28,29), and not broadly on how people would describe their perception of the COVID-19 pandemic on their household. The findings from this study suggest that participants aged 50-96 years in Canada have been substantially impacted by the consequences of the pandemic, with 76% of respondents experiencing at least one stressor and 63% reporting they perceived the consequences of the pandemic as negative or very negative.

Conversely, about 7% of participants perceived the pandemic as positive or very positive, and about 24% reported experiencing no stressors. The prevalence of both stressors and the perceived consequences of the pandemic varied by socioeconomic factors, with adults aged 50-64 and females more likely to experience most of the stressors.

Few Canadian studies have described stress during the pandemic. A national online survey of 2000 adults early in the pandemic found that 45% of adults agreed the pandemic was stressful and consistent with our study results, participants in Ontario were more likely to report stress (25). The variation in the perception of the consequences of the pandemic may be related to different public health responses and preventive measures that were implemented by different provinces (30). A study conducted in the United States found people reported experiencing a high number of stressors during the pandemic (15), and the most commonly reported stressors were reading/hearing others talk about the severity and contagiousness of COVID-19 (96.6%) and uncertainty surrounding quarantine/social distancing requirements (88.3%). Although these specific stressors were different than what we measured, the overall report of increases in stress related to changes in daily routines is consistent.

Strengths of our study included that the CLSA is a nationally generalizable sample with a population-based sampling strategy. Surveys were collected by both phone and web to accommodate participants with limited internet access. Further, the longitudinal data availability with extensive pre-pandemic data collected at CLSA baseline (2011-2015) and follow-up 1 (2015-2018) allowed for a comprehensive assessment of sociodemographic factors. Future waves of data being collected by the CLSA (20), will

allow for longitudinal research on how the experiences of stress during the pandemic impact both short- and long-term health outcomes. The CLSA COVID-19 Questionnaire Study collected in-depth information on stressors and perceived consequences during the pandemic on a large sample of older adults in Canada. However, limitations of our study are that a perceived stress scale was not included, and the stressor list was developed early in the pandemic and may not include all possible stressors (e.g., loss of job, inability to attend community centres or places of worship) that may have been experienced. Although the outcome measures have been widely used in previous disaster research (10,11,21,22) to assess objective and subjective reactions to stressful events and were modified from gold-standard measurement tools (10), they have not yet been validated in the current CLSA sample. Further, the response rate was relatively low (68%), and study participants were primarily white and were limited to community-dwelling adults at baseline, with only a small proportion of participants moving into long-term care and subsequently followed throughout the CLSA surveys. Thus, potentially introducing a selection bias, with results that are not representative of all Canadian adults 50 years of age and older. It is also important to note that the data from this study were collected in the first two waves of the pandemic in Canada with the stress measures collected from September 2020 to December 2020 which also was before the general population was eligible for vaccination. Following December 2020, Canada has experienced subsequent waves of the pandemic (31). The results from this study may vary from the experiences of stressors or the overall perception of the pandemic during subsequent waves or when people were eligible to be vaccinated, as this may have impacted the stress Canadians

may have experienced. Understanding the indirect impact of the pandemic on Canadian adults is critical. Stress is one indirect impact that may have a profound effect on the long-term health consequences of Canadians. Both acute and chronic stress are established risk factors for mental health, chronic diseases and mortality (32). Describing the prevalence of stressors by socioeconomic factors is crucial to identify health inequalities and to prevent further disparities (33,34). As the pandemic continues to progress, and as future follow-ups of the CLSA are collected and subsequently become available, this will allow for continued investigation of the impact of stress during the pandemic on long-term health outcomes.

Table 1. Characteristics of participants from the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Questionnaire study (n=23,785)

Characteristic	N (%) (n=23,785)
Sex[1]	
Male	11145 (47%)
Female	12640 (53%)
Age group[2]	
50-64 years	8269 (35%)
65-74 years	8705 (37%)
75-96 years	6811 (29%)
Racial background[1]	
White	23091 (97%)
Non-white	668 (3%)
Missing	26
Education[1]	
Secondary school graduation or less	3426 (14%)
Some post-secondary education	17106 (7%)
Post-secondary degree or diploma	18609 (78%)
Missing	44
Total household income[3]	
Less than $50,000	5663 (25%)
$50,000 to less than $100,000	8514 (38%)
$100,000 to less than $150,000	4554 (20%)
$150,000 or more	3726 (17%)
Missing	1328
Region[2]	
Atlantic[4]	4297 (18%)
Quebec	4299 (18%)
Ontario	5509 (23%)
Prairies[5]	5091 (21%)
British Columbia	4589 (19%)
Marital status[3]	
Single (never married/never lived with partner)	1992 (8%)
Married or common law relationship	16711 (70%)
Widowed	2311 (10%)
Divorced or separated	2757 (12%)
Missing	14
Essential worker status[2]	
Doesn't work outside the home	17244 (75%)
Essential worker	2478 (11%)
Not essential worker	3392 (15%)
Missing	671
Urban/rural status[2]	
Urban	19447 (82%)
Rural	4214 (18%)
Missing	124

1. Data collected at CLSA Baseline (2011-2015)
2. Data collected at CLSA COVID-19 Questionnaire Baseline Survey (April 2020-June 2020)
3. Data collected at CLSA Follow-up 19 (2015-2018)
4. Newfoundland, New Brunswick, Nova Scotia, Prince Edward Island
5. Manitoba, Saskatchewan, Alberta

Table 2. The adjusted association between socioeconomic characteristics and individual stressors among Canadian adults in the Canadian Longitudinal Study on Aging (CLSA) at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020) (n=21,605)

	Stressors Adjusted PR (95% CI) [1]											
	Participant was ill	Someone close to participant was ill	Someone close to participant died	Loss of income	Unable to access necessary food or supplies	Unable to access healthcare	Unable to access usual prescriptions	Increased conflict	Separation from family	Increased caregiving	Unable to care for those who require assistance	Breakdown in family relationships
Sex												
Male	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Female	1.22 (1.14, 1.33)	1.16 (1.09, 1.24)	1.17 (1.10, 1.25)	0.89 (0.83, 0.96)	1.05 (0.93, 1.18)	1.05 (1.00, 1.09)	1.11 (0.98, 1.26)	1.10 (0.98, 1.23)	1.31 (1.28, 1.35)	1.49 (1.37, 1.62)	1.33 (1.22, 1.45)	1.28 (1.12, 1.45)
Age group												
50-64 years	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
65-74 years	0.90 (0.82, 0.99)	0.84 (0.77, 0.92)	0.96 (0.88, 1.05)	0.62 (0.57, 0.68)	0.63 (0.54 ,0.72)	0.92 (0.87, 0.98)	0.82 (0.70, 0.96)	0.69 (0.60, 0.79)	1.01 (0.97, 1.04)	0.70 (0.63, 0.78)	0.78 (0.70, 0.87)	0.68 (0.58, 0.80)
75-96 years	0.70 (0.62, 0.78)	0.80 (0.72, 0.88)	1.04 (0.95, 1.15)	0.31 (0.26, 0.36)	0.36 (0.29, 0.43)	0.68 (0.63, 0.74)	0.62 (0.51, 0.75)	0.57 (0.47, 0.67)	0.87 (0.83, 0.90)	0.52 (0.46, 0.60)	0.51 (0.44,0.59)	0.50 (0.41, 0.61)
Racial background												
White	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Non-white	0.82 (0.64, 1.04)	0.90 (0.72, 1.10)	1.34 (1.13, 1.57)	1.08 (0.90, 1.28)	0.95 (0.68, 1.29)	0.81 (0.68, 0.94)	0.83 (0.55, 1.19)	0.81 (0.56, 1.12)	0.81 (0.73, 0.88)	0.88 (0.68, 1.11)	0.95 (0.72, 1.21)	0.93 (0.63, 1.33)
Education												
Secondary school graduation or less	0.87 (0.77, 0.97)	0.86 (0.77, 0.95)	0.97 (0.88, 1.07)	0.95 (0.85, 1.07)	0.90 (0.75, 1.07)	0.90 (0.84, 0.98)	0.96 (0.79, 1.15)	0.96 (0.81, 1.13)	0.87 (0.83, 0.91)	0.96 (0.84, 1.09)	0.73 (0.66, 0.85)	0.87 (0.71, 1.05)
Some post-secondary education	1.01 (0.75, 1.15)	1.09 (0.96, 1.23)	1.05 (0.93, 1.18)	1.02 (0.89, 1.16)	1.14 (0.93, 1.38)	1.01 (0.92, 1.10)	1.20 (0.97, 1.47)	1.01 (0.81, 1.23)	0.97 (0.92, 1.01)	0.89 (0.75, 1.04)	1.01 (0.85,1.18)	1.12 (0.88, 1.40)
Post-secondary degree or diploma	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Household income												
Less than $50,000	1.22 (1.08, 1.38)	1.04 (0.93, 1.16)	1.08 (0.98, 1.20)	1.31 (1.17, 1.47)	1.40 (1.16, 1.69)	1.03 (0.95, 1.12)	1.12 (0.92, 1.37)	1.15 (0.96, 1.38)	0.91 (0.87, 0.95)	0.89 (0.77, 1.02)	1.06 (0.92, 1.23)	1.27 (1.03, 1.56)
$50,000 or more, but less than $100,000	1.04 (0.93, 1.15)	1.02 (0.94, 1.12)	0.99 (0.91, 1.09)	1.03 (0.94, 1.14)	1.10 (0.93, 1.29)	1.03 (0.96, 1.10)	0.96 (0.81, 1.14)	0.97 (0.83, 1.12)	0.99 (0.96, 1.03)	1.04 (0.93, 1.16)	0.97 (0.86, 1.09)	1.04 (0.87, 1.24)
$100,000 or more, but less than $150,000	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
$150,000 or more	1.05 (0.93, 1.19)	1.04 (0.94, 1.16)	0.86 (0.77, 0.96)	0.84 (0.76, 0.93)	1.10 (0.92, 1.32)	0.96 (0.88, 1.04)	0.95 (0.78, 1.15)	0.83 (0.69, 0.98)	1.01 (0.97, 1.05)	1.08 (0.96, 1.22)	0.99 (0.87, 1.13)	0.98 (0.80, 1.20)
Region												
Atlantic	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Quebec	1.01 (0.89, 1.14)	1.52 (1.37, 1.69)	0.84 (0.76, 0.94)	1.02 (0.90, 1.16)	0.47 (0.37, 0.60)	0.53 (0.48, 0.58)	0.37 (0.28, 0.48)	1.31 (1.07, 1.59)	0.81 (0.77, 0.85)	0.58 (0.49, 0.67)	0.90 (0.76, 1.06)	2.15 (1.74, 2.67)
Ontario	1.07 (0.95, 1.19)	1.08 (0.97, 1.21)	0.91 (0.83, 1.01)	1.29 (1.14, 1.45)	1.34 (1.13, 1.60)	1.19 (1.11, 1.28)	1.25 (1.04, 1.50)	1.50 (1.25, 1.80)	1.20 (1.15, 1.24)	1.15 (1.02, 1.30)	1.39 (1.21, 1.60)	1.44 (1.15, 1.81)
Prairies	0.96 (0.85, 1.08)	1.16 (1.04, 1.30)	0.88 (0.79, 0.97)	1.50 (1.34, 1.68)	1.19 (0.99, 1.42)	0.70 (0.64, 0.76)	1.11 (0.92, 1.34)	1.40 (1.16, 1.69)	1.15 (1.11, 1.20)	1.08 (0.95, 1.22)	1.32 (1.14, 1.52)	1.47 (1.17, 1.84)
British Columbia	1.13 (1.01, 1.27)	1.09 (0.97, 1.22)	0.83 (0.75, 0.92)	1.44 (1.28, 1.62)	1.41 (1.18, 1.69)	1.03 (0.96, 1.11)	1.10 (0.91, 1.33)	1.54 (1.28, 1.87)	1.10 (1.06, 1.15)	1.15 (1.01, 1.31)	1.28 (1.11, 1.49)	1.50 (1.20, 1.88)
Marital Status												
Single (never married/never lived with partner)	1.18 (1.03, 1.34)	0.85 (0.75, 0.97)	0.94 (0.83, 1.07)	0.95 (0.84, 1.08)	1.06 (0.85, 1.30)	1.06 (0.96, 1.16)	1.27 (1.02, 1.57)	0.81 (0.65, 1.00)	0.89 (0.84, 0.94)	0.72 (0.60, 0.86)	0.82 (0.69, 0.98)	0.99 (0.79, 1.22)
Married or common law relationship	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Widowed	1.06 (0.92, 1.22)	0.82 (0.71, 0.93)	1.01 (0.90, 1.14)	0.86 (0.71, 1.03)	0.98 (0.76, 1.25)	0.95 (0.86, 1.06)	0.93 (0.73, 1.19)	0.67 (0.51, 0.85)	1.00 (0.96, 1.05)	0.61 (0.49, 0.74)	0.85 (0.71, 1.03)	0.93 (0.71, 1.19)
Divorced and separated	1.15 (1.02, 1.29)	0.81 (0.72, 0.91)	1.00 (0.90, 1.11)	1.12 (1.01, 1.24)	1.35 (1.13, 1.59)	1.08 (0.99, 1.16)	1.13 (0.92, 1.37)	0.91 (0.76, 1.09)	1.04 (1.00, 1.08)	0.80 (0.69, 0.93)	0.91 (0.78, 1.05)	1.00 (0.81, 1.21)
Essential worker status												
Doesn't work outside the home	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Essential worker	0.95 (0.83, 1.07)	1.08 (0.97, 1.20)	1.00 (0.89, 1.12)	1.61 (1.43, 1.80)	1.01 (0.85, 1.20)	0.92 (0.85, 1.00)	1.01 (0.83, 1.23)	1.19 (1.00, 1.40)	0.93 (0.88, 0.97)	1.04 (0.92, 1.18)	1.02 (0.89, 1.17)	1.25 (1.03, 1.51)
Not essential worker	0.89 (0.80, 1.00)	1.00 (0.90, 1.10)	0.94 (0.85, 1.04)	3.04 (2.78, 3.32)	0.79 (0.67, 0.94)	0.88 (0.82, 0.95)	0.86 (0.72, 1.04)	1.12 (0.96, 1.31)	0.98 (0.94, 1.02)	1.11 (0.99, 1.24)	1.03 (0.90, 1.16)	1.10 (0.92, 1.31)
Urban/rural status												
Urban	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Rural	1.02 (0.93, 1.12)	0.92 (0.85, 1.01)	1.03 (0.95, 1.12)	1.03 (0.94, 1.13)	0.97 (0.83, 1.13)	1.01 (0.95, 1.08)	1.05 (0.89, 1.22)	1.00 (0.87, 1.16)	0.96 (0.93, 1.00)	0.98 (0.89, 1.09)	1.02 (0.91, 1.14)	1.02 (0.87, 1.20)

1. Adjusted for all variables listed in the table: sex, age group, racial background, education, household income, region, marital status, essential worker status and urban/rural status

Table 3. The adjusted association between socioeconomic characteristics and total number of stressors[1] among Canadian adults in the CLSA at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020) (n=21,605)

	Adjusted PR (95% CI)[2]
Sex	
Male	1.00
Female	1.20 (1.17, 1.23)
Age group	
50-64 years	1.00
65-74 years	0.86 (0.84, 0.89)
75-96 years	0.70 (0.67, 0.73)
Racial background	
White	1.00
Non-white	0.91 (0.85, 0.98)
Education	
Secondary school graduation or less	0.89 (0.86, 0.92)
Some post-secondary education	0.99 (0.95, 1.04)
Post-secondary degree or diploma	1.00
Household income	
$50,000 or less	1.04 (1.00, 1.08)
$50,000 or more, but less than $100,000	1.01 (0.98, 1.05)
$100,000 or more, but less than $150,000	1.00
$150,000 or more	0.99 (0.95, 1.02)
Region	
Atlantic	1.00
Quebec	0.86 (0.82, 0.89)
Ontario	1.17 (1.13, 1.22)
Prairies	1.07 (1.03, 1.11)
British Columbia	1.12 (1.07, 1.16)
Marital Status	
Single (never married/never lived with partner)	0.94 (0.90, 0.98)
Married or common law relationship	1.00
Widowed	0.92 (0.88, 0.97)
Divorced and separated	1.02 (0.98, 1.06)
Essential worker status	
Doesn't work outside the home	1.00
Essential worker	1.02 (0.98, 1.06)
Not essential worker	1.08 (1.05, 1.12)
Urban/rural status	
Urban	1.00
Rural	0.99 (0.96, 1.02)

1. The total number of stressors was calculated by summing the stressors people reported, this ranged from zero to 12.
2. Adjusted for all variables listed in the table: sex, age group, racial background, education, household income, region, marital status, essential worker status and urban/rural status

Table 4. Adjusted prevalence ratio (PRs) and 95% CI for the association between socioeconomic characteristics and negative/very negative versus neutral/positive/very positive perception of the consequences of the COVID-19 pandemic among Canadian adults in the Canadian Longitudinal Study (CLSA) on Aging at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020) (n=20,982)

	Adjusted PR (95% CI)[1]
Sex	
Male	1.00
Female	0.98 (0.97, 1.01)
Age group	
50-64 years	1.00
65-74 years	0.98 (0.95, 1.00)
75-96 years	0.93 (0.90, 0.95)
Racial background	
White	1.00
Non-white	0.89 (0.83, 0.95)
Education	
Secondary school graduation or less	0.90 (0.87, 0.93)
Some post-secondary education	0.97 (0.93, 1.01)
Post-secondary degree or diploma	1.00
Household income	
$50,000 or less	0.94 (0.91, 0.97)
$50,000 or more, but less than $100,000	0.98 (0.96, 1.01)
$100,000 or more, but less than $150,000	1.00
$150,000 or more	0.99 (0.96, 1.03)
Region	
Atlantic	1.00
Quebec	0.87 (0.84, 0.91)
Ontario	1.20 (1.16, 1.24)
Prairies	1.21 (1.17, 1.25)
British Columbia	1.17 (1.13, 1.21)
Marital Status	
Single (never married/never lived with partner)	0.99 (0.95, 1.03)
Married or common law relationship	1.00
Widowed	1.04 (1.00, 1.08)
Divorced and separated	1.02 (0.99, 1.05)
Essential worker status	
Doesn't work outside the home	1.00
Essential worker	0.92 (0.89, 0.95)
Not essential worker	0.96 (0.93, 0.99)
Urban/rural status	
Urban	1.00
Rural	0.93 (0.90, 0.96)

1. Adjusted for all variables listed in the table: sex, age group, racial background, education, household income, region, marital status, essential worker status, education, and urban/rural status

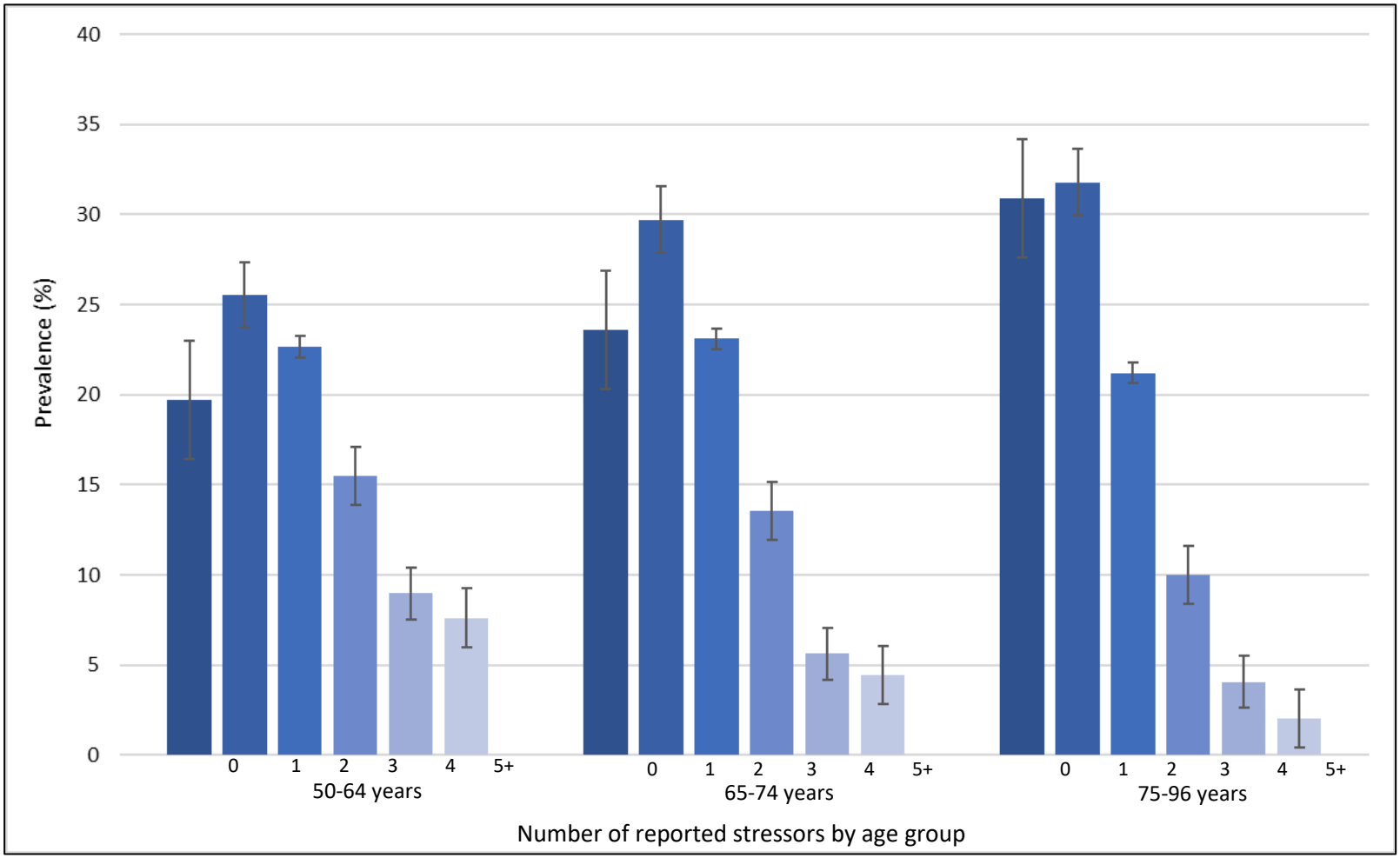

Figure 1. Prevalence of total reported stressors with standard error bars by age group among Canadian adults within the Canadian Longitudinal Study on Aging (CLSA) at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020) (n=23,758)

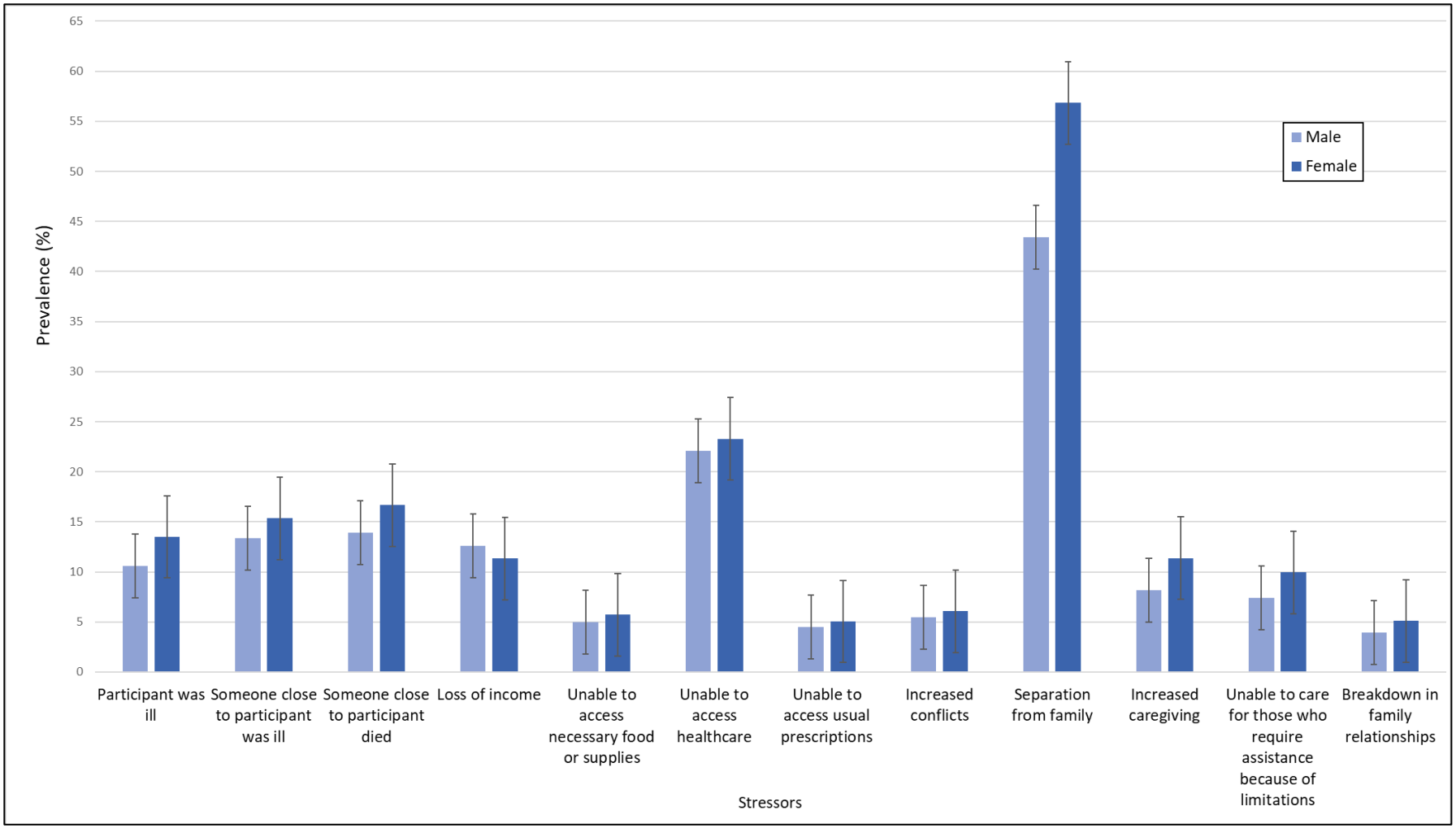

Figure 2. Prevalence of stressors with standard error bars among Canadian adults within the Canadian Longitudinal Study on Aging (CLSA) by sex at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020) (n=23,758)

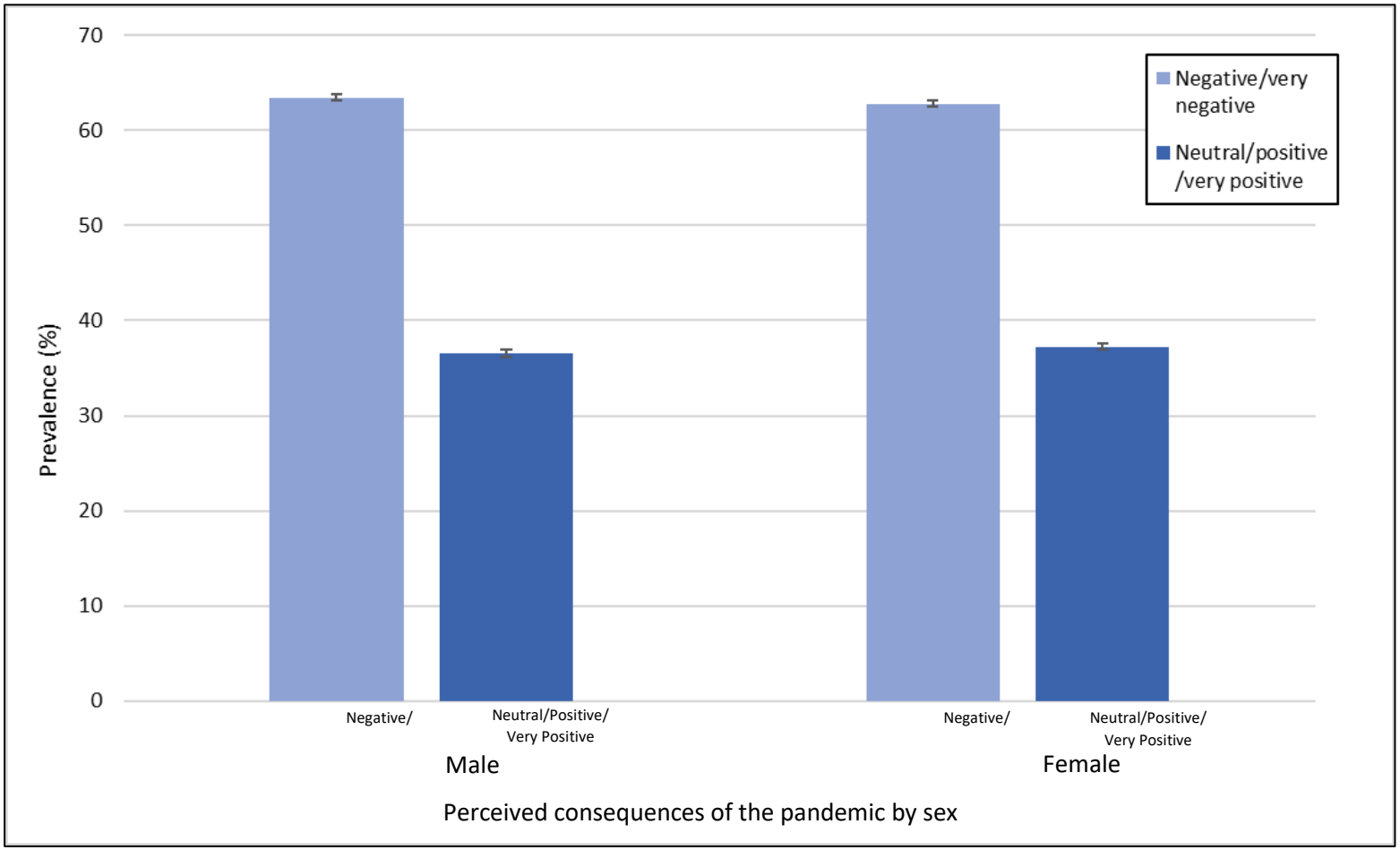

Figure 3. Perceived consequences of the COVID-19 pandemic experienced by Canadian adults within the Canadian Longitudinal Study on Aging (CLSA) (n=23,020) by sex at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020) with standard error bars

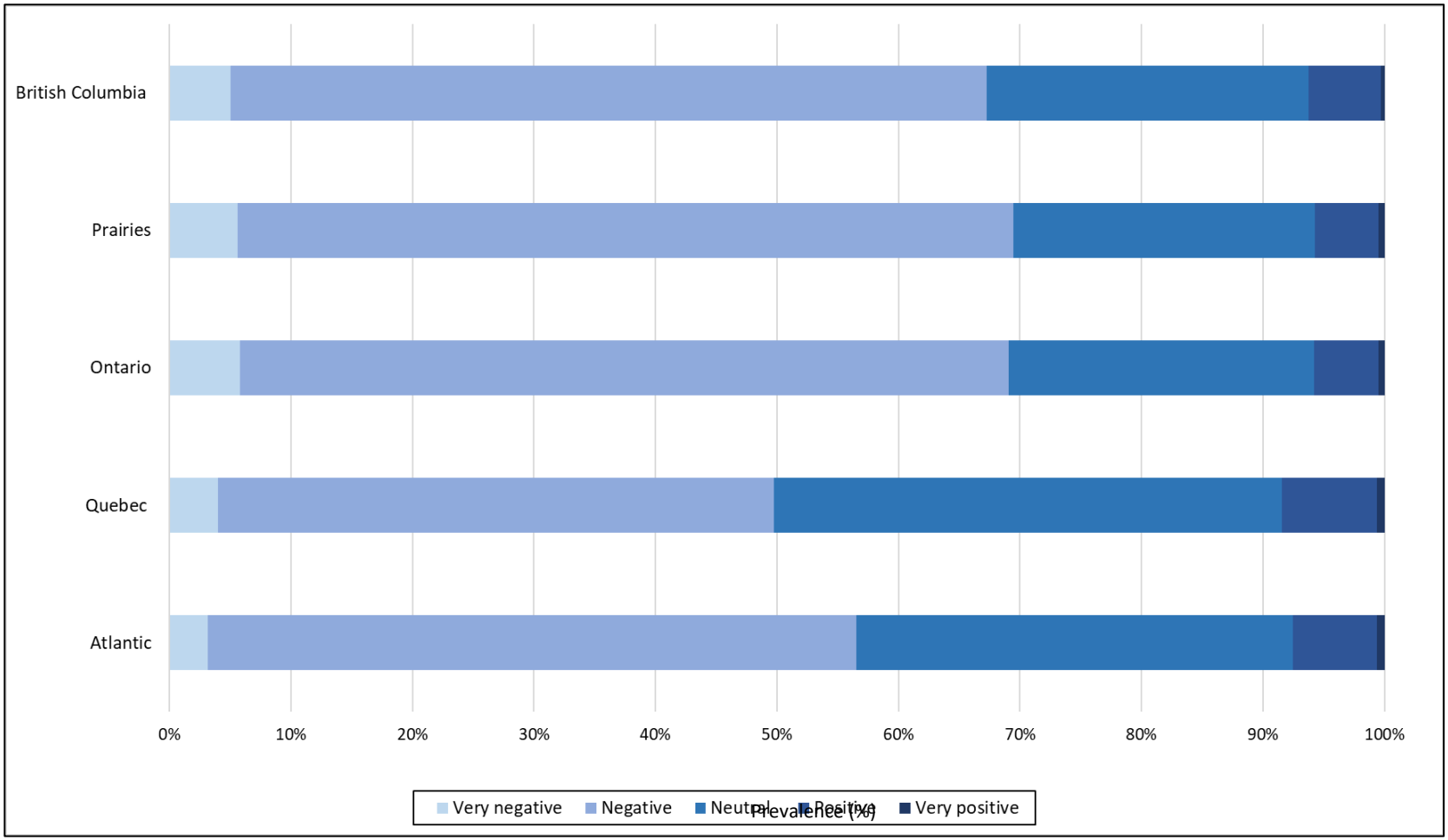

Figure 4. Perceived consequences of the COVID-19 pandemic experienced by Canadian adults within the Canadian Longitudinal Study on Aging (CLSA) (n=23,020) at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020) by region

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Supplementary Information

Brief CLSA Methodology

The Canadian Longitudinal Study on Aging (CLSA) is a nationally generalizable sample of Canadian adults aged 45-85 at the time of recruitment from the 10 provinces across Canada. The CLSA has a sample of 51,338 participants that will be followed for at least 20 years. The sampling frame for the CLSA was based off the Canadian Community Health Survey (CCHS) 4.2 on Healthy Aging implemented by Statistics Canada, with supplementation from provincial healthcare registration databases and random digit dialing to ensure the target sample size was met. Further details on the CCHS 4.2 Health Aging study design can be found elsewhere (1,2). The CLSA inclusion criteria were: able to complete interviews in either English or French, cognitively able to participate on their own, not institutionalized, did not reside in a Canadian territory or on a Federal First Nations reserve, or not full-time members of the Canadian Armed forces. At baseline recruitment, trained interviewers made the decision if someone was unable to provide informed consent on their own or unable to provide reliable information, and thus were excluded from the study.

Participants were recruited into two cohorts within the CLSA, the tracking cohort (n baseline = 21,241) and the comprehensive cohort (n baseline = 30,097). Data on the comprehensive cohort was collected using computer-assisted personal interviews completed in the participants' home and computer-assisted telephone interviews completed over the phone. In addition, participants in the comprehensive cohort also completed face-to-face interviews and visits to local data collection sites (DCS) where

more in-depth information was collected. Data collection has taken place at baseline (2011-2015) (n=51,338) and follow-up 1 (2015-2018) (n=44,817).

In April 2020, the CLSA COVID-19 Questionnaire Study was launched to collect pandemic-related data. The CLSA COVID-19 surveys were developed by CLSA COVID-19 Team. The survey included several questions and validated measurement tools (e.g., CES-D-10), and items that were included in the CLSA baseline and follow-up surveys to allow for longitudinal assessment of participants over time. Of the 51,338 participants within the CLSA, 42,700 participants were invited to participate in the COVID survey. Participants were ineligible to be included if they had withdrawn from the CLSA, required a proxy, for administrative reasons (e.g., current contact information unavailable) or if they had died. Participants were contacted via email (n=34,498) or telephone for those without internet access (n=8,202) by CLSA staff or a private marketing company. Participants were provided with information about the purpose and scope of the study prior to agreeing to participate. Among the 42,700 participants invited to participate, 28,559 (66.9%) agreed to participate in the CLSA COVID-19 study. The CLSA COVID-19 Study collected longitudinal data over a 9-month period with participants. A baseline survey was administered from April 2020-June 2020 and the Exit Survey administered from September 2020-December 2020, which collected information on COVID-19 symptoms, risk factors, healthcare use, health behaviours, psychosocial and economic consequences of the pandemic. There were additional, weekly, bi-weekly, and monthly surveys that were shortened and focused in on COVID-19 symptoms and

status and behaviours. Participants either completed surveys via web (n= 23,832) or by telephone interview (n= 4,727).

All surveys used for the CLSA can be found at the following link: https://www.clsa-elcv.ca/researchers/data-collection

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Table A1. The proportion of Canadian adults reporting stressors by socioeconomic characteristics within the Canadian Longitudinal Study on Aging (CLSA) at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020)

	Stressors N (row %)											
	Participant was ill	Someone close to participant was ill	Someone close to participant died	Loss of income	Unable to access necessary food or supplies	Unable to access healthcare	Unable to access usual prescriptions	Increased conflict	Separation from family	Increased caregiving	Unable to care for those who require assistance	Breakdown in family relationships
Sex												
Male	1182 (11%)	1489 (13%)	1552 (14%)	1432 (11%)	558 (5%)	2457 (22%)	498 (4%)	612 (6%)	4832 (43%)	909 (8%)	827 (7%)	438 (4%)
Female	1704 (14%)	1939 (15%)	2104 (17%)	1402 (13%)	724 (6%)	2939 (23%)	638 (5%)	767 (6%)	7175 (57%)	1436 (11%)	1257 (10%)	644 (5%)
Age group												
50-64 years	1099 (13%)	1388 (17%)	1226 (15%)	1736 (21%)	637(8%)	2085 (25%)	472 (6%)	641 (8%)	4342(53%)	1156 (14%)	957 (12%)	517 (6%)
65-74 years	1093 (13%)	1190 (14%)	1286 (15%)	822 (9%)	435 (5%)	2101 (24%)	414 (5%)	446 (5%)	4607 (53%)	776 (9%)	749 (9%)	356 (4%)
75-96 years	694 (10%)	850 (13%)	1144 (17%)	276 (4%)	210 (3%)	1210 (18%)	250 (4%)	292 (4%)	3058 (45%)	413 (6%)	378 (6%)	209 (3%)
Racial background												
White	2814 (12%)	3332 (14%)	3515 (15%)	2719 (12%)	1239 (5%)	5255 (23%)	1106 (5%)	1340 (6%)	11711 (51%)	2277 (10%)	2015 (9%)	1049 (5%)
Non-white	69 (10%)	91 (14%)	135 (20%)	112 (17%)	43 (6%)	138 (21%)	29 (4%)	38 (6%)	281 (42%)	63 (9%)	67 (10%)	32 (5%)
Education												
Secondary school graduation or less	369 (11%)	421 (12%)	537 (16%)	314 (9%)	156 (5%)	661 (19%)	150 (4%)	181 (5%)	1447 (42%)	267 (8%)	204 (6%)	142 (4%)
Some post-secondary education	219 (13%)	259 (15%)	283 (17%)	197 (12%)	111 (7%)	409 (24%)	101 (6%)	98 (6%)	880 (52%)	157 (9%)	155 (9%)	82 (5%)
Post-secondary degree or diploma	2293 (12%)	2740 (15%)	2827 (15%)	2317 (12%)	1014 (5%)	4317 (23%)	882 (5%)	1096 (6%)	9660 (52%)	1917 (10%)	1723 (9%)	854 (5%)
Household income												
Less than $50,000	768 (14%)	763 (14%)	965 (17%)	591 (10%)	319 (6%)	1208 (21%)	273 (5%)	313 (6%)	2570 (45%)	380 (7%)	438 (8%)	274 (5%)
$50,000 to less than $100,000	993 (12%)	1215 (14%)	1290 (15%)	905 (11%)	409 (5%)	1932 (23%)	373 (4%)	468 (6%)	4351 (51%)	832 (10%)	692 (8%)	364 (4%)
$100,000 to less than $150,000	512 (11%)	671 (15%)	690 (15%)	630 (14%)	242 (5%)	1088 (24%)	233 (5%)	291 (6%)	2404 (53%)	501 (11%)	445 (10%)	203 (5%)
$150,000 or more	454 (12%)	590 (16%)	478 (13%)	556 (15%)	239 (6%)	892 (24%)	187 (5%)	221 (6%)	2031 (55%)	501 (14%)	399 (11%)	178 (5%)
Region												
Atlantic	500 (12%)	530 (12%)	743 (17%)	424 (10%)	212 (5%)	1081 (25%)	212 (5%)	180 (4%)	2007 (47%)	422 (10%)	322 (8%)	131 (3%)
Quebec	527 (12%)	797 (19%)	627 (15%)	431 (10%)	109 (3%)	589 (14%)	81 (2%)	244 (6%)	1643 (38%)	232 (5%)	283 (7%)	281 (7%)
Ontario	670 (12%)	742 (13%)	868 (16%)	655 (12%)	342 (6%)	1628 (30%)	322 (6%)	338 (6%)	3139 (57%)	629 (11%)	553 (10%)	235 (4%)
Prairies	584 (12%)	737 (14%)	762 (15%)	709 (14%)	301 (7%)	898 (18%)	285 (6%)	317 (6%)	2826 (56%)	545 (11%)	490 (10%)	228 (5%)
British Columbia	604 (13%)	622 (14%)	656 (14%)	615 (13%)	318 (7%)	1200 (26%)	236 (5%)	300 (7%)	2392 (52%)	517 (11%)	436 (10%)	207 (5%)
Marital Status												
Single (never married/never lived with partner)	284 (14%)	285 (14%)	303 (15%)	295 (15%)	115 (6%)	465 (23%)	113 (6%)	114 (6%)	876 (44%)	157 (8%)	158 (8%)	106 (5%)
Married or common law relationship	1932 (12%)	2523 (15%)	2503 (15%)	2009 (12%)	884 (5%)	3837 (23%)	781 (5%)	1016 (6%)	8507 (51%)	1843 (11%)	1547 (9%)	747 (5%)
Widowed	272 (12%)	265 (11%)	402 (17%)	127 (6%)	85 (4%)	428 (19%)	91 (4%)	84 (4%)	1141 (50%)	121 (5%)	144 (6%)	78 (3%)
Divorced and separated	395 (14%)	354 (13%)	448 (16%)	400 (15%)	198 (7%)	660 (24%)	151 (5%)	164 (6%)	1476 (54%)	224 (8%)	234 (9%)	149 (5%)
Essential worker status												
Doesn't work outside the home	2077 (12%)	2394 (14%)	2717 (16%)	1213 (7%)	857 (5%)	3863 (22%)	797 (5%)	896 (5%)	8705 (51%)	1519 (9%)	8705 (51%)	694 (4%)
Essential worker	308 (12%)	418 (17%)	371 (15%)	430 (17%)	187 (8%)	595 (24%)	143 (6%)	193 (8%)	1220 (49%)	317 (13%)	1220 (49%)	164 (7%)
Not essential worker	404 (12%)	511 (15%)	465 (14%)	1059 (31%)	191 (6%)	780 (23%)	160 (5%)	240 (7%)	1774 (52%)	442 (13%)	1774 (52%)	190 (6%)
Urban/rural status												
Urban	2352 (12%)	2832 (15%)	2966 (15%)	2321 (12%)	1056 (5%)	4398 (23%)	925 (5%)	1134 (6%)	9925 (51%)	1920 (10%)	1700 (9%)	884 (5%)
Rural	517 (12%)	575 (14%)	671 (16%)	497 (12%)	215 (5%)	966 (23%)	202 (5%)	236 (6%)	1358 (48%)	413 (10%)	374 (9%)	193 (5%)
Overall	2886 (12%)	3428 (14%)	3656 (15%)	2834 (5%)	1282 (5%)	5396 (23%)	1136 (5%)	1379 (6%)	12007 (50%)	2345 (10%)	2084 (9%)	1082 (5%)

Table A2. Self-reported perception of the consequences of the COVID-19 pandemic by socioeconomic characteristics among Canadian adults within the Canadian Longitudinal Study on Aging (CLSA) at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020)

	Consequences of the COVID-19 pandemic on the study participant and their household		
	Negative/very negative n=14520 N (row %)	**Neutral** n=6962 N (row %)	**Positive/very positive** n=1538 N (row %)
Sex			
Male	6937 (63%)	3383 (31%)	615 (6%)
Female	7583 (63%)	3579 (30%)	923 (8%)
Age group			
50-64 years	5183 (64%)	2243 (28%)	616 (8%)
65-74 years	5378 (64%)	2560 (30%)	507 (6%)
75-96 years	3959 (61%)	2159 (33%)	415 (6%)
Racial background			
White	14130 (63%)	6768 (30%)	1465 (7%)
Non-white	374 (59%)	186 (29%)	72 (11%)
Education			
Secondary school graduation or less	1801 (55%)	1218 (38%)	229 (7%)
Some post-secondary education	1046 (63%)	508 (31%)	97 (6%)
Post-secondary degree or diploma	11643 (64%)	5223 (29%)	1211 (7%)
Household income			
Less than $50,000	3153 (58%)	1855 (34%)	399 (7%)
$50,000 to less than $100,000	5203 (63%)	2529 (31%)	499 (6%)
$100,000 to less than $150,000	2939 (66%)	1262 (28%)	261 (6%)
$150,000 or more	2455 (67%)	927 (25%)	281 (8%)
Region			
Atlantic	2350 (57%)	1494 (36%)	315 (8%)
Quebec	2040 (50%)	1717 (42%)	346 (8%)
Ontario	3704 (69%)	1349 (25%)	312 (6%)
Prairies	3410 (70%)	1215 (25%)	283 (6%)

British Columbia	3016 (67%)	1187 (26%)	282 (6%)
Marital Status			
Single (never married/never lived with partner)	1152 (60%)	626 (33%)	130 (7%)
Married or common law relationship	10335 (64%)	4819 (30%)	1100 (7%)
Widowed	1363 (62%)	699 (32%)	128 (6%)
Divorced and separated	1663 (63%)	814 (31%)	177 (7%)
Essential worker status			
Doesn’t work outside the home	10555 (63%)	5120 (31%)	998 (6%)
Essential worker	1468 (61%)	748 (31%)	197 (8%)
Not essential worker	2114 (64%)	911 (28%)	288 (9%)
Urban/rural status			
Urban	12105 (64%)	5507 (30%)	1214 (6%)
Rural	2331 (57%)	1424 (35%)	317 (8%)

Table A3. The unadjusted association between socioeconomic characteristics and individual stressors among Canadian adults in the Canadian Longitudinal Study on Aging at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020)

	Stressors Unadjusted PR (95% CI)											
	Participant was ill	Someone close to participant was ill	Someone close to participant died	Loss of income	Unable to access necessary food or supplies	Unable to access healthcare	Unable to access usual prescriptions	Increased conflict	Separation from family	Increased caregiving	Unable to care for those who require assistance	Breakdown in family relationships
Sex												
Male	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Female	1.27 (1.19, 1.37)	1.15 (1.08, 1.22)	1.20 (1.13, 1.27)	0.90 (0.84, 0.97)	1.14 (1.02, 1.27)	1.05 (1.01, 1.11)	1.13 (1.01, 1.27)	1.11 (1.00, 1.23)	1.31 (1.28, 1.34)	1.39 (1.29, 1.51)	1.34 (1.23, 1.46)	1.30 (1.15, 1.46)
Age group												
50-64 years	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
65-74 years	0.94 (0.87, 1.02)	0.81 (0.76, 0.87)	1.00 (0.93, 1.07)	0.45 (0.42, 0.49)	0.65 (0.58, 0.73)	0.96 (0.91, 1.01)	0.83 (0.73, 0.95)	0.66 (0.59, 0.74)	1.01 (0.98, 1.04)	0.64 (0.59, 0.69)	0.74 (0.68, 0.81)	0.65 (0.57, 0.75
75-96 years	0.77 (0.70, 0.84)	0.74 (0.69, 0.80)	1.13 (1.05, 1.22)	0.19 (0.17, 0.22)	0.40 (0.34, 0.47)	0.70 (0.66, 0.75)	0.64 (0.55, 0.75)	0.56 (0.48, 0.63)	0.86 (0.83, 0.88)	0.43 (0.39, 0.48)	0.48 (0.43, 0.54)	0.49 (0.42, 0.57
Racial background												
White	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Non-white	0.85 (0.67, 1.05)	0.95 (0.77, 1.14)	1.33 (1.13, 1.54)	1.42 (1.19, 1.68)	1.20 (0.88, 1.59)	0.91 (0.77, 1.05)	0.91 (0.62, 1.28)	0.99 (0.72, 1.33)	0.83 (0.76, 0.91)	0.96 (0.75, 1.20)	1.15 (0.90, 1.44)	1.06 (0.73, 1.46
Education												
Secondary school graduation or less	0.87 (0.79, 0.97)	0.83 (0.76, 0.92)	1.03 (0.95, 1.12)	0.74 (0.66, 0.82)	0.84 (0.71, 0.98)	0.83 (0.77, 0.89)	0.92 (0.78, 1.10)	0.90 (0.77, 1.04)	0.81 (0.78, 0.85)	0.76 (0.67, 0.85)	0.64 (0.56, 0.74)	0.90 (0.76, 1.07
Some post-secondary education	1.04 (0.91, 1.18)	1.03 (0.92, 1.16)	1.09 (0.97, 1.22)	0.93 (0.81, 1.06)	1.19 (0.98, 1.44)	1.03 (0.95, 1.13)	1.25 (1.02, 1.52)	0.98 (0.79, 1.19)	0.99 (0.95, 1.04)	0.89 (0.76, 1.04)	0.98 (0.84, 1.14)	1.05 (0.83, 1.30
Post-secondary degree or diploma	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Household income												
Less than $50,000	1.21 (1.09, 1.34)	0.92 (0.83, 1.01)	1.13 (1.03, 1.23)	0.75 (0.68, 0.84)	1.06 (0.90, 1.25)	0.89 (0.83, 0.96)	0.94 (0.80, 1.12)	0.87 (0.74, 1.01)	0.86 (0.83, 0.90)	0.61 (0.54, 0.69)	0.79 (0.70, 0.90)	1.09 (0.91, 1.30
$50,000 to less than $100,000	1.04 (0.94, 1.15)	0.97 (0.89, 1.06)	1.00 (0.92, 1.09)	0.75 (0.70, 0.85)	0.90 (0.78, 1.06)	0.95 (0.89, 1.01)	0.86 (0.73, 1.01)	0.86 (0.75, 0.99)	0.97 (0.94, 1.00)	0.89 (0.81, 0.99)	0.83 (0.74, 0.93)	0.96 (0.81, 1.14
$100,000 to less than $150,000	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
$150,000 or more	1.08 (0.96, 1.22)	1.08 (0.97, 1.19)	0.85 (0.76, 0.94)	1.08 (0.97, 1.20)	1.21 (1.02, 1.44)	1.00 (0.93, 1.08)	0.98 (0.81, 1.18)	0.93 (0.78, 1.10)	1.03 (0.99, 1.08)	1.22 (1.09, 1.37)	1.10 (0.96, 1.25)	1.07 (0.88, 1.30
Region												
Atlantic	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Quebec	1.05 (0.94, 1.18)	1.50 (1.36, 1.67)	0.84 (0.77, 0.93)	1.02 (0.90, 1.15)	0.51 (0.41, 0.64)	0.54 (0.50, 0.60)	0.38 (0.30, 0.49)	1.36 (1.12, 1.64)	0.82 (0.78, 0.86)	0.55 (0.47, 0.64)	0.88 (0.75, 1.03)	2.15 (1.76, 2.64
Ontario	1.05 (0.94, 1.17)	1.09 (0.98, 1.21)	0.91 (0.83, 1.00)	1.21 (1.07, 1.35)	1.26 (1.07, 1.49)	1.17 (1.10, 1.26)	1.18 (1.00, 1.40)	1.46 (1.23, 1.75)	1.22 (1.17, 1.27)	1.16 (1.04, 1.31)	1.34 (1.18, 1.53)	1.40 (1.14, 1.73
Prairies	0.99 (0.88, 1.11)	1.17 (1.06, 1.30)	0.87 (0.79, 0.95)	1.41 (1.26, 1.58)	1.20 (1.01, 1.42)	0.70 (0.65, 0.76)	1.14 (0.96, 1.35)	1.49 (1.25, 1.78)	1.19 (1.14, 1.24)	1.09 (0.97, 1.23)	1.28 (1.12, 1.47)	1.47 (1.19, 1.82
British Columbia	1.13 (1.01, 1.26)	1.10 (0.99, 1.22)	0.83 (0.75, 0.91)	1.36 (1.21, 1.53)	1.40 (1.19, 1.67)	1.04 (0.97, 1.12)	1.04 (0.87, 1.25)	1.56 (1.31, 1.87)	1.12 (1.07, 1.16)	1.15 (1.02, 1.30)	1.27 (1.11, 1.46)	1.48 (1.20, 1.84
Marital Status												
Single (never married/lived with partner)	1.23 (1.10, 1.38)	0.95 (0.84, 1.06)	1.02 (0.91, 1.13)	1.23 (1.10, 1.38)	1.09 (0.90, 1.31)	1.02 (0.93, 1.10)	1.21 (1.00, 1.46)	0.94 (0.78, 1.13)	0.86 (0.82, 0.91)	0.71 (0.61, 0.83)	0.86 (0.73, 1.00)	1.19 (0.97, 1.44
Married or common law relationship	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Widowed	1.02 (0.90, 1.15)	0.76 (0.67, 0.85)	1.16 (1.06, 1.28)	0.46 (0.38, 0.54)	0.70 (0.56, 0.86)	0.81 (0.74, 0.88)	0.84 (0.68, 1.04)	0.60 (0.48, 0.74)	0.97 (0.93, 1.01)	0.48 (0.40, 0.57)	0.67 (0.57, 0.97)	0.76 (0.60, 0.94
Divorced and separated	1.24 (1.12, 1.37)	0.85 (0.77, 0.94)	1.09 (0.99, 1.19)	1.21 (1.09, 1.33)	1.36 (1.17, 1.57)	1.04 (0.97, 1.12)	1.17 (0.99, 1.39)	0.98 (0.83, 1.15)	1.05 (1.01, 1.09)	0.74 (0.64, 0.84)	0.92 (0.80, 1.04)	1.21 (1.02, 1.43
Essential worker status												
Doesn't work outside the home	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Essential worker	1.03 (0.92, 1.15)	1.22 (1.10, 1.33)	0.95 (0.86, 1.05)	2.47 (2.23, 2.73)	1.52 (1.30, 1.76)	1.07 (0.99, 1.15)	1.25 (1.05, 1.48)	1.50 (1.29, 1.74)	0.98 (0.93, 1.02)	1.45 (1.29, 1.62)	1.33 (1.11, 1.50)	1.64 (1.39, 1.93
Not essential worker	0.99 (0.99, 1.09)	1.09 (0.99, 1.18)	0.87 (0.79, 0.95)	4.44 (4.12, 4.78)	1.13 (0.97, 1.32)	1.03 (0.96, 1.10)	1.02 (0.86, 1.20)	1.36 (1.18, 1.56)	1.04 (1.00, 1.08)	1.48 (1.34, 1.63)	1.29 (1.15, 1.43)	1.39 (1.19, 1.62
Urban/rural status												
Urban	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Rural	1.01 (0.93, 1.11)	0.94 (0.86, 1.02)	1.04 (0.97, 1.13)	0.99 (0.90, 1.09)	0.94 (0.81, 1.08)	1.01 (0.95, 1.08)	1.01 (0.87, 1.17)	0.96 (0.84, 1.10)	0.94 (0.90, 0.97)	0.99 (0.90, 1.10)	1.01 (0.91, 1.13)	1.01 (0.86, 1.17

Table A4. The unadjusted association between socioeconomic characteristics and total number of stressors[1] among Canadian adults in the Canadian Longitudinal Study on Aging at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020)

	Unadjusted PR (95% CI)
Sex	
Male	1.00
Female	1.20 (1.17, 1.23)
Age group	
50-64 years	1.00
65-74 years	0.83 (0.81, 0.86)
75-96 years	0.67 (0.65, 0.69)
Racial background	
White	1.00
Non-white	0.99 (0.92, 1.06)
Education	
Secondary school graduation or less	0.83 (0.80, 0.86)
Some post-secondary education	1.02 (0.97, 1.06)
Post-secondary degree or diploma	1.00
Household income	
Less than $50,000	0.90 (0.87, 0.93)
$50,000 to less than $100,000	0.94 (0.91, 0.97)
$100,000 to less than $150,000	1.00
$150,000 or more	1.04 (1.00, 1.08)
Region	
Atlantic	1.00
Quebec	0.86 (0.83, 0.90)
Ontario	1.17 (1.13 1.21)
Prairies	1.08 (1.04, 1.12)
British Columbia	1.12 (1.08, 1.16)
Marital Status	
Single (never married/never lived with partner)	0.98 (0.93, 1.02)
Married or common law relationship	1.00
Widowed	0.83 (0.80, 0.87)
Divorced and separated	1.05 (1.01, 1.08)
Essential worker status	
Doesn’t work outside the home	1.00
Essential worker	1.18 (1.14, 1.23)
Not essential worker	1.23 (1.19, 1.27)
Urban/rural status	
Urban	1.00
Rural	0.98 (0.95, 1.00)

1. The total number of stressors was calculated by adding the number of stressors people reported, this ranged from zero to 12.

Table A5. Unadjusted prevalence ratios (PRs) and 95% CI for the association between socioeconomic characteristics and negative/very negative versus neutral/positive/very positive perception of the consequences of the COVID-19 pandemic among Canadian adults in the Canadian Longitudinal Study on Aging at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020)

	Unadjusted PR (95% CI)
Sex	
Male	1.00
Female	0.99 (0.97, 1.01)
Age group	
50-64 years	1.00
65-74 years	0.99 (0.97, 1.01)
75-96 years	0.94 (0.92, 0.96)
Racial background	
White	1.00
Non-white	0.94 (0.87, 1.00)
Education	
Secondary school graduation or less	0.86 (0.83, 0.89)
Some post-secondary education	0.98 (0.95, 1.02)
Post-secondary degree or diploma	1.00
Household income	
Less than $50,000	0.89 (0.86, 0.91)
$50,000 to less than $100,000	0.96 (0.93, 0.99)
$100,000 to less than $150,000	1.00
$150,000 or more	1.02 (0.99, 1.05)
Region	
Atlantic	1.00
Quebec	0.88 (0.84, 0.92)
Ontario	1.22 (1.18, 1.26)
Prairies	1.23 (1.19, 1.27)
British Columbia	1.19 (1.15, 1.23)
Marital Status	
Single (never married/never lived with partner)	0.95 (0.91, 0.99)
Married or common law relationship	1.00
Widowed	0.98 (0.94, 1.01)
Divorced and separated	0.99 (0.95, 1.02)
Essential worker status	
Doesn’t work outside the home	1.00
Essential worker	0.96 (0.93, 0.99)
Not essential worker	1.01 (0.98, 1.04)
Urban/rural status	
Urban	1.00
Rural	0.89 (0.86, 0.92)

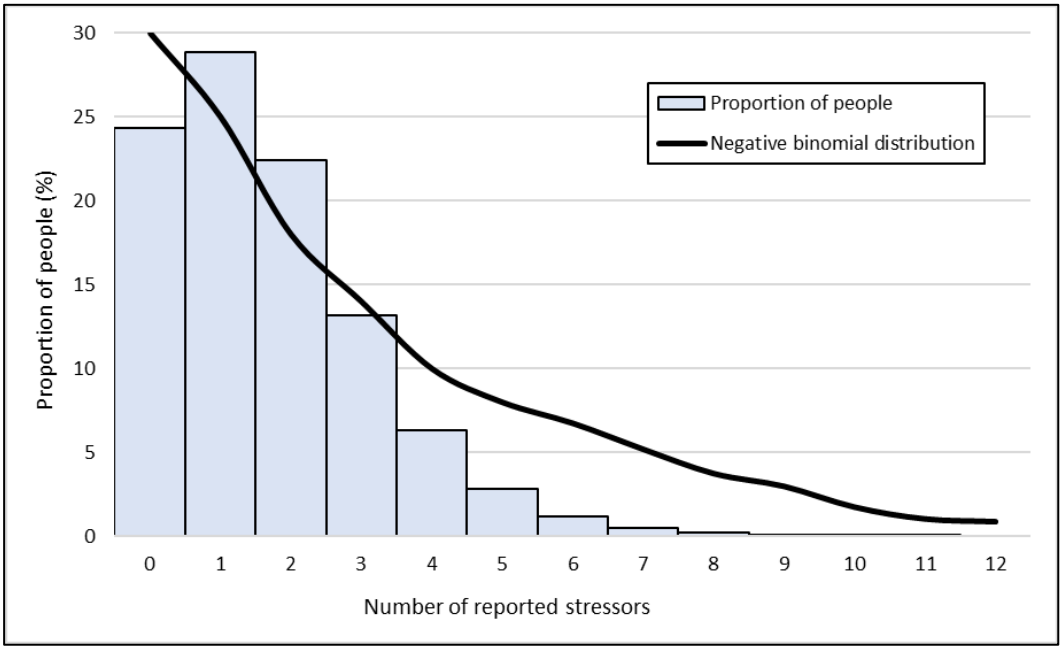

Figure A1. Histogram of the prevalence of total reported stressors (range: 0-12) with overlay of negative binomial distribution

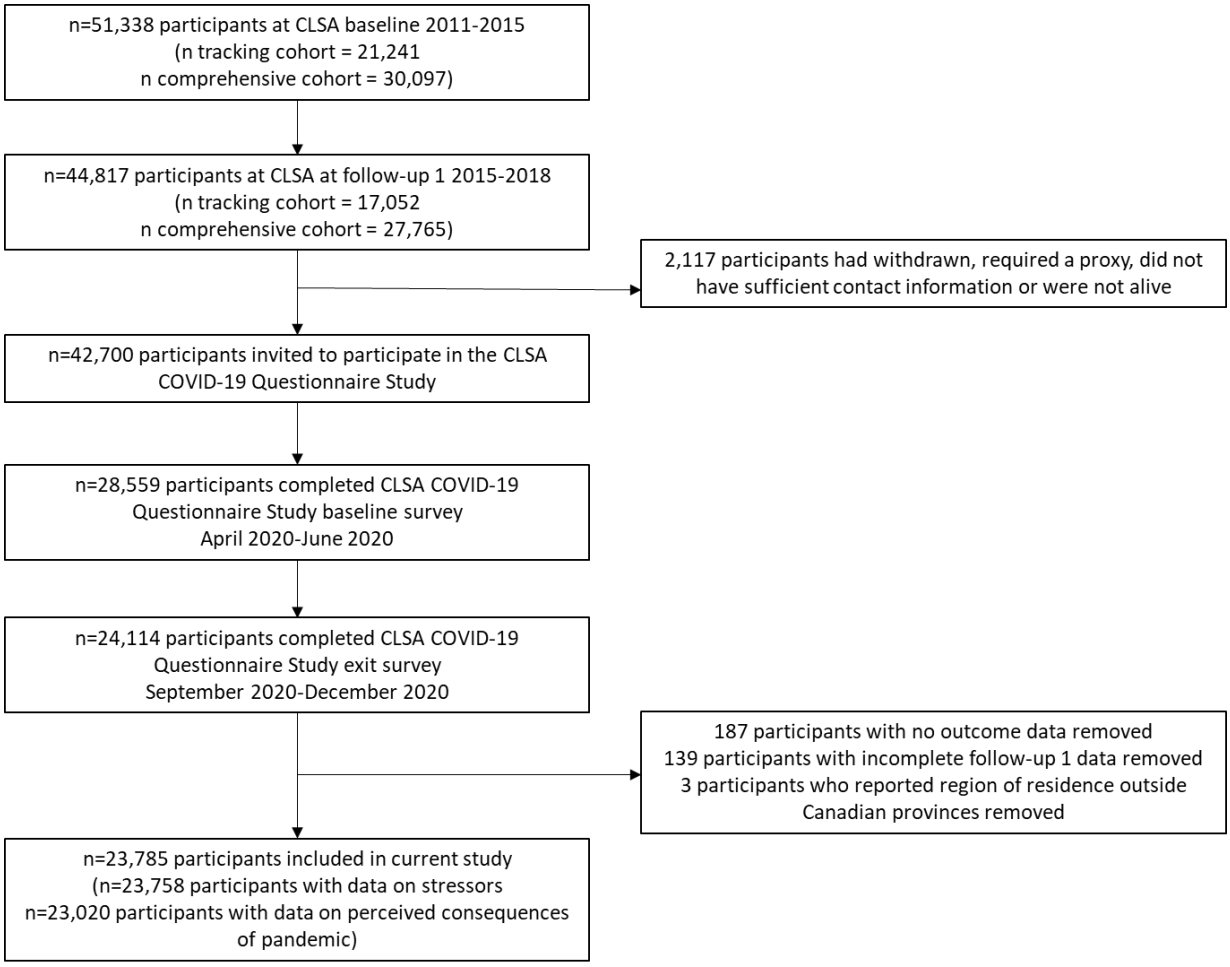

Figure A2. Participant flow diagram of analytic sample from the Canadian Longitudinal Study on Aging (CLSA) at CLSA COVID-19 Questionnaire Exit Survey (September-December 2020)

Chapter 4: Obesity and adverse childhood experiences in relation to stress during the COVID-19 pandemic: an analysis of the Canadian Longitudinal Study on Aging

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Chapter 4 Summary

Summary: People with obesity are at risk for increased stress, which is likely to hold true for stress experienced during the COVID-19 pandemic. In addition, people who have experienced adversity during childhood are at a greater risk of developing obesity during adulthood, thus making it more likely for ACEs to modify the association between obesity and stress experienced during the COVID-19 pandemic. This study aimed to evaluate the associations between obesity, ACEs, and stress during the pandemic, and to determine if ACEs modified the association between obesity and stress. It was evident that experiences across the life course, including ACEs and adulthood obesity were strongly associated with experiences during the COVID-19 pandemic, highlighting the importance of identifying subgroups of people who may be at the greatest risk of negative long-term outcomes following the pandemic.

ABSTRACT

Background*:* People with obesity are at increased risk of chronic stress, and this may have been exacerbated during the COVID-19 pandemic. Adverse childhood experiences (ACE) are also associated with both obesity and stress and may modify risk of stress among people with obesity. The objectives of this study were to evaluate the associations between obesity, ACEs, and stress during the pandemic, and to determine if the association between obesity and stress was modified by ACEs.

Methods: A longitudinal study was conducted among adults aged 50-96 years (n=23,972) from the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Study. Obesity and ACEs were collected pre-pandemic (2015-2018), and stress was measured at COVID-19 Exit Survey (Sept-Dec 2020). We used logistic, Poisson, and negative binomial regression to estimate relative risks (RRs) and 95% confidence intervals (CIs) for the associations between obesity, ACEs, and stress outcomes during the pandemic. Interaction by ACEs was evaluated on the additive and multiplicative scales.

Results: People with obesity were more likely to experience an increase in overall stressors (class III obesity vs. healthy weight RR=1.19; 95% CI: 1.12-1.27) as well as increased health related stressors (class III obesity vs. healthy weight RR: 1.25; 95% CI: 1.12-1.39) but did not perceive the consequences of the pandemic as negative. ACEs were also associated an increase in overall stressors (4-8 ACEs vs. none RR= 1.38; 95% CI: 1.33-1.44) and being more likely to perceive the pandemic as negative (4-8 ACEs vs. none RR=1.32; 95% CI: 1.19-1.47). The association between obesity and stress was not modified by ACEs.

Conclusions: Increased stress during the first year of the COVID-19 pandemic was observed among people with obesity or ACEs. The long-term outcomes of stress during the pandemic need to be determined.

Keywords: COVID-19, stressors, adverse childhood experiences, obesity, effect measure modification, CLSA

INTRODUCTION

Stress and obesity share a complex relationship, with cyclical and bidirectional associations across the life course (1,2). As described in a conceptual model by van der Valk et al., the bidirectional interplay between obesity, chronic stress, and glucocorticoid action is impacted by numerous individual level characteristics, including genetics, lifestyle, medications and mental distress (1). "It is well known that stress and obesity are associated, and many mechanistic pathways that lead to disease development exist, including health behaviours, glucocorticoid activation, and mental health (1,3,4). However, having obesity has also been found to increase stress due to several reasons, including comorbidities that limit daily activities, and weight stigma or bias, which may induce a prolonged stress response (3). Adverse childhood experiences (ACEs), defined as a wide range of negative events, including abuse, neglect, witnessing violence, parental mental illness or incarceration of a family member (5), are one example of an individual level factor that may impact both obesity and stress (4–8). Although ACEs take place early in life, the effects have been found to extend beyond childhood or adolescence into older adulthood (4). Following exposure to ACEs there may be a prolonged stress response, which is also known as toxic stress, which may make people with ACEs more susceptible to stress or worse experiences during a stressful event (5–7,9).

In Canada, throughout the first year of the pandemic (March 2020-March 2021), strict public health preventive measures were in place including work and school closures, and travel bans (10). In turn, this created wide-reaching implications on population health including an increase in stress (11–13). Obesity was identified as a risk

factor for increased COVID-19 morbidity and mortality early in the pandemic and this may have contributed to increased weight bias and stress among people living with obesity (14–16). There is limited research on the impact of living with obesity on stress during the COVID-19 pandemic. A systematic review has found that exposure to disasters increases cardiometabolic risk, including obesity, across the life course, however, research has not yet explored how obesity may influence stress experienced during a disaster (17) . Stress during a disaster can be measured objectively, using reports of stressors, or subjectively, measuring perceptions of a disaster (18). ACEs are an established risk factor for both stress (5–7) and later life obesity (4,8). ACEs have been associated with higher psychological symptoms following a natural disaster (19) and it is possible people with obesity who experienced ACEs may have experienced an added burden of stress during the pandemic (20–22). Differences also exist by sex, whereby females have higher psychological symptoms following a disaster (19), and the prevalence of ACEs and obesity vary among males and females (23,24).

It is possible people with obesity may have experienced greater stress during the COVID-19 pandemic, and life course epidemiology frameworks help to identify potential distal risk factors, such as ACEs, that may have led to differential experiences (25). This is of importance in the context of the pandemic, and beyond, as the findings from this research will contribute to understanding the complex relationship stress and obesity share. The objectives of this study were to evaluate the association between both obesity and ACEs and stress during the pandemic (stressors and perceived consequences) and to

determine if the association between obesity and stress was modified by ACEs. Differences in the association between obesity and ACEs by sex were also evaluated.

METHODS

Study Design and Participants

We conducted an analysis using longitudinal data collected as part of the Canadian Longitudinal Study on Aging (CLSA). The methodology of the CLSA has been published elsewhere (26). Briefly, the CLSA is a national longitudinal study of adults aged 45 to 85 at the time of recruitment (2011-2015). At the time of recruitment, participants provided informed consent. Adults from the 10 Canadian provinces were recruited using population-based sampling strategies (26). Participants were eligible for inclusion into the CLSA if they could complete interviews in English or French, were cognitively able participate on their own, were not in an institution, did not reside in a Canadian territory (The Northwest Territories, the Yukon and Nunavut) or on a Federal First Nations reserve, and were not a full-time member of the Canadian Armed forces. Ethics approval for this study was received from the Hamilton Integrated Research Ethics Board (HiREB).

The CLSA is comprised of the Tracking cohort and the Comprehensive cohort. Data for the Tracking cohort were collected using telephone interviews, whereas data for the Comprehensive cohort were collected via in-home interviews and clinical data collection site visits. Data are collected every three years and all participants will be followed for 20 years, or until death or loss-to-follow-up. Data for this analysis were

collected at baseline in 2011-2015 and at follow-up 1 in 2015-2018. At the start of the COVID-19 pandemic, the CLSA COVID-19 Questionnaire Study was implemented, which collected longitudinal data from April 2020 to December 2020. Specific details about when data for this study were collected can be found in Table 1.

Primary Exposures

Obesity. Obesity was measured at CLSA follow-up 1 (2015-2018). For individuals in the Comprehensive cohort (n=15,582), height and weight were measured by trained research assistants. These measurements were used to calculate body mass index (BMI) (kg/m^2). For individuals in the Tracking cohort (n=8,390), height and weight were assessed using self-report, which were then used to calculate BMI. A correction factor developed by Statistics Canada was applied to the self-reported BMI to account for bias associated with self-report (27). These correction equations were generated using the 2005 Canadian Community Health Survey with consideration of several sociodemographic variables separately for males and females (28). Self-reported BMI was slightly underestimated compared to the corrected BMI, which is consistent with the literature (27). BMI was categorized following World Health Organization standard cut-offs (29): normal weight ($\leq$24.9 kg/m^2), overweight (25 to 29.9 kg/m^2), obesity class I (30-34.9 kg/m^2), obesity class II (35-39.9 kg/m^2) and obesity class III ($\geq$40 kg/m^2). Obesity was further classified into 3 subgroups, as research has found variation in risk of health outcomes across the subtypes (30). Underweight individuals were included in the normal weight category given the small sample size.

Adverse childhood experiences. To measure ACEs, at CLSA follow-up 1, participants were asked about 11 experiences before the age of 16 related to physical abuse, sexual abuse, emotional abuse, neglect, and exposure to intimate partner violence. Participants were also asked about three experiences before the age of 18 related to death of a parent, parental divorce/separation and living with a family member with mental health problems. These questions were adapted from the Childhood Experience of Violence Questionnaire and the National Longitudinal Study of Adolescent to Adult Health Wave III questionnaire (31,32). Based on responses to dichotomized yes/no questions, a cumulative score was created by summing the total number of ACEs participants reported (31). Since only a small proportion of people reported 5 to 8 ACEs (4%), those reporting four or more were collapsed into one group. A cumulative ACEs score was used rather than subgroups by severity, as research has found this to be a better assessment of cumulative exposure, and has been found to be associated with health outcomes (33).

Measurement of Outcomes (stress)

Stress was measured in two ways: 1) stressors and 2) the perceived consequences of the pandemic. These questions have previously been used in disaster research(18,34–36) to study objective and subjective stress following a disaster such as the COVID-19 pandemic. The development of these questions were modified from gold-standard measurement tools (18).

Stressors. Stressors were measured at CLSA COVID-19 Questionnaire Study Exit Survey (September 2020-December 2020). Participants were asked, "*Which of the following have you experienced during the COVID-19 pandemic?"* where participants could select one or more of the following options: participant was ill, someone close to the participant was ill, someone close to the participant died, loss of income, unable to access necessary food and supplies, unable to access healthcare, unable to access usual prescriptions, increased conflict, separation from family, increased caregiving, unable to care for those who require assistance due to limitations, and breakdown in family relationships. The 12 stressors were classified into four domains for this analysis; 1) health (participant was ill, someone close to the participant was ill, someone close to the participant died), 2) resources (loss of income, unable to access necessary food and supplies, unable to access healthcare, unable to access usual prescriptions), 3) relationships (increased conflict, separation from family, breakdown in family relationships), and 4) caregiving (increased caregiving, unable to care for those who require assistance due to limitations). To create each domain, the total number of stressors within each category was summed. The range of values for each domain varied depending on how many stressors fell within the category. For instance, the health domain ranged from 0 to3, whereas the resources domain ranged from 0 to 4. In addition, a cumulative stressor score was created by summing the total number of stressors participants experienced across all domains (37). The cumulative stressor score ranged from 0 to 12.

Perceived consequences of the pandemic. As a subjective measure of perceived stress, participants were asked "*Taking everything about COVID-19 into account, how would you describe the consequences of COVID-19 on you and your household?"* during the CLSA COVID-19 Questionnaire Study Exit Survey (September 2020-December 2020) (18,34,35). Response options were very negative, negative, neutral, positive, and very positive. Very few participants reported the consequences of the pandemic as very negative or very positive, so these categories were combined with negative and positive response options, respectively. The neutral category was further combined with the positive and very positive category to create a binary variable, since the objective of the analysis was to explore negative/very negative perceived consequences of the pandemic compared to all other perceptions.

Measurement of potential confounding variables

All remaining variables were measured at CLSA baseline (2011-2015), CLSA follow-up 1 (2015-2018), CLSA COVID-19 Baseline Survey (April 2020-June 2020) or the CLSA COVID-19 Exit Survey (September 2020-December 2020). These variables were chosen based on the framework proposed by van der Valk et al., identifying characteristics that are related to the association of stress and obesity (1). Participant sex (male or female) and racial background (white or non-white) were collected at CLSA baseline. Participant age at CLSA COVID-19 Baseline Survey was categorized as 50-64 years, 65-74 years, and 75-96 years. Physical activity, household income, alcohol

consumption and depression were measured at CLSA follow-up 1. To assess physical activity, the Physical Activity Scale for the Elderly (PASE) was used which assess level of physical activity for the previous seven days (38). Based on the World Health Organization (WHO) guidelines (39), physical activity was dichotomized into ≤150 min/week of moderate-intensity or ≤75 min/week of vigorous-intensity versus >150 min/week of moderate-intensity or >75 min/week of vigorous-intensity. Household income was categorized into less than $50,000, $50,000 to less than $100,000, $100,000 to less than $150,000, and $150,000 or more and alcohol consumption over the past 12 months was categorized as did not drink in the last 12 months, occasional drinker, and regular drinker (at least once a month). Depression was assessed using the Center for Epidemiologic Studies Short Depression (CESD) scale (40), where a score of ≥10 indicates risk for clinical depression.

Statistical analysis

All statistical analyses were completed using SAS 9.4. Statistical code is available upon request. The associations between both obesity and ACEs were independently evaluated in relation to the three primary outcomes, 1) the stressor domains, 2) total stressor score, and 3) the perceived consequences of the pandemic. PROC GENMOD was used to estimate relative risks (RRs) and 95% confidence intervals (CIs). For all outcomes, a log link function was used, however the distribution used varied for different outcomes. For the stressor domains, a Poisson distribution was assumed as this was a

count variable. Although the total stressor variable was also a count variable, a negative binomial distribution was assumed given the overdispersion. Finally, a binomial distribution was assumed for the binary perceived consequences of the pandemic variable. All models were adjusted for potential confounders that were hypothesized *a priori* to be predictors of both the exposures and outcome variables. These included sex, age group, racial background, physical activity, household income, alcohol consumption and depression (1). For the association between ACEs and stress, an additional model was run adding obesity to the fully adjusted model, given the potential mediating role of obesity. All variables had less than 5% of participants missing, and a complete case analysis was conducted. A sensitivity analysis was conducted to explore differences in associations by severity of ACEs. We explored the association between maltreatment ACEs and measures of stress, and family dysfunction ACEs and measures of stress.

For the association between obesity and measures of stress, interaction by both ACEs and sex were assessed separately on both the additive and multiplicative scales. In epidemiologic research, interaction is often only explored on the multiplicative scale, however, the assessment of interaction on the additive scale has significant public health importance as it can contribute to better allocation of resources and identification of high-risk subgroups (41). STROBE guidelines recommend presenting the separate effects of exposures and modifiers, as well as joint effects to ensure readers can assess interaction on either scale (41). To determine if the associations between obesity and measures of stress were modified by ACEs, a dichotomous ACEs variable was created. Individuals who reported no ACEs were categorized as none, and those who reported one or more

ACES, were categorized as yes. Using the framework proposed by Knol and VanderWeele (41), interaction was tested on the additive scale using the relative excess risk due to interaction (RERI) and on the multiplicative scale using the ratio of relative risk (RRR). The 95% CI for the RERI were calculated using the delta method (41–43).

RESULTS

A total of 23,972 participants were included in this analysis. A detailed flowchart of the analytic sample can be found in Figure 1 and characteristics of the study population are presented in Table 1. The CLSA COVID-19 Questionnaire Study participants are generally comparable to the full CLSA sample; however, this subgroup had a slightly higher mean household income and higher education than the full sample (44). Over three quarters (76%) of the participants reported at least one stressor and 63% reported perceiving the consequences of the pandemic as negative or very negative (Table 2).

Obesity and stress

A consistent dose-response association was observed for the association between obesity and total stressors, and the health and resources domains, whereby as obesity level increased, the risk of reporting an additional stressor also increased. For instance, adults with class III severe obesity (≥40 kg/m^2), compared to normal weight (≤24.9 kg/m^2), had a greater risk of reporting an additional stressor for the total number of

stressors (adjusted RR: 1.19; 95% CI: 1.12, 1.27), within the health domain (adjusted RR: 1.25; 95% CI: 1.12, 1.39), and within the resources domain (adjusted RR: 1.38; 95% CI: 1.25, 1.53) (Table 3). Obesity was slightly associated with an increased risk of perceiving the consequences of the pandemic as negative/very negative (obesity class III adjusted RR: 1.05; 95% CI: 1.00, 1.11) (Table 3). When ACEs were added to the model of obesity and stress the results did not change suggesting that ACEs was not a confounder of this association. Results only slighted changed after adjustment for confounding variables (Supplemental Table A1).

Adverse Childhood Experiences and stress

There were 14,607 (61%) adults who experienced one or more ACE (Table 1). Across all outcomes, there was a strong dose-response association, whereby as the number of ACEs increased, the risk of reporting an additional stressor and within each stressor domain also increased (Table 3). For instance, among those with the highest number of ACEs, the risk of an additional stressor within the resources domain was 53% greater than for those with no ACEs (adjusted RR: 1.53; 95% CI: 1.43, 1.63). Similarly, the adjusted RR estimates for the risk of perceiving the consequences of the pandemic as negative/very negative also increased as the number of ACEs increased (Table 3). Those with 4 to 8 ACEs, compared to none, were 32% more likely to perceive the pandemic as negative/very negative compared to neutral/positive/very positive (adjusted RR: 1.32; 95% CI: 1.19, 1.47). The adjusted results were attenuated slightly but even after

adjustment for potential confounders identified a priori, the results remained similar and statistically significant (Supplementary Table A1). To evaluate whether the association between ACEs and stress was explained fully or in part by obesity we ran a model adjusting for obesity. When adding obesity to the models for ACEs and all outcomes, associations were attenuated only slightly suggesting that obesity may not mediate the association between ACEs and stress (results not shown).

The association between obesity and stress by ACEs

The tests for interaction by ACEs on both the additive and multiplicative scales for the association between obesity and stress are provided in Table 4. There was no consistent evidence of interaction on either the additive or multiplicative scale by ACEs on any of the outcomes. Only the multiplicative interaction between class III obesity and ACEs for stressors within the health domain was statistically significant (RERI=-0.34; 95% CI: -0.71, 0.02; RRR=0.74; 95% CI: 0.58, 0.96), meaning among people with class III obesity, those with ACEs, compared to those with no ACEs, were less likely to report an additional stressor within the health domain.

Sex differences

The tests for interaction of obesity by sex on the additive and multiplicative scale are shown in Supplemental Tables A2 and A3. There was consistent evidence of negative interaction on the multiplicative scale for class III obesity, such that females with class III obesity were less likely to report stress outcomes during the pandemic than males. For

example, the joint exposure of having obesity class III and being female was associated with lower reports of stressors in the health domain (RERI=-0.27; 95% CI: -0.59, 0.05; RRR=0.79; 95% CI: 0.63, 1.00), resources domain (RERI=-0.31; 95% CI: -0.61, -0.01; RRR= 0.80; 95% CI: 0.65, 0.98), caregiving domain (RERI=-0.60; 95% CI: -1.10, -0.09; RRR=0.62; 95% CI: 0.44, 0.88), total stressors (RERI=-0.25; 95% CI: -0.43, -0.07; RRR=0.80; 95% CI: 0.70, 0.91) and perceiving the pandemic as negative or very negative (RERI=0.01; 95% CI: -0.07, 0.09; RRR=0.89; 95% CI: 0.80, 0.99).The tests for interaction of ACEs by sex are shown in Supplemental Table A2. There was limited evidence of interaction on either scale, and all of the tests except one were not statistically significant. The only significant test for interaction was on the multiplicative scale for the perceived consequences of the pandemic such that, females with 4-8 ACEs were less likely to perceive the pandemic as negative or very negative compared to males (RRR=0.91; 95% CI: 0.84, 0.99, p=0.02).

Sensitivity analysis

Sensitivity analyses to explore differences in associations between child maltreatment ACEs and measures of stress, and family dysfunction ACEs and measures of stress can be found in Table A4. For both maltreatment ACEs and family dysfunction ACEs, the greatest risk of reporting an additional stressor, or perceiving the consequences of the pandemic as negative/very negative were among those who reported the most ACEs. Associations were slightly larger for those who reported the most maltreatment ACEs.

DISCUSSION

The findings from this study contribute to our understanding of the experiences of stress among people with obesity during the COVID-19 pandemic and the cyclical relationship between obesity and stress. A dose-response association was found between obesity some measures of stress (total stressors, resources domain, and health domain). Although ACEs did not modify this association, it was found to be independently associated with stress experienced during the pandemic, as we identified a strong dose-response association between ACEs and all measures of stress. It was hypothesized that obesity may mediate the association between ACEs and stress experienced during the pandemic given the cyclical association stress and obesity share, however, the preliminary mediation analysis did not find obesity to be a mediator. This may be related to the timing of the measurement or that there are multiple pathways whereby ACEs influenced pandemic-related stress. Future research exploring the mechanisms behind these associations as it can be used to inform the response to future disasters or stressful events.

The joint exposures of obesity and sex were significant, meaning sex modifies these associations. Females with ACEs and with class III obesity were less likely to report an additional stressor compared to males. Our study appears to be the first to evaluate the joint effect of sex with other distal and proximal factors to stress caused by population-level adversity, such as the COVID-19 pandemic. However, studies that evaluated sex independently found females compared to males typically have higher reports of psychological related outcomes following disasters (19,45).

The findings suggest that people with obesity were more likely to experience stressors during the pandemic, however, we found they were less likely to perceive the consequences of the pandemic as negative or very negative. Similarly, people who experienced increased adversity in childhood, had worse perceptions of experiences during the pandemic, which is consistent with the literature surrounding the psychological changes that occur after exposure to adversity extending beyond childhood and altering experiences later in life (8,46). Understanding the association both ACEs and obesity have with stress during the pandemic, can help to inform future screening programs that can identify who may be at the greatest risk of the worst outcomes or experiences during a stressful event. It is possible that we did not find ACEs to modify the association between obesity and stress during the pandemic due to the measures we used, the population within the study (e.g., community dwelling older adults), or the timing of assessment. For instance, we may have found effect modification by ACEs if we had additional measures of stress after the first year of the COVID-19 pandemic (after December 2020), as people's response may have been different to the prolonged stress associated with the pandemic. Alternatively, it is possible that ACEs really does not modify this association and that stress experienced during the pandemic did not vary by experiences that occurred in early life among those with and without obesity. Future research is needed to understand why individuals with obesity experienced an increased risk of stress and worse perceptions of the pandemic. A potential pathway between obesity and these stressors could be related to weight bias and stigma; there was extensive media coverage highlighting obesity as a potential risk factor for COVID-19 mortality

which may have increased weight stigma (16). This information could be used to inform targeted strategies aimed at individuals who are overweight or have obesity, to help develop coping mechanisms, which in turn could break this cycle between obesity and stress. People with obesity may also have a greater stress response since obesity leads to an stimulation of the stress system within the body, including glucocorticoids or other stress hormones (1). This activation may make them more susceptible to worse experiences. It is also possible that people who have had ACEs respond to stressful situations or events, such as the COVID-19 pandemic, differently. Following ACEs a person may differentially manage or respond to a stressful event making them more susceptible to a greater physiological or emotional stress response (47). In addition, exposure to ACEs had been found to be linked to resilience, meaning the ability to overcome the negative experience, which has been found to lessen negative outcomes (48). Strengths of this study include the availability of longitudinal data, which allowed for an assessment of both proximal (obesity in adulthood) and distal (ACEs) factors that are associated with stressors during the COVID-19 pandemic. This is one of the first studies to explore potential factors that may impact older adults' experiences of stress during the pandemic, using a nationally generalizable cohort of over 23,000 participants. Another strength is the measurement of obesity, where most of the sample (65%) had obesity measured by a trained research assistant, and the remaining particpants (35%) self-reported obesity, which was corrected using validated correction factors to overcome biases associated with self-report. It is also a strength that we evaluated the interactions on both the additive and multiplicative scales as recommended in the epidemiology

methods literature (41). The use of the additive scale provides important evidence for interaction from a causal perspective, as it explains if the presence of one exposure depends on the presence or absence of a second exposure (41,42,49). The findings from this study are consistent with life course epidemiology frameworks that suggest an accumulation of risk can lead to increased disease later in life, as we identified measures of stress during the pandemic varied on both proximal and distal factors (25).

Limitations of this study include the sample demographics, as the current sample is primarily of white racial background which may limit the representativeness of findings. However, the demographics of the CLSA have been found to be similar to other nationally representative Canadian surveys and data from the Canadian census (26). In addition, participants were asked to recall stressors, and the perceptions of the consequences from the start of the pandemic at a relatively early period of the pandemic (September to December 2020). People's experiences may have changed throughout the pandemic as the pandemic is still ongoing as of February 2022. Additional stressors may have also been experienced beyond the 12-items asked in the CLSA COVID-19 Questionnaire survey (e.g., loss of employment). Although the measures used in this study have previously been used in disaster research (18,34–36) and were modified from gold-standard tools, it is a limitation that these tools have not been validated in the CLSA sample. Another potential limitation includes the use of self-reported recall for assessment of ACEs as this may introduce information bias, where individuals with the outcomes of interest recall past experiences differently. Given that CLSA COVID-19 Questionnaire participants were from both the Tracking and Comprehensive cohorts of

the CLSA, data on BMI was collected differently (self-report versus measured). We addressed this issue by applying a correction factor to self-reported BMI to account for any biases associated with self-report (27). It was a limitation that the correction factor used was from 2005, however this is currently the only equation available in the Canadian context to correct for self-reported BMI. We also did not have BMI measures at the time of the CLSA COVID-19 Questionnaire survey, so the use of BMI at CLSA follow-up 1 (2015-2018) may not necessarily reflect participants BMI at the time of the CLSA COVID-19 Exit Survey (Sept-Dec 2020). Finally, selection bias may also be a concern in this study given the age of the participants recruited in the CLSA, and the inability of some people in this age group to participate.

Overall, these findings may be important beyond the COVID-19 pandemic. We found people with obesity were more likely to report stressors but did not perceive the consequences of the pandemic as negative, whereas people who reported childhood adversity reported stressors and perceived the consequences of the pandemic as negative. These findings confirm different subgroups of people perceived themselves to be more susceptible to stress associated with a stressful event, such as the COVID-19 pandemic. These findings build on the framework proposed by van der Valk et al., (1) that outlines the relationship stress and obesity share, however, future research will be needed to further understand why people with obesity were more likely to report stressors but did not perceive the consequences of the pandemic as negative. The findings of this study are important beyond the COVID-19 pandemic, as it is apparent different subgroups are more susceptible to stress, which is likely to extend to other stressful events. Research will be

needed to explore the long-term effects of stress experienced during the pandemic. Given the cyclical association that stress and obesity share, it is likely the pandemic will have lasting effects on future rates of obesity (50). It will be important to determine how stress experienced during the pandemic impacts obesity rates, and potential mechanisms for this association, as it can be used to develop targeted interventions, including emotion regulation and coping strategies, helping to eliminate the cyclical association between stress and obesity, mitigating the burden of disease caused by obesity. The development of these interventions can be incorporated into clinical practice, where health professionals can identify those at the greatest risk, targeting health care to better meet their needs, improving overall health and wellbeing.

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Table 1. Characteristics of participants from the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Questionnaire study (n=23,972), Canada

Characteristics	N (%) (n=23,972)
Sex[1]	
Male	11229 (47%)
Female	12743 (53%)
Age group[2]	
50-64 years	8347 (35%)
65-74 years	8759 (36%)
75-96 years	6866 (29%)
Racial background[1]	
White	23273 (97%)
Non-white	673 (3%)
Missing	26
Total household income[3]	
Less than $50,000	5716 (25%)
$50,000 to less than $100,000	8569 (38%)
$100,000 to less than $150,000	4589 (20%)
$150,000 or more	3758 (17%)
Missing	1340
CESD-10 score ≥10[3]	
No	20548 (87%)
Yes	3096 (13%)
Missing	328
Alcohol consumption[3]	
Did not drink in last 12 months	2777 (12%)
Occasional drinker	2856 (12%)
Regular drinker (at least once a month)	18312 (76%)
Missing	27
Physical activity[3]	
≤150 min/week of moderate-intensity or ≤ 75 min/week of vigorous intensity activity (high risk)	16473 (69%)
>150 min/week of moderate-intensity or >75 min/week of vigorous-intensity activity (low risk)	7485 (31%)
Missing	14
Number of ACEs	
0	9253 (39%)
1	6566 (28%)
2	3652 (15%)
3	2152 (9%)
4-8	2237 (9%)
Missing	112
Body mass index[3]	
Normal weight (≤24.9 kg/m^2)	6710 (28%)
Overweight (25.0-29.9 kg/m^2)	9748 (41%)
Obesity – Class I (30.0-34.9 kg/m^2)	4779 (20%)
Obesity – Class II (35.0-39.9 kg/m^2)	1674 (7%)
Obesity – Class III (≥40.0 kg/m^2)	835 (4%)
Missing	226

ACEs: Adverse childhood experiences; CESD-10: Center for Epidemiologic Studies Short Depression Scale; kg: kilogram; m: meters

1. Data collected at CLSA Baseline (2011-2015)
2. Data collected at CLSA COVID-19 Questionnaire Baseline Survey (April 2020-June 2020)
3. Data collected at CLSA Follow-up 1 (2015-2018)

Table 2. Measures of stress during the COVID-19 pandemic among participants from the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Questionnaire study (n=23,972) measured at CLSA COVID-19 Exit survey (Sept 2020-Dec 2020)

	N (%) (n=23,972)
Total reported stressors	
0	5781 (24%)
1	6856 (29%)
2	5325 (22%)
3	3135 (13%)
4	1508 (7%)
5	673 (3%)
6	279 (1%)
7-12	201 (1%)
Missing	214
Health domain	
0	16098 (68%)
1	5630 (24%)
2	1750 (7%)
3	280 (1%)
Missing	214
Resources domain	
0	15712 (66%)
1	5947 (25%)
2	1656 (7%)
3	383 (2%)
4	60 (0.3%)
Missing	214
Relationship domain	
0	10916 (46%)
1	11444 (48%)
2	1170 (5%)
3	228 (1%)
Missing	214
Caregiving domain	
0	19746 (83%)
1	3595 (15%)
2	417 (2%)
Missing	214
Perceived consequences of the pandemic	
Negative/Very Negative	14520 (63%)
Neutral/Positive/Very positive	8500 (37%)
Missing	952

Table 3. Adjusted relative risks (RRs) and 95% confidence intervals (CIs) for the associations between adverse childhood experiences (ACEs), obesity and measures of stress during the COVID-19 pandemic among older adults in the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Questionnaire Exit Survey

	Stressor domains				**Total number of stressors** (n=22,052)	**Perceived consequences of the pandemic** (n=21,396)
	Health (n=22,052)	**Resources** (n=22,052)	**Relationships** (n=22,052)	**Caregiving** (n=22,052)		
	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)
Number of ACEs						
0	1.00	1.00	1.00	1.00	1.00	1.00
1	1.17 (1.11, 1.23)	1.08 (1.02, 1.13)	1.07 (1.02, 1.12)	1.09 (1.01, 1.18)	1.10 (1.07, 1.13)	1.08 (1.00, 1.15)
2	1.22 (1.15, 1.30)	1.17 (1.10, 1.24)	1.11 (1.05, 1.16)	1.13 (1.03, 1.24)	1.15 (1.11, 1.19)	1.08 (0.99, 1.18)
3	1.38 (1.28, 1.48)	1.30 (1.22, 1.40)	1.15 (1.08, 1.22)	1.22 (1.09, 1.36)	1.25 (1.20, 1.31)	1.22 (1.10, 1.36)
4-8	1.39 (1.30, 1.49)	1.53 (1.43, 1.63)	1.24 (1.17, 1.32)	1.44 (1.20, 1.59)	1.38 (1.33, 1.44)	1.32 (1.19, 1.47)
Obesity	**Stressor domains**				**Total number of stressors** (n=21,932)	**Perceived consequences of the pandemic** (n=21,301)
	Health (n=21,932)	**Resources** (n=21,932)	**Relationships** (n=21,932)	**Caregiving** (n=21,932)		
	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)	Adjusted[1] RR (95% CI)
Normal weight	1.00	1.00	1.00	1.00	1.00	1.00
Overweight	1.03 (0.98, 1.08)	1.05 (1.00, 1.11)	1.01 (0.97, 1.05)	1.01 (0.94, 1.09)	1.02 (0.99, 1.05)	0.97 (0.95, 1.00)
Obesity Class I	1.13 (1.07, 1.20)	1.21 (1.14, 1.28)	1.04 (0.99, 1.09)	1.04 (0.95, 1.14)	1.11 (1.07, 1.15)	0.97 (0.94, 1.00)
Obesity Class II	1.14 (1.04, 1.23)	1.31 (1.22, 1.42)	1.03 (0.96, 1.10)	1.12 (0.98, 1.26)	1.14 (1.09, 1.20)	1.00 (0.96, 1.04)
Obesity Class III	1.25 (1.12, 1.39)	1.38 (1.25, 1.53)	1.04 (0.95, 1.14)	1.08 (0.91, 1.27)	1.19 (1.12, 1.27)	1.05 (1.00, 1.11)

CI: Confidence Intervals; RR: Relative risk

1. Adjusted for sex, age group, racial background, physical activity, household income, alcohol consumption and depression

Table 4. Adjusted relative risks[1] (RRs) and 95% confidence Intervals (CIs) for the joint exposure of obesity and adverse childhood experiences (ACEs) among Canadian adults in the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Questionnaire Exit Survey (September-December 2020) and interaction on the additive and multiplicative scales

Health Domain					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
No ACEs	1.00	1.04 (0.96, 1.14); p=0.34	1.17 (1.05, 1.30); p=0.004	1.06 (0.90, 1.23); p=0.49	1.50 (1.24, 1.81); p<0.0001
ACEs	1.31 (1.19, 1.44); p<0.0001	1.38 (1.26, 1.50); p<0.0001	1.49 (1.35, 1.64); p<0.0001	1.54 (1.36, 1.76); p<0.0001	1.47 (1.24, 1.73); p<0.0001
Additive (RERI) [2]	REF	0.02 (-0.12, 0.17); p=0.74	0.01 (-0.16, 0.19); p=0.87	0.18 (-0.06, 0.42); p=0.15	-0.34 (-0.71, 0.02); p=0.07
Multiplicative (RRR) [3]	REF	1.01 (0.89, 1.14); p=0.90	0.98 (0.85, 1.12); p=0.73	1.12(0.92, 1.37); p=0.27	0.74 (0.58, 0.96); p=0.02
Resources Domain					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
No ACEs	1.00	1.09 (1.00, 1.19); p=0.06	1.21 (1.09, 1.24); p=0.0003	1.35 (1.17, 1.55); p<0.0001	1.38 (1.14, 1.66); p=0.001
ACEs	1.35 (1.23, 1.48); p<0.0001	1.37 (1.26, 1.50); p<0.0001	1.58 (1.44, 1.74); p<0.0001	1.68 (1.49, 1.89); p<0.0001	1.78 (1.54, 2.06); p<0.0001
Additive (RERI)	REF	-0.07 (-0.21, 0.08); p=0.37	0.03 (-0.15, 0.20); p=0.76	-0.02 (-0.28, 0.24); p=0.88	0.05 (-0.30, 0.40); p=0.78
Multiplicative (RRR)	REF	0.93 (0.83, 1.05); p=0.26	0.97 (0.85, 1.11; p=0.68	0.92 (0.77, 1.11); p=0.38	0.96 (0.76, 1.21); p=0.71
Relationships Domain					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
No ACEs	1.00	0.98 (0.92, 1.05); p=0.60	0.97 (0.89, 1.06); p=0.50	1.07 (0.94, 1.20); p=0.30	1.07 (0.90, 1.26); p=0.43
ACEs	1.11 (1.03, 1.20); p=0.01	1.17 (1.09, 1.25); p<0.0001	1.19 (1.09, 1.25); p<0.0001	1.12 (1.00, 1.25); p=0.06	1.14 (0.98, 1.31); p=0.08
Additive (RERI)	REF	0.08 (-0.2, 0.18); p=0.13	0.11 (-0.2, 0.23); p=0.09	-0.06 (-0.24, 0.12); p=0.51	-0.04 (-0.29, 0.20); p=0.72
Multiplicative (RRR)	REF	1.08 (0.97, 1.18); p=0.15	1.10 (0.98, 1.24); p=0.10	0.94 (0.80, 1.11); p=0.49	0.96 (0.77, 1.19); p=0.69
Caregiving Domain					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
No ACEs	1.00	0.98 (0.92, 1.05); p=0.60	0.97 (0.89, 1.06); p=0.50	1.07 (0.94, 1.20); 0p=0.30	1.07 (0.90, 1.25); p=0.43
ACEs	1.11 (1.03, 1.20); p=0.007	1.17 (1.09, 1.25); p<0.0001	1.19 (1.09, 1.28); p<0.0001	1.12 (1.00, 1.25); p=0.06	1.14 (0.98, 1.31); p=0.08
Additive (RERI)	REF	-0.08 (-0.29, 0.12); p=0.42	0.04 (-0.20, 0.28); p=0.76	-0.05 (-0.41, 0.30); p=0.77	0.13 (-0.33, 0.59); p=0.57
Multiplicative (RRR)	REF	0.92 (0.77, 1.10); p=0.38	1.02 (0.83, 1.26); p=0.84	0.93 (0.70, 1.24); p=0.62	1.10 (0.74, 1.63); p=0.65

Total number of stressors					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
No ACEs	1.00	1.03 (0.98, 1.08); p=0.19	1.08 (1.02, 1.15); p=0.01	1.14 (1.05, 1.24); p=0.001	1.25 (1.11, 1.39); p=0.0001
ACEs	1.23 (1.17, 1.30); p<0.0001	1.28 (1.22, 1.34); p<0.0001	1.38 (1.30, 1.45); p<0.0001	1.39 (1.29, 1.50); p<0.0001	1.42 (1.29, 1.55); p<0.0001
Additive (RERI)	REF	0.01 (-0.07, 0.09); p=0.78	0.06 (-0.03, 0.15); p=0.21	0.01 (-0.12, 0.15); p=0.84	-0.06 (-0.25, 0.12); p=0.50
Multiplicative (RRR)	REF	1.00 (0.94, 1.07); p=0.94	1.03 (0.95, 1.11); p=0.47	0.99 (0.88, 1.10); p=0.80	0.92 (0.80, 1.07); p=0.27
Perceived consequences of the pandemic					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
No ACEs	1.00	0.96 (0.93, 1.01); p=0.09	0.99 (0.94, 1.04); p=0.63	0.98 (0.90, 1.05); p=0.53	0.98 (0.88, 1.08); p=0.74
ACEs	1.06 (1.02, 1.11); p=0.006	1.03 (0.99, 1.08); p=0.13	1.00 (0.95, 1.05); p=0.91	1.05 (0.98, 1.12); p=0.17	1.11 (1.02, 1.19); p=0.01
Additive (RERI)	REF	0.003 (-0.05, 0.6); p=0.91	-0.05 (-0.12, 0.02); p=0.18	0.01 (-0.09, 0.11); p=0.89	0.06 (-0.07, 0.20); p=0.36
Multiplicative (RRR)	REF	1.01 (0.95, 1.06); p=0.85	0.95 (0.89, 1.02); p=0.19	1.01 (0.91, 1.11); p=0.87	1.06 (0.93, 1.21); p=0.38

CI: Confidence Intervals; RR: Relative risk; REF: Reference

1. Adjusted for sex, age group, racial background, physical activity, household income, alcohol consumption and depression
2. Interaction on the additive scale using Relative Excess Risk due to Interaction (RERI); Standard error calculated using the delta method (41–43)
3. Interaction on the multiplicative scale using Ratio of Relative Risks (RRR)

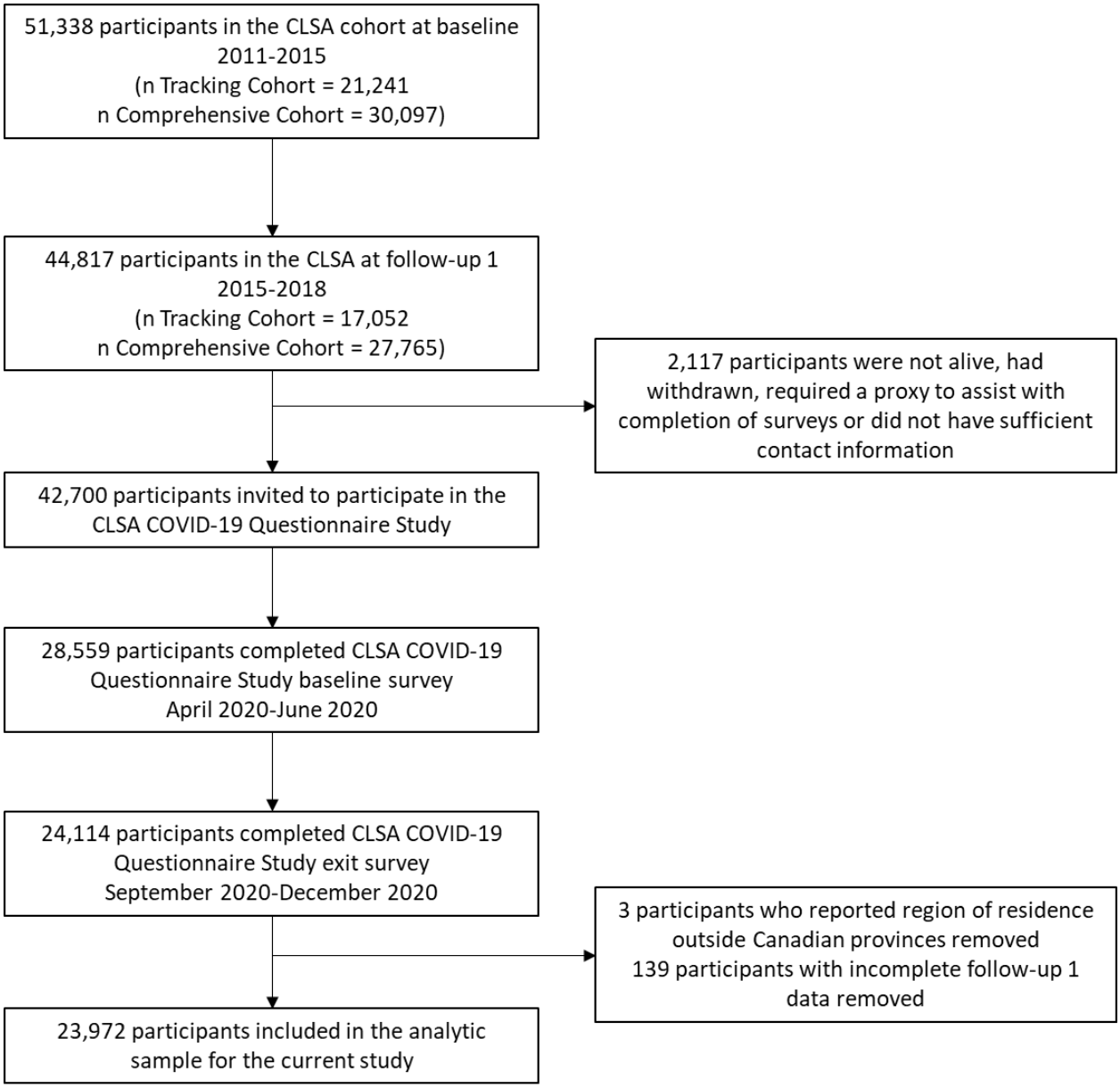

Figure 1. Flowchart of Canadian Longitudinal Study on Aging (CLSA) participants who completed CLSA COVID-19 Questionnaire Exit Survey (September-December 2020)

Consortia

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APPENDIX

Table A1. Unadjusted relative risks (RRs) and 95% confidence intervals (CIs) for the associations between adverse childhood experiences (ACEs), obesity and measures of stress during the COVID-19 pandemic among older adults in the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Questionnaire Exit Survey

	Stressor domains				**Total number of stressors**	**Perceived consequences of the pandemic**
	Health	**Resources**	**Relationships**	**Caregiving**		
	Unadjusted RR (95% CI)	Unadjusted RR (95% CI)	Unadjusted RR (95% CI)	Unadjusted RR (95% CI)	Unadjusted RR (95% CI)	Unadjusted RR (95% CI)
Number of ACEs						
0	1.00	1.00	1.00	1.00	1.00	1.00
1	1.18 (1.12, 1.24)	1.11 (1.05, 1.16)	1.09 (1.04, 1.13)	1.12 (1.04, 1.20)	1.11 (1.09, 1.15)	1.10 (1.03, 1.17)
2	1.25 (1.17, 1.32)	1.24 (1.17, 1.31)	1.15 (1.09, 1.21)	1.18 (108, 1.29)	1.20 (1.16, 1.24)	1.09 (1.01, 1.19)
3	1.42 (1.33, 1.52)	1.42 (1.33, 1.52)	1.21 (1.14, 1.28)	1.31 (1.1, 1.45)	1.33 (1.27, 1.38)	1.26 (1.14, 1.39)
4-8	1.51 (1.41, 1.61)	1.74 (1.64, 1.85)	1.36 (1.29, 1.44)	1.63 (1.48, 1.80)	1.53 (1.47, 1.59)	1.37 (1.24, 1.51)
Obesity						
Normal weight	1.00	1.00	1.00	1.00	1.00	1.00
Overweight	0.99 (0.94, 1.04)	1.02 (0.98, 1.08)	0.96 (0.92, 1.00)	0.93 (0.87, 1.00)	0.97 (0.95, 1.01)	0.98 (0.95, 1.00)
Obesity Class I	1.11 (1.05, 1.17)	1.22 (1.15, 1.29)	1.00 (0.95, 1.05)	0.96 (0.88, 1.05)	1.08 (1.04, 1.11)	0.97 0.94, 1.00)
Obesity Class II	1.15 (1.06, 1.25)	1.37 (1.27, 1.48)	1.03 (0.96, 1.10)	1.07 (0.95, 1.21)	1.15 (1.10, 1.21)	1.00 (0.96, 1.04)
Obesity Class III	1.32 (1.19, 1.46)	1.58 (1.43, 1.73)	1.09 (1.00, 1.19)	1.12 (0.95, 1.21)	1.27 (1.20, 1.35)	1.07 (1.01, 1.12)

CI: Confidence Intervals; RR: Relative risk

Table A2. Adjusted relative risks[1] (RRs) and 95% confidence Intervals (CIs) for the joint exposure of adverse childhood experiences (ACEs) and sex among Canadian adults in the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Questionnaire Exit Survey (September-December 2020) and effect modification on the additive and multiplicative scales

Health Domain					
	0 RR (95% CI)	1 RR (95% CI)	2 RR (95% CI)	3 RR (95% CI)	4-8 RR (95% CI)
Male	1.00	1.24 (1.15, 1.34); p<0.0001	1.23 (1.12, 1.35); p<0.0001	1.43 (1.28, 1.59); p<0.0001	1.46 (1.30, 1.59); p<0.0001
Female	1.20 (1.12, 1.29); p<0.0001	1.34 (1.23, 1.44); p<0.0001	1.46 (1.24, 1.59); p<0.0001	1.60 (1.45, 1.77); p<0.0001	1.62 (1.48, 1.78); p<0.0001
Additive (RERI) [2]	REF	-0.10 (-0.23, 0.03); p=0.12	0.03 (-0.13, 0.18); p=0.73	-0.03 (-0.23, 0.17); p=0.77	-0.04 (-0.25, 0.16); p=0.69
Multiplicative (RRR) [3]	REF	0.90 (0.81, 1.00); p=0.05	0.99 (0.87, 1.12); p=0.84	0.93 (0.81, 1.07); p=0.33	0.92 (0.80, 1.07); p=0.28
Resources Domain					
	0 RR (95% CI)	1 RR (95% CI)	2 RR (95% CI)	3 RR (95% CI)	4-8 RR (95% CI)
Male	1.00	1.07 (1.00, 1.16); p=0.06	1.17 (1.07, 1.27); p-0.0004	1.34 (1.21, 1.48); p<0.0001	1.63 (1.47, 1.80); p<0.0001
Female	0.99 (0.93, 1.06);	1.07 (1.00, 1.06); p=0.86	1.16 (1.06, 1.26); p=0.001	1.26 (1.15, 1.39); p<0.0001	1.46 (1.34, 1.58); p<0.0001
Additive (RERI)	REF	0.004 (-0.10, 0.11); p=0.94	-0.01 (-0.14, 0.13); p=0.93	-0.08 (-0.25, 0.09); p=0.38	-0.17 (-0.35, 0.02); p=0.08
Multiplicative (RRR)	REF	1.00 (0.91, 1.11); p=0.94	1.00 (0.88, 1.12); p=0.95	0.94 (0.82, 1.08); p=0.41	0.90 (0.79, 1.02); p=0.11
Relationships Domain					
	0 RR (95% CI)	1 RR (95% CI)	2 RR (95% CI)	3 RR (95% CI)	4-8 RR (95% CI)
Male	1.00	1.09 (1.02, 1.16); p=0.01	1.11 (1.03, 1.20); p=0.008	1.20 (1.09, 1.21); p=0.0002	1.29 (1.16, 1.42); p<0.0001
Female	1.30 (1.23, 1.38); p<0.0001	1.37 (1.29, 1.46); p<0.0001	1.43 (1.34, 1.54); p<0.0001	1.45 (1.34, 1.58); p<0.0001	1.59 (1.47, 1.71); p<0.0001
Additive (RERI)	REF	-0.02 (-0.12, 0.09); p=0.73	0.02 (-0.11, 0.14); p=0.77	-0.04 (-0.20, 0.11); p=0.60	0.002 (-0.16, 0.17); p=0.98
Multiplicative (RRR)	REF	0.97 (0.89, 1.06); p=0.47	0.99 (0.89, 1.10); p=0.84	0.93 (0.83, 1.06); p=0.28	0.95 (0.84, 1.07); p=0.41
Caregiving Domain					
	0 RR (95% CI)	1 RR (95% CI)	2 RR (95% CI)	3 RR (95% CI)	4-8 RR (95% CI)
Male	1.00	1.13 (1.00, 1.27); p=0.05	1.10 (0.95, 1.28); p=0.19	1.28 (1.08, 1.52); p=0.004	1.55 (1.30, 1.83); p<0.0001
Female	1.38 (1.24, 1.54); p<0.0001	1.47 (1.32, 1.65); p<0.0001	1.58 (1.39, 1.79); p<0.0001	1.63 (1.40, 1.88); p<0.0001	1.92 (1.68, 2.19) p<0.0001
Additive (RERI)	REF	-0.03 (-0.26, 0.18); p=0.75	0.09 (-0.15, 0.33); p=0.45	-0.04 (-0.34, 0.27); p=0.82	-0.01 (-0.33, 0.32); p=0.96
Multiplicative (RRR)	REF	0.95 (0.81, 1.11); p=0.49	1.03 (0.86, 1.25); p=0.73	0.92 (0.74, 1.15); p=0.45	0.90 (0.73, 1.11); p=0.31
Total number of stressors					

	0 RR (95% CI)	1 RR (95% CI)	2 RR (95% CI)	3 RR (95% CI)	4-8 RR (95% CI)
Male	1.00	1.12 (1.08, 1.17); p<0.0001	1.16 (1.10, 1.22); p<0.0001	1.31 (1.23, 1.39); p<0.0001	1.46 (1.37, 1.56); p<0.0001
Female	1.20 (1.15, 1.24); p<0.0001	1.29 (1.23, 1.34); p<0.0001	1.37 (1.31, 1.44); p<0.0001	1.45 (1.38, 1.54); p<0.0001	1.60 (1.52, 1.68) p<0.0001
Additive (RERI)	REF	0.01 (-0.04, 0.06); p=0.64	0.02 (-0.04, 0.08); p=0.48	-0.02 (-0.09, 0.06); p=0.68	-0.03 (-0.10, 0.05); p=0.47
Multiplicative (RRR)	REF	1.01 (0.96, 1.07); p=0.63	1.02 (0.96, 1.09); p=0.48	0.99 (0.92, 1.06); p=0.70	0.98 (0.91, 1.05); p=0.49
Perceived consequences of the pandemic					
	0 RR (95% CI)	1 RR (95% CI)	2 RR (95% CI)	3 RR (95% CI)	4-8 RR (95% CI)
Male	1.00	1.02 (0.98, 1.06); p=0.33	1.02 (0.97, 1.06); p=0.41	1.08 (1.02, 1.12); p=0.003	1.12 (1.06, 1.18); p<0.0001
Female	0.99 (0.96, 1.02); p=0.57	1.02 (0.98, 1.06); p=0.27	1.03 (0.98, 1.08); p=0.16	1.05 (1.00, 1.11); p=0.04	1.08 (1.03, 1.13); p=0.001
Additive (RERI)	REF	-0.03 (-0.10, 0.04); p=0.34	0.02 (-0.06, 0.11); p=0.62	-0.05 (-0.16, 0.06); p=0.38	-0.06 (-0.18, 0.05); p=0.28
Multiplicative (RRR)	REF	0.96 (0.90, 1.02); p=0.14	0.99 (0.93, 1.07); p=0.85	0.93 (0.86, 1.01); p=0.08	0.91 (0.84, 0.99); p=0.02

CI: Confidence Intervals; RR: Relative risk; REF: Reference

1. Adjusted for sex, age group, racial background, physical activity, household income, alcohol consumption and depression
2. Effect modification on the additive scale using Relative Excess Risk due to Interaction (RERI); Standard error calculated using the delta method [36–38]
3. Effect modification on the multiplicative scale using Ratio of Relative Risks (RRR)

Table A3. Adjusted relative risks[1] (RRs) and 95% confidence Intervals (CIs) for the joint exposure of obesity and sex among Canadian adults in the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Questionnaire Exit Survey (September-December 2020) and effect modification on the additive and multiplicative scales

Health Domain					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
Male	1.00	1.06 (0.98, 1.15); p=0.17	1.19 (1.08, 1.31); p=0.0003	1.09 (0.95, 1.26); p=0.21	1.47 (1.22, 1.76); p<0.0001
Female	1.21 (1.12, 1.32); p<0.0001	1.23 (1.13, 1.34); p<0.0001	1.33 (1.21, 1.46); p<0.0001	1.41 (1.26, 1.59); p<0.0001	1.42 (1.23, 1.63); p<0.0001
Additive (RERI) [2]	REF	-0.05 (-0.17, 0.07); p=0.45	-0.07 (-0.22, 0.07); p=0.32	0.11 (-0.10, 0.31); p=0.31	-0.27 (-0.59, 0.05); p=0.10
Multiplicative (RRR) [3]	REF	0.95 (0.86, 1.06); p=0.39	0.92 (0.81, 1.04); p=0.18	1.06 (0.89, 1.27); p=0.48	0.79 (0.63, 1.00); p=0.04
Resources Domain					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
Male	1.00	1.08 (1.00, 1.17); p=0.05	1.24 (1.14,1.36); p<0.0001	1.37 (1.21, 1.54); p<0.0001	1.60 (1.36, 1.88); p<0.0001
Female	1.04 (0.96, 1.13); p=0.03	1.08 (1.00, 1.17); p=0.05	1.23 (1.13, 1.35); p<0.0001	1.34 (1.20, 1.50); p<0.0001	1.34 (1.17, 1.52); p<0.0001
Additive (RERI)	REF	-0.04 (-0.15, 0.07); p=0.45	-0.05 (-0.19, 0.08); p=0.44	-0.07 (-0.27, 0.13); p=0.48	-0.31 (-0.61, -0.01); p=0.04
Multiplicative (RRR)	REF	0.96 (0.87, 1.06); p=0.44	0.95 (0.85, 1.07); p=0.40	0.94 (0.80, 1.10); p=0.42	0.80 (0.65, 0.98); p=0.03
Relationships Domain					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
Male	1.00	0.99 (0.93, 1.06); p=0.86	1.04 (.96, 1.12); p=0.34	0.99 (0.97, 1.11); p=0.82	1.13 (0.95, 1.34); p=0.16
Female	1.27 (1.19, 1.36); p<0.0001	1.30 (1.21, 1.39); p<0.0001	1.32 (1.22, 1.43); p<0.0001	1.35 (1.23, 1.49); p<0.0001	1.29 (1.14, 1.49); p<0.0001
Additive (RERI)	REF	0.03 (-0.07, 0.13); p=0.55	0.01 (-0.11, 0.13); p=0.87	0.09 (-0.07, 0.26); p=0.27	-0.12 (-0.36, 0.12); p=0.33
Multiplicative (RRR)	REF	1.02 (0.94, 1.12); p=0.58	1.00 (0.90, 1.11); p=0.98	1.08 (0.93, 1.25); p=0.33	0.89 (0.73, 1.10); p=0.27
Caregiving Domain					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
Male	1.00	1.06 (0.93, 1.21); p=0.38	1.15 (0.99, 1.33); p=0.06	1.13 (0.91, 1.40); p=0.26	1.50 (1.13, 1.97); p=0.004
Female	1.48 (1.30, 1.69); p<0.0001	1.47 (1.30, 1.67); p<0.0001	1.44 (1.25, 1.66); p<0.0001	1.65 (1.38, 1.96); p<0.0001	1.38 (1.10, 1.71), p=0.004
Additive (RERI)	REF	-0.06 (-0.26, 0.13); p=0.52	-0.19 (-0.43, 0.05); p=0.13	0.04 (-0.29, 0.38); p=0.80	-0.60 (-1.10, -0.09); p=0.02
Multiplicative (RRR)	REF	0.94 (0.80, 1.10); p=0.46	0.85 (0.70, 1.02); p=0.08	0.99 (0.76, 1.29); p=0.93	0.62 (0.44, 0.88) p=0.01

Total number of stressors					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
Male	1.00	1.04 (0.99, 1.09); p=0.09	1.15 (1.09, 1.21); p<0.0001	1.14 (1.05, 1.23); p=0.001	1.39 (1.24, 1.54); p<0.0001
Female	1.21 (1.16, 1.27); p<0.0001	1.24 (1.18, 1.30); p<0.0001	1.31 (1.24, 1.28); p<0.0001	1.39 (1.30, 1.49); p<0.0001	1.35 (1.24, 1.46); p<0.0001
Additive (RERI)	REF	-0.02 (-0.08, 0.05); p=0.59	-0.05 (-0.13, 0.03); p=0.25	0.04 (-0.07, 0.16); p=0.48	-0.25 (-0.43, -0.07); p=0.09
Multiplicative (RRR)	REF	0.98 (0.92, 1.04); p=0.48	0.94 (0.88, 1.02); p=0.10	1.01 (0.92, 1.11); p=0.86	0.80 (0.70, 0.91); p=0.0009
Perceived consequences of the pandemic					
	Normal weight RR (95% CI)	Overweight RR (95% CI)	Obesity class I RR (95% CI)	Obesity class II RR (95% CI)	Obesity class III RR (95% CI)
Male	1.00	0.96 (0.93, 1.00); p=0.05	0.96 (0.92, 1.00); p=0.10	0.99 (0.93, 1.06); p=0.86	1.14 (1.04, 1.22); p=0.002
Female	0.99 (0.95, 1.03); p=0.48	0.96 (0.93, 1.00); p=0.07	0.96 (.92, 1.00); p=0.09	0.99 (0.93, 1.05); p=0.74	1.00 (0.93, 1.07); p=0.92
Additive (RERI)	REF	0.02 (-0.03, 0.06); p=0.54	0.01 (-0.05, 0.07); p=0.74	0.01 (-0.07, 0.09); p=0.82	0.01 (-0.07, 0.09); p=0.82
Multiplicative (RRR)	REF	1.02 (0.97, 1.07); p=0.55	1.01 (0.95, 1.07); p=0.75	1.01 (0.93, 1.10); p=0.83	0.89 (0.80, 0.99); p=0.03

CI: Confidence Intervals; RR: Relative risk; REF: Reference

1. Adjusted for sex, age group, racial background, physical activity, household income, alcohol consumption and depression
2. Effect modification on the additive scale using Relative Excess Risk due to Interaction (RERI); Standard error calculated using the delta method [36–38]
3. Effect modification on the multiplicative scale using Ratio of Relative Risks (RRR)

Table A4. Sensitivity analysis exploring the association between maltreatment ACEs and measures of stress during the COVID-19 pandemic, and family dysfunction ACEs and measures of stress during the COVID-19 pandemic among older adults in the Canadian Longitudinal Study on Aging (CLSA) COVID-19 Questionnaire Exit Survey

	Stressor domains				Total number of stressors	Perceived consequences of the pandemic
	Health	**Resources**	**Relationships**	**Caregiving**		
	Adjusted RR (95% CI)[1]	Adjusted RR (95% CI)[1]	Adjusted RR (95% CI)[1]	Adjusted RR (95% CI)[1]	Adjusted RR (95% CI)[1]	Adjusted RR (95% CI)[1]
Number of maltreatment ACEs						
0	1.00	1.00	1.00	1.00	1.00	1.00
1	1.18 (1.11-1.24)	1.12 (1.06-1.17)	1.10 (1.06-1.15)	1.12 (1.04-1.21)	1.13 (1.10-1.16)	1.13 (1.06-1.22)
2	1.20 (1.12-1.28)	1.27 (1.19-1.35)	1.14 (1.08-1.20)	1.22 (1.11-1.33)	1.20 (1.15-1.24)	1.20 (1.10-1.32)
3	1.30 (1.20-1.40)	1.41 (1.31-1.52)	1.21 (1.14-1.29)	1.22 (1.09-1.36)	1.29 (1.23-1.34)	1.39 (1.25-1.56)
4	1.53 (1.36-1.71)	1.67 (1.49-1.84)	1.27 (1.15-1.40)	1.57 (1.34-1.83)	1.47 (1.38-1.57)	1.22 (1.02-1.46)
Number of family dysfunction ACEs						
0	1.00	1.00	1.00	1.00	1.00	1.00
1	1.12 (1.07-1.18)	1.09 (1.04-1.14)	1.05 (1.01-1.09)	1.13 (1.06-1.21)	1.09 (1.06-1.11)	1.03 (0.97-1.10)
2	1.23 (1.14-1.33)	1.23 (1.14-1.32)	1.15 (1.08-1.22)	1.15 (1.03-1.28)	1.19 (1.14-1.24)	1.06 (0.95-1.19)
3	1.36 (1.11-1.65)	1.39 (1.15-1.66)	1.15 (0.97-1.35)	1.63 (1.26-2.07)	1.33 (1.19-1.48)	1.17 (0.86-1.61)

CI: Confidence Intervals; RR: Relative risk

2. Adjusted for sex, age group, racial background, physical activity, household income, alcohol consumption and depression
3. Maltreatment ACEs include physical abuse, sexual abuse, emotional abuse, neglect, intimate partner violence
4. Family dysfunction ACEs include parental divorce/separation, living with a family member with mental health problems, death of a parent

Chapter 5: A longitudinal study evaluating adverse childhood experiences and obesity in adulthood using the Canadian Longitudinal Study on Aging (CLSA)

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Chapter 5 Summary

Adversity during childhood is a risk factor for obesity during adulthood, however, the mechanistic pathway to disease development is not understood. To develop targeted prevention strategies and interventions, understanding the pathway leading to obesity is needed. This study aimed to evaluate the association between ACEs and adulthood obesity, and to investigate mediation by nutrition. ACEs were strongly associated with obesity during adulthood, and although nutrition was not found to be a mediator, given the high prevalence of ACEs and obesity, and the established association, future research must continue to understand the pathway to disease development.

ABSTRACT

Introduction: Adverse childhood experiences (ACEs) are a risk factor for obesity; however, the causal mechanisms are not well understood. Objectives were to measure the impact of ACEs on adulthood obesity, and to investigate if the association was mediated by nutrition.

Methods: A longitudinal study was conducted using adults aged 46-90 years (n=26,615) from the Canadian Longitudinal Study on Aging (CLSA). Participants were asked to recall ACEs ≤18 years of age. Body mass index (BMI), waist circumference, and percent body fat were measured (2015-2018) and obesity was defined using standard cut-points. Nutrition was measured using data from the Short Diet Questionnaire. Multinomial logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for each obesity measure. Causal mediation methods were used to determine if nutrition was a mediator.

Results: There were 66% of adults who experienced one or more ACE. The odds of obesity defined by BMI and waist circumference increased in a dose-response manner with increasing number of ACEs (*p* trend <0.001). For instance, adults with 4-8 ACEs, compared to 0, had greater odds of obesity, defined by BMI (adjusted OR: 1.42; 95% CI: 1.21-1.67) and waist circumference (adjusted OR: 1.15; 95% CI: 1.02-1.31). There was no evidence of mediation by nutrition.

Conclusion: Adversity experienced in early life is strongly associated with obesity among Canadian adults. Further research is needed in identifying other mechanisms for this association to inform obesity prevention strategies.

Key Words: Adverse childhood experiences; Obesity; Nutrition; CLSA

KEY MESSAGES

- A high proportion of Canadian adults have experienced at least one adverse childhood experience, and have obesity defined by body mass index, waist circumference and percent body fat.
- People who reported 4-8 adverse childhood experiences have the greatest odds of obesity in adulthood defined by body mass index, waist circumference and percent body fat.
- No evidence was found that nutrition mediates the association between adverse childhood experiences and obesity, thus future research is needed to continue to explore this mechanistic pathway.

BACKGROUND

National data suggest that 27% of Canadians aged 18 years or older have obesity, which is about 7.3 million adults (1). Although body mass index (BMI) is typically used in epidemiologic research to measure obesity, other measures of adiposity, such as waist circumference and percent body fat may provide further information in terms of disease risk (2). Waist circumference provides an indication of excess fat that is located in the abdominal region, which may put an individual at greater risk of disease compared to fat that is located in other regions of the body. Similar to many chronic diseases, obesity has a long latency period. Therefore, it is important to understand the early life determinants for obesity and mechanisms across the life course to inform obesity prevention (4). Although numerous genes and epigenetic variations in multiple biologic pathways have been associated with obesity, environmental factors during early life are also critical, diseases signifying the importance of exploring early origins of obesity (5-7).

Adverse childhood experiences (ACEs) have a profound impact on disease risk across the life course (8-9). There are several possible frameworks that could explain how experiences in early life alter the body's functioning leading to development of diseases, including obesity (10-12). These include sensitive or critical periods of develop, chain of risk, or accumulation of risk (12). Systematic reviews have consistently reported that people with a history of adversity in childhood had 1.12-1.46 greater odds of developing obesity across the life course (13-16). It was noted that regardless of method of assessment and with either continuous or categorical assessment of body weight, the association between early life adversity and obesity remained (14). There has been a call

for future research to use large, population-based samples to further explore the association between ACEs and obesity, and to explore sex differences, as it has been found that females typically report more ACEs, but it is not clear how this impacts obesity development (13,17).

A recent systematic review exploring plausible mechanisms following exposure to ACEs to obesity development noted availability of data often limits the exploration of potential pathways to disease development (13). Expanding on the Developmental Origins of Health and Disease (DOHaD) framework may inform pathways to obesity development, as it hypothesizes disease development works through nutrition pathways (5,18). ACEs have been linked to changes in diet (19, 20), which is also linked to obesity (21,22), therefore making this a potential mediator. Thus, the objectives of this study were to evaluate the association between ACEs and obesity in adults aged 46-90 years in Canada and to investigate if the association between ACEs and obesity was mediated by nutrition using causal mediation methods. Sex differences were also examined.

METHODS

Study design and participants. A longitudinal was conducted study using data from the Canadian Longitudinal Study on Aging (CLSA). The CLSA has collected data on over 50,000 community dwelling adults from Canada. The complete description of the methodology of the CLSA can be found elsewhere (23). Briefly, participants were recruited using a population-based sampling strategy. People who resided in the 10

Canadian provinces, could complete interviews in either English or French, did not reside in an institution or on a Federal First Nations reserve, were not a full-time member of the Canadian Armed forces, and were cognitively able to participate on their own were eligible for inclusion. This study uses data collected at baseline (2011-2015) and follow-up 1 (2015-2018). The CLSA has two cohorts: the Tracking cohort (n=21,241) and the Comprehensive cohort (n=30,097), which vary in how data was collected. Only participants in the Comprehensive cohort were eligible for inclusion into this study, as they provided anthropometric measures to define obesity, as well as biomarkers which were used to generate the measure of stress. Ethics approval for the current study was obtained from the Hamilton Integrated Research Ethics Board (HiREB) on November 24th, 2020.

Measurement of adverse childhood experiences. At follow-up 1 (2015-2018), participants were asked to recall events that occurred before the age of 16 within their family related to physical abuse, sexual abuse, emotional abuse, neglect, and exposure to intimate partner violence. Participants were also asked if they experienced the death of a parent, parental divorce/separation or living with a family member with mental health problems before the age of 18. Questions asked were adapted from the Childhood Experience of Violence Questionnaire and the National Longitudinal Study of Adolescent to Adult Health Wave III questionnaire (24,25). The number of reported ACEs were summed to create a total ACEs variable, ranging from 0 to 8. This method has previously been used in the CLSA (26). Since relatively few people reported more than five ACEs, four or more ACEs were collapsed into one group.

Measurement of obesity. All obesity measures were taken by trained research assistants at follow-up 1 (2015-2018), who followed standardized protocols to ensure valid and reliable measurement (27,28). Participant's measured height and weight were used to calculate body mass index (kg/m^2). BMI was categorized using the World Health Organization (WHO) standard cut-offs for defining obesity (29,30): normal weight ($\leq$24.9 kg/m^2), overweight (25 to 29.9 kg/m^2) and obesity ($\geq$30 kg/m^2). A cut-off of $\geq$88 cm for females and $\geq$102 cm for males was used to define obesity by waist circumference. Participants' body fat (%BF) was measured using Hologic Discovery A Dual Energy X-Ray Absorptiometry (DXA) machines (31). Although there are no well-established cut points to define obesity using %BF, the WHO suggests using >35% for females and >25% for males (32).

Measurement of nutrition (mediator). To measure nutrition, the unhealthy diet score was derived using data from the CLSA Short Diet Questionnaire (SDQ) (33) at CLSA baseline (2011-2015). The unhealthy diet score was created based off a methodology from the Prospective Urban Rural Epidemiological (PURE) healthy diet score and has previously been applied to the CLSA data (34). Seven food groups (fruits, vegetables, legumes, nuts, fish, dairy, and meat), measured in the number of servings per day, were divided into quintiles based on the sample distribution. A cumulative score was created by adding the quintile of consumption for each food group, creating a score ranging from 0 to 28 (where 0 is the healthiest diet and 28 is the unhealthiest diet).

Measurement of other variables. Potential confounding variables included participant's age, sex, education level, racial background, household income, smoking status, and

alcohol intake. Participant's sex was categorized as male or female and age at follow-up 1 (2015-2018) was grouped into categories of 46-54, 55-64, 65-74, 75-90 years. At baseline, participants were asked to report their highest level of education, which was categorized into less than secondary school graduation, secondary school graduation, some post-secondary education or post-secondary degree or diploma, and racial background was categorized into white and other. At follow-up 1, data on household income (categorized as <$20,000, $20,000-$50,000, $50,000-$100,000, $100,000-150,000, ≥$150,000 CDN), smoking status (categorized as never, former, or current smoker), and alcohol intake (categorized as did not drink in the last 12 months, occasional drinker, and regular drinker (at least once a month) was collected.

STATISTICAL ANALYSIS

All statistical analyses were conducted using SAS 9.4. Multinomial logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Unadjusted and adjusted models (adjusted for age, sex, racial background, education, household income, smoking status, and alcohol intake) were run separately for all three obesity outcome measures. Models were also stratified by sex. Inflation weights were applied to descriptive analyses to account for sample misrepresentation, coverage error and non-response, which improved the overall precision of estimates (38). Analytic weights were used for regression analyses to ensure results represent the association among variables at the population-level, rather than the association between variables

within the selected sample (38). Complete case analysis was conducted as there was minimal missing data (no variable had >10% missing).

Causal mediation analysis was conducted following the principles outlined by VanderWeele (39,40). Exposure-mediator, mediator-outcome, and exposure-outcome confounders were identified to control potential biases and to meet the assumptions of causal mediation analysis (Figure 1). We allowed for exposure-mediator interaction in all models. PROC CAUSALMED was used to estimate the total effect, direct effect, and indirect effects. This procedure can not handle multicategory exposure or outcome variables (40). ACEs were dichotomized as (0-3 ACEs) vs (4-8 ACEs), this categorization was chosen as 4-8 ACEs has consistently been found to be associated with increased outcomes (8). Obesity was also dichotomized as no obesity ($\leq$29.9 kg/m^2) vs obesity ($\geq$30 kg/m^2). Separate mediation analyses were run for all three obesity outcomes (BMI, waist circumference and %BF). Unadjusted mediation analyses were run to ensure the fourth assumption (no mediator-outcome confounding that is influenced by the exposure) was not violated, as controlling for mediator-outcome confounders that are influenced by the exposure could hide mediation.

SENSITIVITY ANALYSIS

As a sensitivity analysis, we ran the unadjusted and adjusted associations between the exposure (ACEs) and mediators (nutrition and stress), and the mediators (nutrition and stress) and outcomes (obesity defined by BMI, waist circumference and %BF), to

explore the individual associations. We also conducted a sensitivity analysis to explore how the severity of ACEs influenced the association between ACEs and obesity, and the subsequent mediation analyses by creating a new ACEs score and rerunning the mediation analysis without parental separation/divorce. To determine the potential protective effect obesity has as people age (41), we removed those in the oldest age group (75-90 years).

RESULTS

This study included 26,615 participants from the CLSA at follow-up 1 (2011-2015) (Figure 2). Over 63% of participants reported one or more ACE (n=16,745) (Figure 3). A high proportion of people had obesity defined by BMI (31%), waist circumference (43%), and %BF (74%). A more detailed description of the included participants can be found in Table 1.

As the number of reported ACEs increased, the odds of obesity also increased for obesity defined by BMI and waist circumference, however, this pattern was not consistent for obesity defined by %BF. The *p* trend for obesity defined by BMI and waist circumference was p=0.001, indicating a dose-response association (Table 2). For all three obesity measures, people who reported 4-8 ACEs, compared to those who reported no ACEs, had the highest odds of obesity in adulthood defined by BMI (adjusted OR: 1.42; 95% CI: 1.21-1.67), waist circumference (adjusted OR: 1.15; 95% CI: 1.02-1.31) and %BF (adjusted OR: 1.17; 95% CI: 1.00-1.36) (Table 2). Adjustment for confounders

slightly attenuated the associations for BMI and waist circumference to the null, whereas for %BF some associations increased (unadjusted results are shown in Table 2).

When the results were stratified by sex, similar associations remained. For instance, males who reported 4-8 ACEs, compared to none, were 60% more likely to have obesity defined by BMI (adjusted OR: 1.60; 95% CI: 1.23-2.09), whereas females who reported 4-8 ACEs, compared to none, were 26% more likely to have obesity (adjusted OR: 1.26; 95% CI: 1.03-1.54) (Table 3). Similarly, obesity defined by waist circumference, the association was higher among males (adjusted OR: 1.18; 95% CI: 0.99-1.44) compared to females (adjusted OR: 1.12; 95% CI: 0.95-1.32) (Table 3). Whereas for %BF, females with 4-8 ACEs, compared to none, had higher odds of obesity (adjusted OR: 1.21; 95% CI: 0.98-1.49), compared to males with 4-8 ACEs compared to 0 (adjusted OR: 1.12; 95% CI: 0.89-1.40).

Mediation by nutrition

We did not find exposure-mediator interactions for any models; therefore, it can be assumed the controlled direct effect and natural direct effect were not different, and therefore, we only present the natural direct effect (Table 4). There was limited evidence of mediation by nutrition for obesity defined by BMI, waist circumference and %BF as all indirect effects were null and confidence intervals included one (Table 4). The percentage mediated also suggested limited mediation by nutrition as the percentage was close to zero with wide confidence intervals that included zero. Mediation analyses were

stratified by sex; however, results did not differ between males and females (results not shown). Unadjusted mediation analyses were similar to adjusted analyses suggesting violation of the 4th assumption was not a concern in this study (Table A2).

Sensitivity analysis

Results for all sensitivity analyses can be found in the Supplementary Information. Although we found an association between ACEs and nutrition (adjusted b= -0.32; 95% CI: -0.60- -0.05) (Table A3), we did not find an association between nutrition and all obesity outcomes (Table A4). Conversely, we did not find an association between ACEs and stress (Table A3), but we did, however, find an association between stress and all obesity outcomes (Table A4). The findings provide further evidence that suggests stress and nutrition are not mediators in the association between ACEs and obesity. Results of our sensitivity analysis evaluating the type of ACEs, suggest that both maltreatment ACEs and family dysfunction ACEs were associated with increased odds of obesity defined by each measure (Table A5). Removal of parental separation or divorce from the ACE score did not appear to change results (Table A6). Restricting the age of the sample to a younger group did not appear to change results (Table A7).

DISCUSSION

Consistent with previous research, the results of our study demonstrate a strong, dose-response association between ACEs and obesity in adults aged 46-90 years, however, our findings are novel given the use of multiple obesity measures taken by trained research assistants, rather than self-report. We found those who reported 4-8

ACEs had the greatest odds of obesity, which was consistent across all measures of obesity. When exploring factors that explained the association between ACEs and obesity, our study did not find evidence that nutrition mediated this association.

In our large population-based sample of 26,615 Canadian adults, two-thirds reported experiencing at least one ACE. This is similar to other estimates of population-based studies (42), which is concerning since ACEs are a known risk factors for several conditions (20). Given the public health impact of obesity, understanding risk factors in early life are important, leading to new strategies for obesity prevention or treatment (1). While, ACEs have consistently been shown to increase the risk of obesity, the pathways to disease development are understudied and not well understood (13, 14, 43). A recent systematic review evaluating associations between ACEs and adulthood obesity, identified few studies that specifically studied obesity as the outcome, none of which were conducted in the Canadian population (13). The most commonly cited explanations of this association included social disruption, health behaviours, chronic stress response and mental health (13). Another review that focused more broadly on adversity throughout childhood, obesity and binge eating disorder, found the most common pathways were depression, post-traumatic stress disorder (PTSD), interpersonal and neurobiological factors (11). There are several pathways that explain how adversity during childhood leads to obesity development, and it is possible these pathways are intertwined, meaning they work together after exposure to the development of obesity. For instance, there is some evidence on mediation through mental health, however, this was not explored in our study (44,45). It has been suggested that intervention strategies

should be aimed at different pathways of disease development following exposure to ACEs, which should be considered in the context of obesity development (26,46). It has been found that that nutrition explains the pathway between ACEs and the development of other diseases (26,46). Although we did not find this to be a mediator, it is still possible these could explain the development of obesity following ACEs, and null findings may be related to the timing of assessment or that these factors work in tandem with other pathways (e.g., mental health, lifestyle or health behaviours factors, interpersonal factors or neurobiological factors) (11,13). Future researchers who have access to different measures of nutrition may consider further exploring its role in this association, as well as studying multiple mediators along this pathway. The findings from this study still remain to be an important contribution to the literature as it has been noted there is limited availability of data to explore potential mechanistic pathways (13).

Similar to previous research, our study did find that females reported experiencing more adverse experiences, compared to males (17). However, when evaluating the impact ACEs has on outcomes later in life, stronger associations have been found with other outcomes including PTSD (17), multimorbidity (26) among females. This is consistent with our findings for obesity defined by %BF but not obesity defined by BMI or waist circumference. The differences in outcome development across males versus females may be related to how ACEs are biologically embedded, and what physiological changes occur following adversity which may predispose someone to have an increased risk of disease development, including obesity (47).

There are several strengths of our study including the large population-based sample and the use of longitudinal data. This study also is one of the first to use objective measures of obesity rather than self-report on a large sample, including the assessment of body fatness using DXA scans. The use of mediation methodologies is also a strength of this study as it has been noted that there are biases associated with more traditional approaches, for instance, the inability to control for exposure-outcome and mediator-outcome confounders (48). Limitations of this study include the lack of ethnic diversity which limits the ability to generalize results. Temporality is a requirement for causal mediation, in our study ACEs were specific to experiences that occurred before the age of 18, and measurements of nutrition and obesity were prospectively collected later in adulthood; however, ACEs were based on self-reported recall and we can not exclude the possibility that the temporality assumption could have been violated by recall bias. Yet, previous studies have reported that ACEs can be recalled in later adulthood accurately (49). In addition, people with obesity and ACEs may have differentially participated in our study, therefore potentially introducing selection bias in this study. Assessment of nutrition was taken relatively close to when obesity measures were taken potentially limiting the ability to identify them as mediators. Future research may consider assessment of nutrition earlier in life, or assessment at different time points allowing for a multiple mediation analysis to be conducted since it is possible that the development of obesity following exposure to ACEs occurs through multiple pathways. We defined obesity using standard cut-offs for BMI, waist circumference, and %BF, however, these cut-offs have been noted to be vary across different samples or groups of people (50). For

instance, there is limited consensus on a standard cut-off to define obesity using %BF (32). For this current study, we identified a cut-off that is often used in research (32, 51, 52) since there is no established cut-off from the WHO, however, this may be a potentially liberal cut-off, which would explain the high prevalence of obesity defined by %BF found in our study. Continued research on cut-offs to define obesity is needed, as this may improve obesity prevention and interventions. Although we controlled for exposure-mediator, mediator-outcome, and exposure-mediator confounders, it is possible there is residual confounding, which could potentially bias findings as the assumptions of causal mediation may be violated (53). However, unmeasured exposure-mediator confounding, and unmeasured mediators are only a concern if exposure-mediator interaction is present, which was not in our study (40,53).

ACEs dramatically influence obesity later in life, whereby the more ACEs a person had experienced, the greater the risk of obesity in later life. Although we did not find evidence to support the role of nutrition as a mediator along the pathway to disease development, these findings can be used to inform future research questions or hypotheses to possible plausible mechanisms. Understanding the pathway to obesity development following ACEs is critical to inform strategies to identify people at a greater risk of disease later in life, allowing for potential interventions. Although adversity may occur very early on in life, it is apparent the detrimental effects last beyond childhood, contributing to negative outcomes later in life.

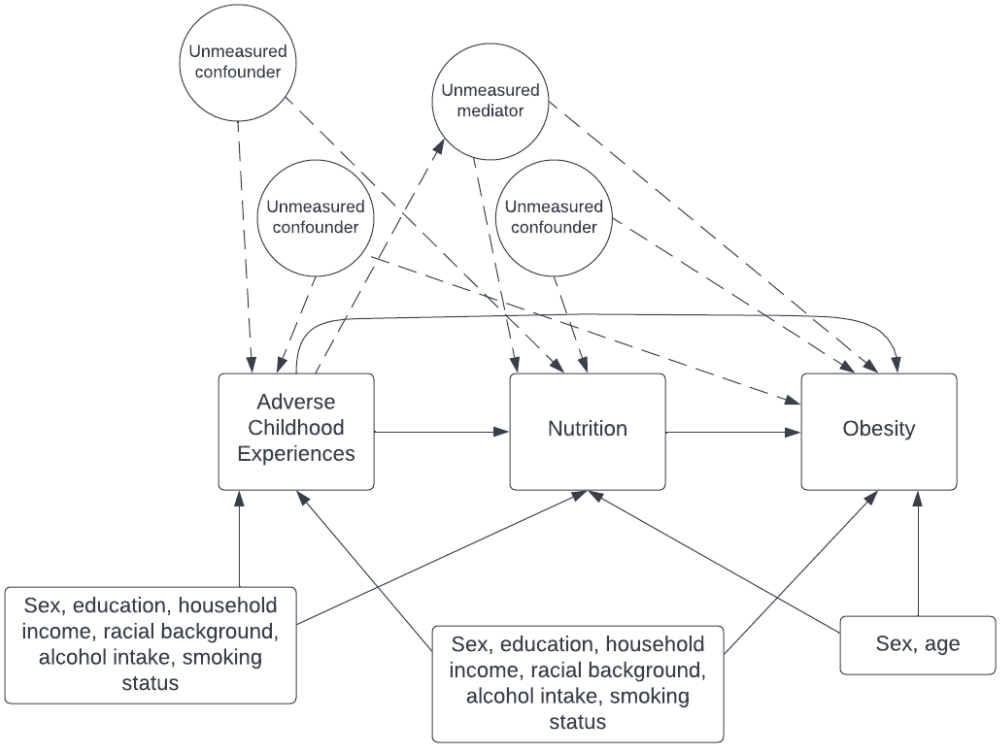

Figure 1. Directed Acyclic Graph (DAG) for the association between ACEs and obesity among adults in the Canadian Longitudinal Study (CLSA) mediated by nutrition while controlling for all known and unknown confounding variables

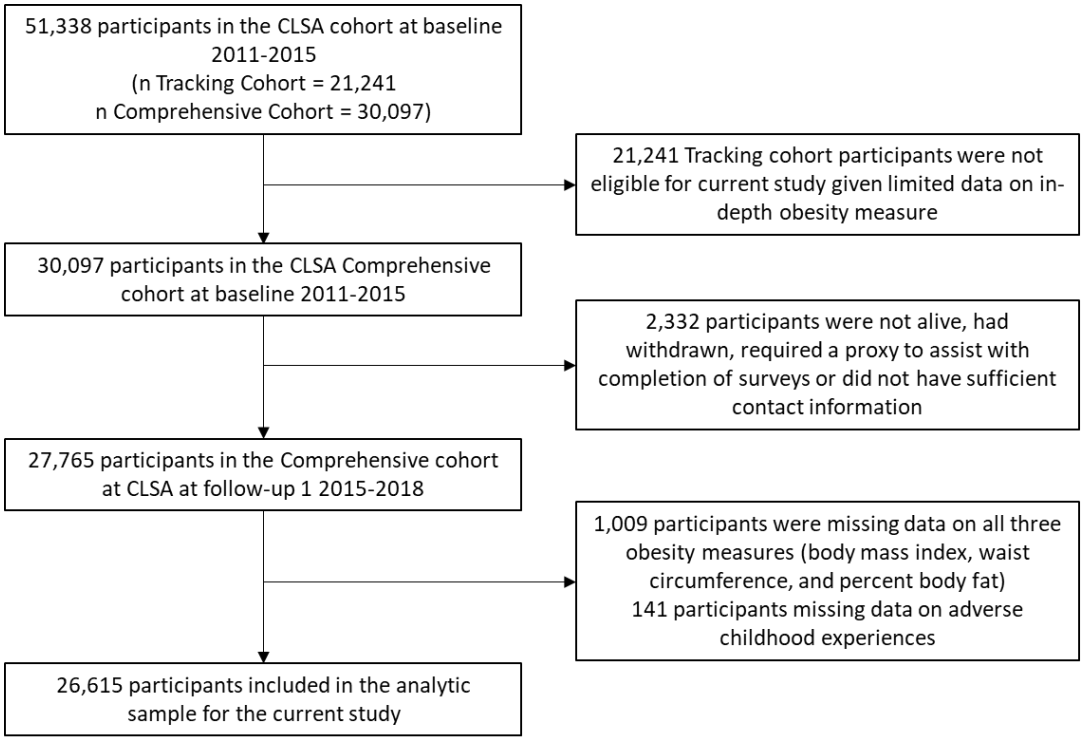

Figure 2. Description of analytic sample from the Canadian Longitudinal Study on Aging (n=26,615)

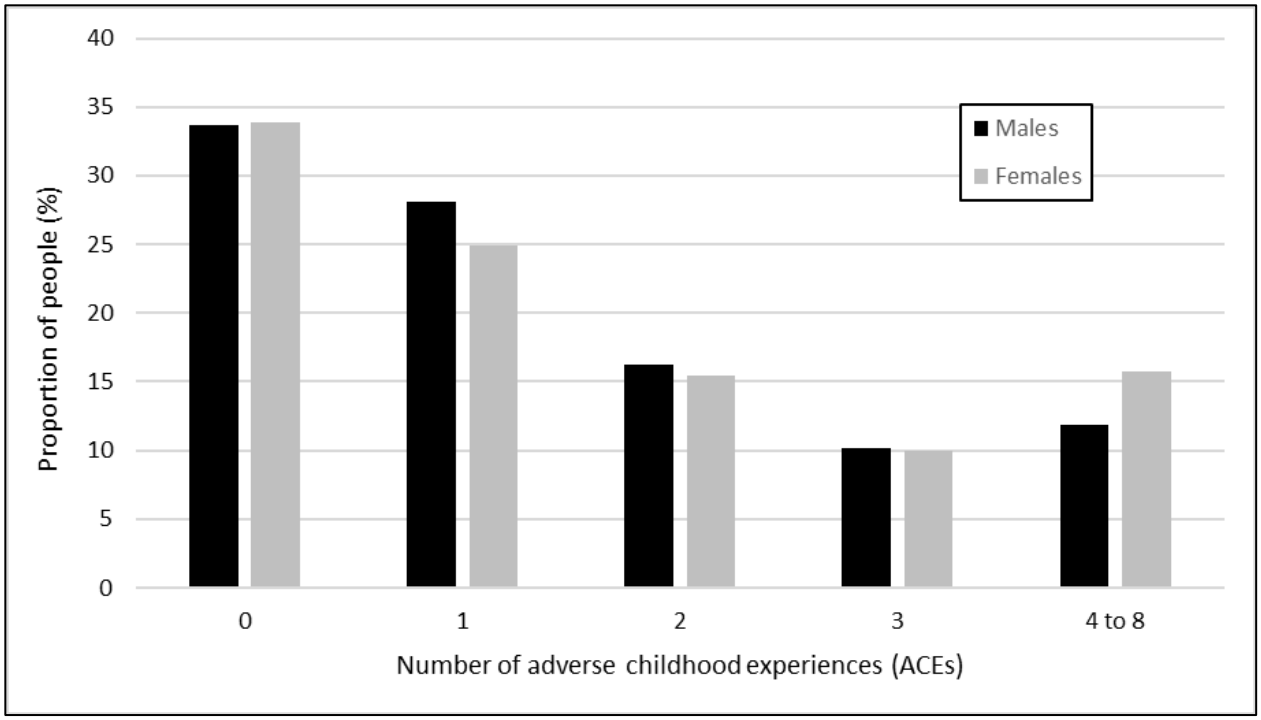

Figure 3. Proportion of adverse childhood experiences (ACEs) index among Canadian adults within the Canadian Longitudinal Study on Aging (CLSA) by sex at CLSA Follow-up 1 (2015-2018)

Table 1. Characteristics of participants from the Canadian Longitudinal Study on Aging (CLSA) at CLSA follow-up 1 (2015-2018) (n=26,615)

Characteristics	**Total %**	**Male %**	**Female %**
Age group[1]			
46-54	27.6	28.5	26.8
55-64	34.8	35.5	34.2
65-74	23.7	23.3	24.1
75-90	13.8	12.7	14.9
Education[1]			
Less than secondary school	15.3	14.9	15.6
Secondary school graduation	11.2	10.3	11.9
Some post-secondary education	9.2	9.2	9.2
Post-secondary degree or diploma	64.3	65.5	63.2
Alcohol intake[1]			
Did not drink in the last 12 months	13.3	11.8	14.6
Occasional drinker	12.6	8.8	15.9
Regular drinker (at least once a month)	74.2	79.4	69.5
Smoking[1]			
Never	9.8	10.1	9.5
Former	47.3	44.3	50.0
Current	42.9	45.6	40.5
Racial background[2]			
White	94.5	93.9	94.9
Other	5.5	6.1	5.1
Household income[1]			
<$20,00	5.1	3.7	6.5
$20,000-$50,000	20.6	16.9	24.0
$50,000-$100,000	34.4	34.9	33.8
$100,000-150,000	20.9	22.3	19.6
≥$150,000	19.0	21.2	16.0
Mediator	**Total mean (SD)**	**Male mean (SD)**	**Female mean (SD)**
Unhealthy score[2]	14.5 (0.06)	15.3 (0.09)	13.7 (0.08)
Outcomes	**Total %**	**Male %**	**Female %**
BMI[1]			
Normal (≤24.9 kg/m^2)	29.9	23.5	35.7
Overweight (25 to 29.9 kg/m^2)	38.8	44.9	33.3
Obesity (≥30 kg/m^2)	31.3	31.6	31.0
Waist Circumference[1]			
No obesity (<88 cm for females and <102cm for males)	56.1	58.5	53.9
Obesity (≥88 cm for females and ≥102 cm for males)	43.0	41.5	46.1
Percent body fat			
No obesity (≤35% for females and ≤25% for males)	26.4	29.6	23.5
Obesity (>35% for females and >25% for males)	73.6	70.4	76.5

1. Data collected at CLSA Follow-up 1 (2015-2018)
2. Data collected at CLSA Baseline (2011-2015)

Table 2. Associations between adverse childhood experiences (ACEs) and adulthood obesity, defined by body mass index (BMI) (kg/m^2), waist circumference (cm) and precent body fat (%BF) among adults in the Canadian Longitudinal Study on Aging (CLSA)

	Overall Unadjusted OR (95% CI)		Overall Adjusted OR[1] (95% CI)	
Body mass index[2]	**Overweight (25 to 29.9 kg/m^2)**	**Obesity (≥30 kg/m^2)**	**Overweight (25 to 29.9 kg/m^2)**	**Obesity (≥30 kg/m^2)**
ACEs				
0	1.00	1.00	1.00	1.00
1	0.99 (0.90-1.10)	1.06 (0.95-1.18)	0.99 (0.89-1.10)	1.07 (0.95-1.20)
2	1.03 (0.91-1.17)	1.24 (1.08-1.42)	1.04 (0.92-1.20)	1.19 (1.03-1.37)
3	0.96 (0.82-1.11)	1.24 (1.06-1.45)	1.03 (0.88-1.20)	1.21 (1.03-1.43)
4-8	0.95 (0.82-1.10)	1.50 (1.28-1.75)	1.04 (0.89-1.21)	1.42 (1.21-1.67)
p trend	<.0001			
Waist circumference[3]	**Obesity (≥88 cm for females and ≥102 cm for males)**		**Obesity (≥88 cm for females and ≥102 cm for males)**	
ACEs				
0	1.00		1.00	
1	0.97 (0.89-1.06)		0.97 (0.89-1.06)	
2	1.08 (0.97-1.21)		1.06 (0.95-1.19)	
3	1.08 (0.95-1.22)		1.08 (0.95-1.24)	
4-8	1.25 (1.11-1.42)		1.15 (1.02-1.31)	
p trend	<.0001			
Percent Body Fat[4]	**Obesity (>35% for females and >25% for males)**		**Obesity (>35% for females and >25% for males)**	
ACEs				
0	1.00		1.00	
1	1.02 (0.92-1.13)		1.04 (0.94-1.16)	
2	1.05 (0.922-1.20)		1.10 (0.96-1.26)	
3	0.84 (0.72-0.98)		0.91 (0.77-1.07)	
4-8	1.13 (0.97-1.31)		1.17 (1.00-1.36)	
p trend	0.2898			

1. Adjusted for age, sex, racial background, education, household income, smoking status and alcohol intake
2. Reference group: Normal weight (≤24.9 kg/m^2)
3. Reference group: No obesity (<88 cm for females and <102cm for males)
4. Reference group: No obesity (≤35% for females and ≤25% for males)

Table 3. Adjusted[1] associations between adverse childhood experiences (ACEs) and adulthood obesity, defined by body mass index (BMI) (kg/m^2), waist circumference (cm) and precent body fat (%BF) among adults in the Canadian Longitudinal Study on Aging (CLSA) stratified by sex

	Males Adjusted OR (95% CI)		Females Adjusted OR (95% CI)		p-value for interaction	
Body mass index[2]	**Overweight (25 to 29.9 kg/m^2)**	**Obesity (≥30 kg/m^2)**	**Overweight (25 to 29.9 kg/m^2)**	**Obesity (≥30 kg/m^2)**	**Overweight (25 to 29.9 kg/m^2)**	**Obesity (≥30 kg/m^2)**
ACEs						
0	1.00	1.00	1.00	1.00		
1	0.90 (0.77-1.05)	1.09 (0.92-1.30)	1.11 (0.96-1.29)	1.03 (0.89-1.21)	0.0133	0.2896
2	1.14 (0.93-1.40)	1.43 (1.14-1.79)	1.00 (0.84-1.19)	1.03 (0.85-1.24)	0.1218	0.0707
3	1.04 (0.82-1.33)	1.25 (0.97-1.62)	1.01 (0.82-1.24)	1.17 (0.94-1.45)	0.5310	0.7453
4-8	1.01 (0.79-1.29)	1.60 (1.23-2.09)	1.08 (0.88-1.31)	1.26 (1.03-1.54)	0.6537	0.4804
Waist circumference[3]	**Obesity (≥102 cm)**		**Obesity (≥88 cm)**		p-value for interaction	
ACEs						
0	1.00		1.00			
1	0.98 (0.86-1.12)		0.97 (0.85-1.10)		0.4062	
2	1.22 (1.03-1.43)		0.93 (0.80-1.08)		0.0158	
3	1.09 (0.90-1.32)		1.08 (0.91-1.29)		0.5918	
4-8	1.18 (0.97-1.44)		1.12 (0.95-1.32)		0.8376	
Percent Body Fat[4]	**Obesity (>25%)**		**Obesity (>35%)**		p-value for interaction	
ACEs						
0	1.00		1.00			
1	1.08 (0.93-1.26)		1.01 (0.86-1.19)		0.2644	
2	1.12 (0.92-1.37)		1.07 (0.88-1.29)		0.4717	
3	0.85 (.68-1.07)		0.97 (0.77-1.22)		0.3928	
4-8	1.12 (0.89-1.40)		1.21 (0.98-1.49)		0.4601	

1. Adjusted for age, racial background, education, household income, smoking status and alcohol intake
2. Reference group: Normal weight (≤24.9 kg/m^2)
3. Reference group: No obesity (<88 cm for females and <102cm for males)
4. Reference group: No obesity (≤35% for females and ≤25% for males)

Table 4. Total, direct, and indirect effects for the association between adverse childhood experiences (ACEs) and obesity defined by body mass index (BMI) (kg/m^2), waist circumference (cm) and percent body fat (%) mediated by nutrition among adults from the Canadian Longitudinal Study on Aging (CLSA)[1]

	Total Effect OR (95%CI)	Natural direct effect OR (95% CI)	Natural indirect effect OR (95% CI)	Percent Mediated
BMI				
Mediator: Nutrition[2]	1.29 (1.18-1.40)	1.30 (1.19-1.41)	0.99 (0.99-1.00)	-2.42 (-5.18-0.33)
Waist circumference				
Mediator: Nutrition[2]	1.21 (1.11-1.31)	1.21 (1.11-1.32)	1.00 (0.99-1.00)	-2.51 (-6.15-1.13)
Percent body fat				
Mediator: Nutrition[2]	1.14 (1.02-1.26)	1.16 (1.04-1.28)	0.99 (0.98-1.00)	-10.86 (-21.82-0.10)

1. All outcomes are binary (obesity vs no obesity), where no obesity is the reference group
2. Nutrition measured using the unhealthy diet score (range: 0 to 28; where 0 is the lowest healthiest diet and 28 is the unhealthiest diet).

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Supplementary Information

Table A1. Unadjusted associations between adverse childhood experiences (ACEs) and adulthood obesity, defined by body mass index (BMI) (kg/m^2), waist circumference (cm), and percent body fat (%) overall and stratified by sex

	Males OR (95% CI)		Females OR (95% CI)	
Body mass index[1]	**Overweight (25 to 29.9 kg/m^2)**	**Obesity (≥30 kg/m^2)**	**Overweight (25 to 29.9 kg/m^2)**	**Obesity (≥30 kg/m^2)**
ACEs				
0	1.00	1.00	1.00	1.00
1	0.88 (0.76-1.03)	1.10 (0.93-1.30)	1.10 (0.96-1.26)	0.99 (0.85-1.15)
2	1.10 (0.91-1.34)	1.10 (0.91-1.34)	1.00 (0.85-1.17)	1.09 (0.91-1.31)
3	0.99 (0.78-1.25)	1.36 (1.07-1.73)	0.92 (0.76-1.13)	1.15 (0.93-1.40)
4-8	0.93 (0.73-1.14)	1.73 (1.33-2.25)	1.08 (0.90-1.31)	1.41 (1.17-1.71)
Waist circumference[2]	**Obesity (≥102 cm)**		**Obesity (≥88 cm)**	
ACEs				
0	1.00		1.00	
1	0.89 (0.87-1.12)		0.96 (0.85-1.09)	
2	1.20 (1.03-1.41)		0.99 (0.85-1.14)	
3	1.10 (0.91-1.33)		1.06 (0.89-1.25)	
4-8	1.24 (1.02-1.52)		1.22 (1.04-1.43)	
Percent Body Fat[3]	**Obesity (>25%)**		**Obesity (>35%)**	
ACEs				
0	1.00		1.00	
1	1.06 (0.92-1.23)		0.99 (0.85-1.15)	
2	1.04 (0.86-1.26)		1.06 (0.89-1.27)	
3	0.81 (0.64-1.01)		0.88 (0.72-1.09)	
4-8	1.01 (0.81-1.27)		1.18 (0.97-1.44)	

1. Reference group: Normal weight (≤24.9 kg/m^2)
2. Reference group: No obesity (<88 cm for females and <102cm for males)
3. Reference group: No obesity (≤35% for females and ≤25% for males)

Table A2. Unadjusted total, direct, and indirect effects for the association between adverse childhood experiences (ACEs) and obesity defined by body mass index (BMI) (kg/m^2), waist circumference (cm) and percent body fat (%) mediated by nutrition among adults from the Canadian Longitudinal Study on Aging (CLSA)[1]

	Total Effect OR (95%CI)	Natural direct effect OR (95% CI)	Natural indirect effect OR (95% CI)	Percent Mediated
BMI				
Mediator: Nutrition[2]	1.44 (1.33-1.56)	1.45 (1.34-1.56)	1.00 (1.00-1.00)	-0.30 (-1.71-1.09)
Waist circumference				
Mediator: Nutrition[2]	1.28 (1.18-1.39)	1.28 (1.18-1.39)	1.00 (1.00-1.00)	-0.60 (-1.96-0.76)
Percent body fat				
Mediator: Nutrition[2]	1.15 (1.03-1.26)	1.15 (1.04-1.26)	1.00 (0.98-1.00)	-2.76 (-9.57-4.06)

1. All outcomes are binary (obesity vs no obesity), where no obesity is the reference group
2. Nutrition measured using the unhealthy diet score (range: 0 to 28; where 0 is the lowest healthiest diet and 28 is the unhealthiest diet).

Table A3. Unadjusted and adjusted associations between exposure, ACEs, and mediator, nutrition.

	Nutrition (Unhealthy diet score)	
	Unadjusted b (95% CI)	Adjusted[1] b (95% CI)
ACEs		
0-3	1.00	1.00
4-8	0.02 (-0.26-0.30)	-0.32 (-0.60- -0.05)

1. Adjusted for sex, age, racial background, education, household income, smoking status and alcohol intake

Table A4. Associations between mediator, nutrition, and outcomes[1]

	Obesity defined by BMI		Obesity defined by waist circumference		Obesity defined by perfect body fat	
	Unadjusted OR (95% CI)	Adjusted[2] OR (95% CI)	Unadjusted OR (95% CI)	Adjusted[2] OR (95% CI)	Unadjusted OR (95% CI)	Adjusted[2] OR (95% CI)
Nutrition (Unhealthy diet score)	1.03 (1.03-1.04)	1.02 (1.01-1.03)	1.03 (1.02-1.04)	1.03 (1.02-1.03)	1.04 (1.03-1.05)	1.04 (1.03-1.05)

1. All outcomes are binary (obesity vs no obesity), where no obesity is the reference group
2. Adjusted for sex, age, racial background, education, household income, smoking status and alcohol intake

Table A5. Sensitivity analysis exploring severity of ACEs, with two ACEs scores 1) maltreatment (physical abuse, sexual abuse, emotional abuse, neglect, intimate partner violence) 2) family dysfunction (parental divorce/separation or living with a family member with mental health problems, death of a parent). Adjusted associations between ACEs scores and obesity (measured by BMI, waist circumference and percent body fat)

	Obesity defined by BMI[1] Adjusted OR[2] (95% CI)	Obesity defined by waist circumference[1] Adjusted OR[2] (95% CI)	Obesity defined by percent body fat[1] Adjusted OR[2] (95% CI)
Maltreatment ACEs[3,5]			
0	1.00	1.00	1.00
1	1.07 (0.97-1.18)	0.97 (0.89-1.07)	1.06 (0.95-1.19)
2	1.13 (1.00-1.28)	1.06 (0.95-1.19)	0.94 (0.82-1.08)
3	1.30 (1.13-1.50)	1.04 (0.91-1.19)	1.14 (0.96-1.34)
4	1.33 (1.08-1.63)	1.22 (0.99-1.49)	1.16 (0.90-1.48)
5	1.78 (1.18-1.51)	1.67 (1.09-2.56)	1.36 (0.78-2.37)
Family dysfunction ACEs[4,5]			
0	1.00	1.00	1.00
1	1.16 (1.07-1.27)	1.07 (0.99-1.16)	1.10 (1.00-1.22)
2	1.15 (0.99-1.34)	1.11 (0.97-1.28)	0.95 (0.80-1.12)
3	1.17 (0.81-1.69)	1.26 (0.87-1.82)	1.12 (0.73-1.71)

1. All outcomes are binary (obesity vs no obesity), where no obesity is the reference group
2. Adjusted for sex, age, racial background, education, household income, smoking status and alcohol intake
3. Range from 0 to 5 (5 ACEs: physical abuse, sexual abuse, emotional abuse, neglect, intimate partner violence)
4. Range from 0 to 3 (3 ACEs: parental divorce/separation or living with a family member with mental health problems, death of a parent)
5. Cut-off was not applied since severe ACE score and Less severe ACE score have different ranges

Table A6. Sensitivity analysis exploring potential mediator, nutrition, for the association between ACEs and obesity[1] (defined by BMI, waist circumference, and %BF), with parental separation/divorce removed from the ACEs score[2,3]

	Total Effect OR (95%CI)	Natural direct effect OR (95% CI)	Natural indirect effect OR (95% CI)	Percent Mediated
BMI				
Mediator: Nutrition[4]	1.34 (1.22-1.47)	1.36 (1.23-1.48)	0.99 (0.99-1.00)	-2.48 (-0.02-0.001)
Waist circumference				
Mediator: Nutrition[4]	1.26 (1.14-1.37)	1.27 (1.15-1.38)	0.99 (0.99-1.00)	-4.40 (-7.56- -1.25)
Percent body fat				
Mediator: Nutrition[4]	1.13 (1.00-1.26)	1.13 (1.00-1.26)	1.00 (0.99-1.00)	-3.62 (-11.53-4.28)

1. All outcomes are binary (obesity vs no obesity), where no obesity is the reference group
2. ACE score for sensitivity analysis ranges from 0 to 7, since parental separation/divorce has been removed
3. Adjusted for sex, age, racial background, education, household income, smoking status and alcohol intake
4. Nutrition measured using the unhealthy diet score (range: 0 to 28; where 0 is the lowest healthiest diet and 28 is the unhealthiest diet).

Table A7. Sensitivity analysis exploring if nutrition is a mediator for the association between ACEs and obesity[1] (defined by BMI, waist circumference, and %BF), with people aged 75-90 years of age removed[2]

	Total Effect OR (95%CI)	Natural direct effect OR (95% CI)	Natural indirect effect OR (95% CI)	Percent Mediated
BMI				
Mediator: Nutrition[3]	1.29 (1.17-1.40)	1.29 (1.18-1.41)	0.99 (0.99-1.00)	-2.52 (-5.51-0.47)
Waist circumference				
Mediator: Nutrition[3]	1.19 (1.08-1.29)	1.19 (1.09-1.30)	1.00 (0.99-1.00)	-3.22 (-7.68-1.24)
Percent body fat				
Mediator: Nutrition[3]	1.10 (0.98-1.21)	1.10 (0.98-1.22)	0.99 (0.99-1.00)	-5.90 (-16.66-4.85)

1. All outcomes are binary (obesity vs no obesity), where no obesity is the reference group
2. Adjusted for sex, age, racial background, education, household income, smoking status and alcohol intake
3. Nutrition measured using the unhealthy diet score (range: 0 to 28; where 0 is the lowest healthiest diet and 28 is the unhealthiest diet)

Chapter 6. Conclusion

Overview

This thesis explored the complex relationships between stress and obesity across the life course using four unique objectives while applying novel epidemiologic methodologies. Findings from this thesis suggest that regardless of the type of stress and at which point of the life course a person is exposed, it is likely that it will influence obesity development, and obesity also influences experiences of stress. The findings also suggest that specific groups of people may be more susceptible to worse experiences, and this may be related to adversity during childhood, chronic diseases, including obesity, or other sociodemographic characteristics. This concluding chapter highlights the key conclusions of this thesis, a comparison to existing frameworks, methodological contributions, future research, and conclusions.

Key conclusions

Chapter 1 introduced obesity and stress, specifically focusing on two examples of stress: ACEs and the COVID-19 pandemic, and the complex relationship obesity and stress share. More specifically, a literature review was conducted on previous research highlighting the prevalence and burden of obesity, measurement of obesity, the prevalence and burden of ACEs and the COVID-19 pandemic, measurement of stress, and how stress (ACEs and the COVID-19 pandemic) and obesity are interrelated. Chapter 2 is a systematic review that contributed to our understanding of the impact of disasters, including pandemics, on cardiometabolic risk and more specifically obesity. The review

found that regardless of the type of disaster, implications extend beyond the direct harms, and it is evident exposure to disasters affects the future risk of obesity. It was also apparent literature did not explore the mechanisms behind this association, or subgroups who were at the greatest risk. Chapter 3 aimed to determine variation in stress experienced during the COVID-19 pandemic, which found differences existed on several sociodemographic characteristics. For instance, females and adults aged 50-64 reported experiencing more stressors and perceived the consequences of the pandemic as negative. Chapter 4 aimed to explore if people with ACEs and obesity were more susceptible to different experiences during the COVID-19 pandemic, and to determine if ACEs exacerbated the association between obesity and stress during the pandemic. People with obesity were more likely to experience stress, and although we did not find ACEs to modify this association, we did find that ACEs also independently increased stress during the pandemic. Chapter 5 used a life course perspective to understand how ACEs impact adulthood obesity and the mechanistic pathway behind this association. This study found that people who experienced ACEs were more likely to have obesity in adulthood, and although nutrition was not found to be a mediator, the findings still indicate the importance of further exploration of the pathway to disease development as ACEs were found to increase the odds of the most severe type of obesity.

Comparison to existing frameworks

This thesis builds on the current literature aiming to understand the complex relationship shared between obesity and stress. The framework (Thesis Figure 1) proposed by van der

Valk et al., states that obesity and stress are constantly impacting each other (1), which is consistent with the findings of this thesis. This framework was created before the COVID-19 pandemic but can still inform the interrelatedness of stress and obesity in the context of the pandemic. This framework suggested mediation by glucocorticoid activation, meaning the release of cortisol in response to a stress stimuli, however, this thesis was unable to measure this (1). Rather, mediation by nutrition was evaluated. The lack of mediation may be related to methodologic limitations or the timing of measurement. As suggested, there are several potential pathways to obesity development (49,71), the findings from this thesis can be used to inform future hypotheses about other potential pathways, at different periods throughout the life course.

Another important framework that informed this thesis was the life course epidemiology framework (53). Life course epidemiology is defined as "*the study of long term effects on later health or disease risk of physical or social exposures during gestation, childhood, adolescence, young adulthood and later adult life*" (53). This framework also outlines the different pathways to disease development, including biological, psychological or social (72). This framework is commonly applied when exploring metabolic conditions including obesity, cardiovascular disease, mental health, socioeconomic outcomes or behavioural outcomes (73). Within the life course epidemiology framework, different theoretical models are applied to better understand how a disease may develop. Examples include accumulation of risk, chains of risk model, or the critical period model. This thesis was unable to evaluate or identify the exact model which explains the findings across the chapters, but the concept applied by each of these models and overall by the

life course epidemiology framework was evident throughout the thesis as the effects of ACEs influence both adulthood obesity and experiences during the pandemic (74). The methodologies used in this thesis can be used by future research that plan to apply or study a research question that is framed or designed following the life course epidemiology framework.

Methodological contributions

This thesis applied several epidemiologic study designs including a systematic review, cross-sectional study, and cohort study to answer both descriptive and analytic research questions. Further, this thesis applied epidemiologic and statistical methods including longitudinal analysis of big data, effect measure modification, and causal mediation methods. The variation in methodologies used allowed for unique questions to be answered. The systematic review allowed us to identify all relevant literature on the impact of disasters, including pandemics, on long-term cardiometabolic outcomes, including obesity. Given the diversity of the studies included, such as the different types of disasters, study periods and outcomes assessed, the findings can be used to inform future research on the COVID-19 pandemic and long-term outcomes, and more broadly for other future disasters, including both human-made and natural. Causal mediation is a relatively new epidemiologic method; however, it is important given the ability to explore and understand pathways leading to disease development. This mediation method overcomes limitations associated with traditional methods, as they fail to account for all potential confounding variables and interactions between the exposure and mediator. Few

studies have used causal mediation methodologies (67), and given the established association between ACEs and obesity (49,51,52), it further signifies the need for causal analyses. In addition, the assessment of effect modification on both the additive and multiplicative scales are an important contribution to the literature. Studies often only focus on the multiplicative interaction, however, the additive interaction allows a better understanding if the effect of an exposure depending on the presence or absence of a second variable (68).

Strengths and limitations

There are specific strengths and limitations of each study within this thesis which are explained in detail within each manuscript. However, this thesis overall has several key strengths and limitations. The use of the CLSA allowed for complex research questions to be answered using a large population-based sample. For each chapter of this thesis that used CLSA data, comprehensive data were available, such as measured anthropometric data to measure obesity or key COVID-19-related data. Although the CLSA is limited by a predominately white, high-income sample, the findings from this work are representative of people who share similar characteristics to those within the CLSA but may not represent the general Canadian population. This in turn is similar to generalizing these findings beyond the Canadian population, where findings can be generalized to other countries or jurisdictions that share similar characteristics to the people included in the CLSA sample. The CLSA had an overall participation rate of 45% and overall response rate of 10%, which is relatively low contributing to the limited

representativeness of the Canadian population (75). Selection biases exist when recruiting participants, including volunteer bias, whereby those who are willing participate in a study are systematically different than those who are not willing to participate (76). The CLSA participants have a higher education, higher household income, better self-rated general health, and a higher percentage who are born in Canada relative to the comparable Canadian population (75). Given the unexpected and unpredictable nature of the COVID-19 pandemic, there was a need for research to understand who was more susceptible to worse experiences during the pandemic. However, at the time this thesis was conducted the COVID-19 pandemic was ongoing, limiting the ability to study the long-term effects of the pandemic, such as how stress experienced during the pandemic impacts the future risk of obesity.

Future research

Several measures of stress were used in this thesis including ACEs, and both objective stressors and perceived consequences of the COVID-19 pandemic, however, there are several other examples of how and when stress could be measured in relation to obesity. These may include measuring cortisol, validated checklists or scales including *The Impact of Event Scale* (77), or different objective stressors in relation to the exposure of stress (2,23). Measurement of stress can take place across the life course, applying a life course perspective when evaluating stress allows for a better assessment of cumulative exposure. Given the wide range of methods for assessing stress, having a clearly defined research question, or stress exposure helps guide selection. For example, if data on biological

measurements of stress are not available, then the research question of interest may incorporate a broader definition of stress, rather than for instance focusing in on stress measured by cortisol. Given the complexities associated with measuring stress, future research with similar objectives to this thesis can use the method methodology and findings to inform future work.

To develop prevention strategies and interventions, a better understanding of the mechanistic pathways between stress and obesity, and obesity and stress are needed. There are several potential pathways between these associations, and it is likely outcome development operates through several mediators. Using the findings from this thesis, and from previous research (49,78), lifestyle (e.g., nutrition), social (e.g., education, household income, etc.), biological (e.g., cortisol) or psychological (e.g., depression, anxiety) pathways may warrant further exploration. Longitudinal research is needed to better understand how various factors at different points of the life course may lead to increased stress or obesity following exposure to either of these. In addition, it is apparent people with obesity experienced greater stress during the pandemic. Exploration into why this occurred is needed. People with obesity face stigma in everyday society, but more specifically this was amplified during the COVID-19 pandemic and within the healthcare system (8,64). If this is the reason for the increased stress, prevention strategies addressing this stigma are urgently needed.

Several unanswered questions remain surrounding the lasting effects of the COVID-19 pandemic. It is evident that ACEs and obesity influenced how people experienced the pandemic, but it is unclear how stress experienced during the pandemic will influence

future rates of obesity. It is also likely that those who have past ACEs exposure may have experienced differential long-term effects following the COVID-19 pandemic, similar to how their experiences varied during the pandemic. Future research will be needed to determine the long-term effects, and these questions can be answered using the CLSA. Future data collection follow-ups are planned for the CLSA allowing for the research conducted in this thesis to inform this work and continue to answer these unknown questions.

Conclusions

Obesity and stress share complex relationships across the life course. This thesis confirms that obesity and stress are interrelated, and that beginning in early life experiences shape the trajectory of a person's life. This signifies the importance of using a life course perspective as it is apparent experiences that throughout the life course, including ACEs or chronic disease development, such as obesity, may make people more susceptible to worse experiences during a stressful event, and may also further increase the risk of disease development. The findings from this thesis will be imperative in continuing to explore and understand the indirect impacts of the COVID-19 pandemic on chronic disease risk.

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